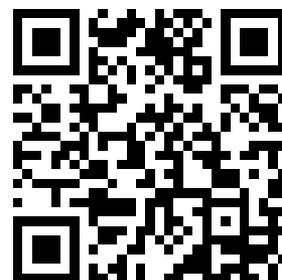

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**NEW RESEARCH
FRONTIERS IN
BEHAVIORAL
MEDICINE**



**PROCEEDINGS OF THE
NATIONAL CONFERENCE**

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NATIONAL INSTITUTES OF HEALTH
National Institute of Mental Health

New Research Frontiers in Behavioral Medicine: Proceedings of the National Conference

Editors

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EXECUTIVE SUMMARY

Under the leadership of the NIH Health and Behavior Coordinating Committee and the National Institute of Mental Health, the National Working Conference on Research Frontiers in Behavioral Medicine was held July 11-14, 1993 at the Westfields Conference Center in Chantilly, Virginia. Co-sponsored by all NIH institutes, centers and divisions with active "behavioral medicine/health and behavior" research programs, this meeting provided a unique opportunity to bring the "old" and "new" NIH institutes together to consider how the new structure could most effectively coordinate, and where appropriate, expand behavioral medicine/"health and behavior" research both within and across institutes' mandates.

The objectives of this conference were to:

- (1) identify and prioritize the most important unresolved biobehavioral research issues, both generic and categorical;
- (2) review the spectrum of existing and planned program initiatives in this area across all NIH institutes, centers and divisions; and
- (3) develop recommendations for a comprehensive, NIH-wide behavioral medicine/health and behavior research agenda.

Participants included nationally recognized scientists representing the broad spectrum of biobehavioral research and NIH program and review staff representatives.

The conference was "matrix"-designed to explore four major behavioral medicine/health

and behavior research domains, using a "life course" approach to each domain. The four major topic domains, **Disease Processes, Biobehavioral Risk Factors, Treatment Interventions and Disease Prevention/Health Promotion**, were addressed by four Life Course Task Groups: **Prenatal/Infant/Child, Adolescent/Young Adult, Midlife Adult and Senior Adult**. Each of the four Task Groups were asked to propose four initiatives in each area, for a total of 64 research program initiatives being developed over the two and one-half days of the conference. Plenary papers introduced each topic area and synthesis papers attempted to summarize the deliberations of the groups, again by topic area. Each Task Group Leader also provided an overview of the deliberations of each life course group on each topic, resulting in over 90 separate contributions to these proceedings, including the Opening Session addresses and papers. These proceedings are intended to serve as a blueprint for the "expanded" NIH behavioral medicine/health and behavior research agenda.

Because these papers and reports describe in detail the conference products, in this section, we highlight the major themes that crosscut the Task Group Reports according to the four key domains.

A. Disease Processes

1. **Genetic/environmental Interactions:** As molecular biology continues to unravel the human genome, the role of the environment in modulating gene expression assumes

increasing importance in understanding why all individuals with similar genetic reservoirs are not equally susceptible to biological/environmental challenges. Understanding how psychological, social and cultural variables interact with genetic predispositions will provide the basis for developing assessment criteria and instruments for identifying persons at high risk as well as critical guidance to the design of biobehavioral interventions to increase resistance/decrease vulnerability to disease/disorder.

2. **Utility of Animal Models:** It is essential to develop biobehavioral analog models to understand the disease process as it unfolds, under the carefully controlled conditions of the laboratory. Animal models which take into account the complexity of biological/behavioral interactions are necessary to replicate the multiple dimensions of the human experience in real life circumstances.
3. **Exposure to Toxic Environments Across the Life Span:** Exposure to toxic environments, both physically and psychologically toxic, can have different effects on health, depending on when exposed, type and length of exposure, and intensity. For example, substance use and abuse (e.g., alcohol, tobacco, licit and illicit drugs) on the part of the pregnant woman can have teratogenic effects, influencing growth and development as well as future health status of the unborn child. Similarly, exposure to positive environments at critical points may protect individuals from health-damaging effects at later points in the life span. The extent to which the sequelae during one critical period influences the sequelae during another critical period is largely unknown.
4. **Interactions among Social, Psychological, Cultural and Biological Systems on Premature Morbidity and Mortality:** The effects of such interactions on basic immune and endocrine functions associated with the

development and progression of chronic disease. Studying co-morbidity of physical and mental disorders may also increase our understanding of underlying common pathways. A major longitudinal study, a behavioral "Framingham" study, could provide extremely valuable data on the interaction of behavioral, biological and environmental variables on multiple disease outcomes.

5. **Inclusion of Behavioral Science Concepts in Studies of Disease Processes:** Integration of psychosocial variables into models of disease will result in much faster progress in understanding the pathogenesis of disease than segregation of those variables into separate models. Funding of projects that combine psychosocial and biological variables should be given highest priority.

B. Biobehavioral Risk Factors

1. **Development and Maintenance of Health-related Behaviors Across the Life Span:** The interaction of biological and behavioral factors in increasing or decreasing health behaviors related to disease or injury has been and continues to be an important arena for research. The factors that lead to adoption of a healthy life style at one age may be different than the factors that lead to adoption at a later age. Studying the exceptions to the rule, i.e., the resilient, hardy children and adults from "high risk" familial and social environments, may elucidate protective mechanisms that could be capitalized upon in interventions. Similarly, studying the characteristics of those individuals able to make health behavior change without formal intervention may provide clues for intervention design.
2. **Clustering of Health-related Behaviors:** Evidence suggests that some biobehavioral risk factors "cluster" together, suggesting common determinants may be involved,

whether they be psychosocial, genetic, behavioral, or environmental. These factors may interact in synergistic, catalytic, additive or inhibitory patterns which may be modulated by socioeconomic, familial and/or cultural/normative factors. The extent to which the common determinants can be identified, more efficient interventions can be designed and tested.

- 3. Social Norms and Health Behaviors:** Social norms are powerful determinants of human behavior. Studying the process by which social norms for health behaviors are established, maintained, and modified can provide critical guidance in the design of population-based interventions to promote healthier lifestyles (e.g., cardiovascular risk-reduction, HIV/AIDS prevention and injury reduction programs in schools, communities, worksites).
- 4. Sociodemographic Context of Health Behaviors and Disease Processes:** Clearly socioeconomic status, ethnicity, and gender are strong predictors of health behaviors and health status. Yet there are often treated analytically as nuisance variables, rather than as markers reflecting fundamental processes. The study of specific biobehavioral risk factors and disease processes and intervention/prevention of those factors and processes should be tied specifically to the socio-demographic context of the individual in an effort to understand how these macro-variables affect individual health behavior and disease risk.

C. Treatment Interventions

- 1. Improving Treatment Outcomes:** Although behavioral/pharmacologic treatments alone or in combination have had some success in modifying outcomes, it is widely accepted that new methods of behavioral treatment

need to be developed. Among the issues for further analysis or development should be the following: individual differences and matching patient to treatment; interventions based on groups, peers, and techniques of marketing; utility of community-based vs. clinical models as well as social or physical environmental interventions, particularly for the elderly.

- 2. Health Behavior Change/Maintenance:** It is increasingly clear that the newest challenge to health behavior change has shifted from the design of high quality health education materials and excellent programs to begin the behavior change process to the maintenance of behavior change and prevention of relapse. The "modifiability" of health-related behaviors depends on complex interactions among behavioral, psychosocial, environmental and biological factors. Maintaining the desired behavior pattern may involve additional and/or different factors than those related to "changing" behavior per se.
- 3. Multi-center Trials of Behavioral Interventions:** Multi-center trials of behavioral and biobehavioral interventions are needed to develop an adequate database to test promising treatment or prevention strategies in representative samples of the U.S. population. Ethnic, gender, age and socioeconomic variables must be addressed to evaluate the effectiveness of these interventions for all segments of the population. Not only will such interventions allow the testing of the adequacy of techniques in diverse regions, population, laboratories, it will also require the exporting of techniques developed in one center/laboratory to other sites, which will improve the reliability of study findings.
- 4. Design and Methodology Considerations:** Alternative research designs must be considered to fully exploit the potential of

biobehavioral research concerning treatment efficacy. The design of biobehavioral interventions present unique challenges to traditional scientific processes and models. Issues such as the adequacy of control groups, placebos/expectancy, single/double blinding, informed consent, assessment of outcome must take into account the special constraints of biobehavioral research without compromising scientific rigor. Technological advances in assessment must be more effectively utilized in the measurement of treatment outcomes.

D. Disease Prevention/Health Promotion

- 1. Environmental Interventions to Prevent Illness and Injury:** Reducing risk of exposure to toxins, sports injury, and workplace hazards typically involves the adopting of safety-oriented behaviors. Increasing the use of safety belts, bicycle helmets, worksite safety equipment may require behavioral and environmental modification to encourage individual adoption and maintenance of health protective behavior patterns.
- 2. Making the Health Care System More Responsive to Patient Needs:** Although the patient is traditionally thought to be the target of intervention, the health care provider should also be the target of intervention. Improvement in patient-provider communication regarding the specifics of the regimen should enhance health outcomes. Health care provider communication regarding their patients' health behaviors can be a strong stimulus for behavior change. Moreover, to be successful, all medical interventions require behavior change on the part of the patient. Interventions will be more successful if health care providers receive some behavioral training to teach their patients how to succeed.

- 3. Inclusion of Quality of Life, Functional Measures in Intervention Studies:** Efficacy of disease prevention and health promotion should be evaluated in terms of improvement in quality of life and avoidance of dysfunction, in addition to standard measures of morbidity and mortality.

Implementation:

A final plenary session among the scientists and NIH officials and administrators led to a constructive discussion of next steps to implement the products of the conference. Perhaps most relevant here were the suggestions that each NIH Institute review the proceedings for themes and issues most relevant to their Institute and to follow up this conference with disease-specific workshops to elucidate more precisely the behavioral medicine issues within the mission of their Institute. Further exploration of behavioral medicine approaches would be aided by preliminary discussion of focus groups made up of NIH staff and outside consultants discussing the applicability of concepts and domains to the mission of each Institute. Some of the themes and issues above concern common processes, approaches, or outcomes that are within the purview of multiple Institutes. Co-funding by Institutes of initiatives on common issues should be explored. Use of existing fellowships for training of behavioral medicine researchers at each Institute should be encouraged and new short term fellowships, e.g. 1-3 months, for training in specific behavioral intervention techniques should be developed to allow the multi-center approach to treatment and to test the limits of exportability of techniques by individuals not trained specifically in behavioral change methods. Finally, with the reorganization of the IRGs and the assimilation of the NIMH into the NIH, it is critical that the study sections be aware of the importance of the behavioral medicine approach and that their members include scientists with experience in multidisciplinary research.

Welcome to Participants

*Jay Moskowitz, Ph.D.
Deputy Director for Science Policy and Technology Transfer
National Institutes of Health*

It is a pleasure to welcome you on behalf of the staff of NIH and our Acting Director, Dr. Kirschstein, to this National Working Conference on Research Frontiers in Behavioral Medicine.

As this is an after dinner program and since we recognize behavioral aspects of proper nutrition and eating diseases as part of the multifactorial bases for the control and prevention of certain chronic diseases, I will start with an easy reference to nutrition and behavior.

Nearly 40 years ago, the nutrition writer Adele Davis complained that "thousands upon thousands of persons have studied disease. Almost no one has studied health." Since 1954, when Davis penned those words in *Let's Eat Right to Keep Fit*, research on the underpinnings of good health has come a long, long way. Scientists have demonstrated that many of today's most prevalent diseases can be prevented, delayed, or controlled through changes in behavior and lifestyle. As important, we have solid evidence that this understanding—along with the public health programs built on this foundation of knowledge—can make a difference.

For example, recent results announced by the NIH National Cholesterol Education Program and by the CDC document significant gains in efforts, through behavioral modification, to reduce the prevalence of high blood cholesterol and its sequelae, coronary heart disease. Clearly, a growing number of Americans are trying to change their behavior to eat right and keep

fit. But not enough are; almost 30 percent of the adult population require dietary intervention for high blood cholesterol.

Even though we have come far over the past four decades, we have much farther to go in uncovering the biological, behavioral, and social underpinnings of health. At NIH, we are continually increasing our emphasis on research that is vital to the success of efforts to foster adoption of disease prevention and health-promoting behaviors by all Americans. At the same time we are taking aim on the disparities in the health status of large segments of the population—women, minorities, and the underserved. Progress on these research fronts is fundamental to our Administration's national strategy to reduce the burdens of illness and to safeguard the quality of life.

Joint sponsorship of this conference by the NIH Health and Behavior Coordinating Committee, the National Institute of Mental Health, and each of the other NIH institutes with behavioral medicine research programs exemplifies the kind of cooperation that is so urgently needed if we are to accomplish national health goals. In research, we need a combined effort—one that leverages and merges contributions from molecular biology, genetics, structural biology, the neurosciences, and the behavioral and social sciences. If research is cordoned off by disciplinary boundaries, then efforts to broaden and deepen our understanding of human behavior and how it affects health will be disjointed. And as a result, new knowledge in public

health, education, and disease prevention will be delayed. That climate must be prevented. This conference and its resultant research agenda and implementation will assure that this does not occur.

This conference is especially timely in several regards. As many of you may know, the NIH has just concluded a two-year strategic planning process that has culminated in the recently completed NIH Strategic Plan, entitled "Investment for Humanity: A Strategic Vision for the National Institutes of Health." The Plan identifies nine "critical health needs" and describes NIH initiatives to promote general health and prevent disease. Prominent among these is the area of "Behavior and Health." This area includes two major initiatives: "Neuroscience and Behavior" and "Behavior and Health Across the Life Span: Biobehavioral Medicine."

Major goals in the area of Behavior and Health, whether implemented as part of the Strategic Plan process or the Institutes' Task Force as a result of this conference will include, among others:

- ▶ Evaluation of the integration of the scientific programs of NIAAA, NIMH, and NIDA into NIH.
- ▶ Establishment of mechanisms, within the Office of the NIH Director, to coordinate and promote trans-NIH efforts in behavioral medicine.

The work of the outstanding panels that have been assembled for this conference will clearly complement, augment, and extend the planning process embodied in each of our Institutes. I am pleased to note that over the next few days you will not only identify important unresolved behavioral research issues and address the

research needs and opportunities in behavioral medicine but will also establish a comprehensive trans-NIH set of priorities and assess the resources required.

This conference coincides with and will contribute to an evaluation that the NIH is conducting, through the National Academy of Sciences, to establish the nation's overall need for biomedical and behavioral research personnel. And it will define the extent and nature of the of training that should be provided. The results of this conference will aid greatly the deliberations of the NAS Committee. Your input will strengthen the validity of the recommendations for meeting future needs for behavioral research personnel. I am hopeful that this conference will also yield suggestions for improving training programs. We must produce adequate numbers of high-quality behavioral and social scientists—investigators who have the skills and creativity necessary to unravel the complexities of health and disease and who are willing to cross disciplinary boundaries.

On June 10, President Clinton signed into law legislation authorizing the establishment of an Office of Behavioral and Social Sciences Research within the Office of the NIH Director. The new Office is charged with the responsibility to, in the language of the legislation:

- a. coordinate research conducted or supported by the agencies of the National Institutes of Health; and
- b. identify projects of behavioral and social sciences research that should be conducted or supported by the national research institutes, and develop such projects in cooperation with such institutes."

The report of this conference will also undoubtedly serve as a valuable resource document for

this new Office as it plans and coordinates NIH programs in behavioral medicine. This new Office will also be aided greatly by the to be expanded activities of the NIH Health and Behavior Coordinating Committee. Under the able chairmanship of Dr. Susan Blumenthal, this body will serve as the principal integrating

focus for NIH activities related to the behavioral aspects of health.

I wish to thank each of you for contributing your time and effort to this important endeavor and I look forward with great enthusiasm to the report of this conference.

*Fredrick Goodwin, M.D.
Director, National Institute of Mental Health
National Institutes of Health*

Let me first express our appreciation to the organizers of this conference, Dr. Susan Blumenthal, Chief of the Basic Prevention and Behavioral Medicine Research Branch, at the National Institute of Mental Health (NIMH) and her colleague, Dr. Stephen Weiss, a pioneer in this field. As the primary sponsor for this conference, NIMH is pleased that twelve other institutes of the National Institutes of Health (NIH) have joined us as co-sponsors. When the NIMH returned to NIH last October after a 25 year absence, the issue of integrating our behavioral research with that conducted and supported by our sister Institutes was among our foremost priorities; this session promises to facilitate that task in a very significant way.

I mentioned our "return" to NIH last year. I should note that when I first came to NIMH 27 years ago, the Institute was still part of NIH, as it had been ever since its authorization in 1946 as one of the four original Institutes; between 1968 and 1992, however, it was reauthorized as a "separate but equal" research agency outside of the NIH. In its early years, under the NIH aegis, NIMH research support, both extramural and intramural, largely built the modern field of behavioral sciences. Today, of course, that knowledge base constitutes a solid foundation

for behavioral medicine across the NIH campus and across the health care spectrum.

The NIMH's early basic behavioral and psychopharmacologic research also laid much of the groundwork for contemporary neuroscience, as well as many of the clinical evaluation technologies so widely used throughout clinical research and clinical practice today. In light of our history of pioneering involvement and leadership in these areas, and in light of the NIH's track record of nurturing specific aspects of these fields, we view our return as quite promising for health research in its entirety. We are gaining a lot by rejoining the mainstream of biomedical and behavioral research, and I believe NIH is gaining a lot by having us back.

Reasons for the significance of our return to the NIH reflect the pivotal nature of this era for the health and behavior fields generally. That is, not only has the generic fallacy of "separate but equal" become as evident in science as in any other sphere, but the advance of health research has shown program separation to be antiquated and untenable. As ideology is replaced by data and information, the dichotomy between "mind" and "brain" is rapidly breaking down, and,

along with it, the rationale for any split between "general" health and "mental" health. An example of this accelerating convergence can be seen in one of the most exciting areas of neuroscience, that concerned with explaining mechanisms by which even subtle psychosocial events translate into alterations in brain biology and, often in turn, changes in behavior, expressed as illness as well as healthy behaviors.

This also is a critical moment for all of us who are interested in research on behavior because public awareness of health and behavior issues has never been higher. Consider how often you see increasingly sophisticated coverage of "behavioral" topics in virtually any major media outlet today. This coverage is contributing substantially to the destigmatization of mental illnesses, but also is having a profound effect on people's appreciation of the complexity and interconnectedness of health and behavior.

A third and, perhaps, bottom-line reason why it is critical for us to be thinking these issues through as carefully as we can right now is the health care reform process that is well underway. In a certain sense, behavioral science offers much of the potential and promise for truly reforming our health care system as well as influencing and directly enhancing individual health. At the same time, despite the more enlightened public perceptions of the role of behavior in health, it is clear that behavioral issues are among the least understood facets of health care services, and thus an area that those who are myopically cost-conscious about health care reform may find easiest to jettison. The task of educating policymakers about the relevance of basic behavioral research, without overstating its immediate relevance to short-term health care needs, can be difficult, but is vitally necessary.

Our purpose here is to set research agendas. Not to set agendas in the sense of creating a planning straightjacket, but rather to identify opportunities and generate a climate for cross-fertilization among all parties involved in behavioral research. The government, through NIH, does not intend to *define* research priorities for the field. You, the research community, must define them in terms of the scientific opportunities that exist now and evolve continuously. It is our task to shape your input—offered at this meeting and on other occasions—into Program Announcements (PAs), Requests for Applications (RFAs), and budgetary allocations that are responsive to scientific as well as public health needs.

Of course, we all are aware that this is a tight time for research budgets. This is unfortunate, for the budgetary constraints coincide with very rapidly expanding scientific opportunities and public health needs in the areas represented at this gathering. Put the two together, and what it means is that we within the NIH have to attend more diligently to the search for opportunities for synergistic efforts. I don't think there is much raw duplication to be found among funding sources, but certainly opportunities exist for greater collaboration between and among Institutes and disciplines. If we are to achieve this, your help and guidance about priority setting is crucial, particularly in this era of fiscal constraint.

An important new NIH-wide policy that will help diminish turf consciousness among the Institutes and enhance synergy, is the recent decision that all Institutes involved in joint sponsorship of a project now will get "credit" for their involvement. In an era in which we are seeing evermore "earmarking" of funds for specific purposes (not to mention what has been

described as micromanagement of the research enterprise), the focus on ensuring Institute "credit" is more than a matter of bookkeeping vanity. Having that policy in effect should help all of us at the NIH work more effectively with each other.

The background material provided to all conference participants reveals considerable variability among NIH's Institutes as to what is included under the rubric of health and behavior or behavioral medicine. I hope that one outcome of this meeting will be to sharpen those definitions. We do not want to be overly restrictive; we want to be inclusive. On the other hand, if a description or definition of a field gets too broad, it loses its punch.

Traditionally, the National Institute of Mental Health always has kept its behavioral research—including, of course, behavioral medicine studies—closely integrated with our other areas of research; this is true across the spectrum, from basic, to clinical, to services research. In many ways, the Basic Prevention and Behavioral Medicine Research Branch, which is headed by Dr. Blumenthal, is as neuroscience-related as it is behaviorally related. Such functional and organizational integration simply reflects the trends and data coming out of your research.

Several of you may recall—indeed, may have participated in—the 1977 Yale Conference on Behavioral Medicine, one of the first comprehensive efforts to come up with a definition of what was then a emerging field. One product of the conference was a recommended definition of behavioral medicine as *"..concerned with the development of behavioral science knowledge and techniques relevant to the understanding of physical health and illness and with the application of this knowledge and human techniques to prevention, diagnosis,*

treatment, and rehabilitation." In the intervening years, of course, we have seen a number of expansions and elaborations of that definition. Last summer, one session of NIMH's Extramural Science Advisory Board (ESAB) was devoted to discussion of our activities in "health and behavior;" at that time, we identified no less than five definitions of "behavioral medicine." These included: 1) behavioral aspects of medical disorders (which essentially captures the Yale definition); 2) behavioral aspects of mental disorders—that is, to the extent that they involve homeostatic behaviors such as sleep, circadian physiology, eating behaviors, and the like that cross over mental and physical disorders; 3) a focus on behavioral techniques for altering and changing health behaviors, again, I think, which was implicit in the Yale definition; 4) the relationship between lifestyle and illness, also implicit in the Yale definition; and, 5) the "behavior" of health care systems, a definition which underscores the relevance of this area to the current attention being directed to health care reform.

My interest in having health and behavior put on the NIMH Science Board's agenda last summer was influenced by the prospect of health care reform, but was driven principally by my anticipation of our return to NIH. I felt then—as I do now—that one of our first and most important tasks in these first months of our reunion with NIH would be to figure out who's doing what across the campus, and to sharpen the focus of our existing programs in this area.

Our Extramural Science Advisory Board issued several recommendations as to what NIMH, which among the NIH Institutes has the largest investment in behavioral science, ought to be doing. In the hope of stimulating discussion later on, let me mention a couple of the Board's recommendations. Their first, and by far their

most important recommendation, was that we focus on **basic mechanisms** of how psychosocial and behavioral events get translated into health consequences. Obviously, we are talking here about studies of immune system physiology, endocrine physiology, and so forth. In these areas particularly, extraordinary opportunities exist for all NIH research programs.

A second recommendation was that we focus on **method development** in a number of areas. The Board felt that we need improved methods for diagnosis and rating systems, particularly as they relate to comorbid states. They wanted us to do more on life assessment measures, an area in which the National Cancer Institute (NCI) has invested heavily. They wanted us to work on an enhanced definition of "caseness" for behavioral medicine studies, with particular focus on integrating *categorical* and *dimensional* measures—a conundrum for many years in this and many other areas of research. They recommended that we look at some new constructs of personality types; that is, move away from the classic personality types, which were derived from psychoanalytic constructs, to new formulations that include psychophysiological measures such as risk-taking behavior and impulsivity. They wanted us to focus on subsyndromal mental disorders and, particularly, how they impact on primary care. When seeking help, the majority of people with depressive and anxiety symptoms go first to their primary care physician for treatment of those conditions, but only in one out of four of those help-seeking episodes is the problem recognized. This sorry statistic underscores the importance of studies to improve methodologies for identifying the so-called subsyndromal.

The Board also recommended that NIMH should **not** put its primary focus on health and

behavior as it relates primarily to so-called physical conditions, but rather that we focus on those physical conditions that have comorbid mental conditions with them. Of course, that focus encompasses very large pieces of both the mental illness pie and the physical illness pie. For those physical disorders with behavioral components, our Board recommended that we not take over what is now being done very successfully at many Institutes at NIH, but rather that we collaborate with those Institutes to enhance and exchange ideas about methodological work.

An important ESAB recommendation in my estimation, was that all NIH Institutes direct more attention to **behavioral change research**. This is an issue that unfortunately gets trivialized by many people in other areas of science. I believe that an NIH-wide affirmation of its fundamental importance would do much toward changing those unfortunate—and incorrect—perceptions that it is trivial.

The ESAB recommended that we do much more research on mechanisms and methods for educating primary care providers in the recognition of behavioral pathologies and symptoms of mental disorders. They discussed user-friendly, time-efficient interview scales for primary care. They discussed research on integrating, within primary care settings, medical and non-medical personnel to assure appropriate expertise in and attention to behavioral problems. It is no secret that our health care reimbursement system cheapens provider *time* in contrast to very expensive *techniques* and *technologies*; until that imbalance (which reflects, essentially, a philosophic position) is corrected, unless we can do something that makes assessment time-efficient, behavioral concerns are not going to get the attention they warrant from busy, harassed practitioners.

Finally, the ESAB urged us to expand our studies on the cost offset effect of including mental health services in the primary health care system. There is a substantial body on work in this area that goes back a couple of decades—I believe Dr. Regier will review some of it—but much remains to be done. Cost offset research is another area which offers a specific and fairly near-term means of demonstrating the relevance of our research and its applicability to pressing policy questions in the health care arena now.

I hope that these recommendations serve to stimulate your thinking and discussion during this meeting about the opportunities for behavioral research in the years ahead, and about the role of the National Institute of Mental Health in contributing to progress in this area. I realize that this meeting will not entail a long series of formal presentations, but that it is a working meeting designed to generate a product which will be useful to all of the NIH. You have an ambitious agenda set out for yourselves, but looking at the talent present here, I am confident that you will achieve your aims.

Introductory Remarks: New Frontiers in Behavioral Medicine Research

Susan J. Blumenthal, M.D., M.P.A.

Chair, NIH Health and Behavior Coordinating Committee

Chief, Basic Prevention and Behavioral Medicine Research Branch, NIMH

On behalf of the Health and Behavior Coordinating Committee of the National Institutes of Health (NIH) and the Basic Prevention and Behavioral Medicine Research Branch of the National Institute of Mental Health (NIMH), I welcome you to this most important conference that will chart a new course and direction for the growing field of behavioral medicine within the National Institutes of Health, in the broader Public Health Service, and across the overall research and clinical care communities. I hope you share my enthusiasm about our work over the next three days, work that brings hope for the improved health and well-being of Americans.

I want to thank Dr. Jay Moskowitz both for his ongoing support of the health and behavior research agenda at the NIH. I also applaud his leadership and vision in the development of an Office of Alternative Medicine at the NIH. I further appreciate the support lent to behavioral medicine research by National Institute for Mental Health Director Dr. Fred Goodwin. His willingness to expand the existing behavioral medicine program at the NIMH lent impetus to this conference, a convening that is cosponsored by the NIMH, one of the three Institutes that have rejoined the NIH in recent months. With the National Institute on Drug Abuse and the National Institute on Alcoholism and Alcohol Abuse, the NIMH stands in the forefront of the important relationship between mind and body, between behavior and health. The Health and Behavior Coordinating Committee also extends

its deep gratitude to Dr. Lynn Gordon and the Fetzer Institute for their co-sponsorship of this important conference.

Further, I would like to express our thanks to each of the NIH Institutes and Offices. The collegiality and cooperation lent by the staff of these Institutes in the planning and organization of this meeting are hallmark indicators that a new spirit of collaboration has been born at the NIH, a collaboration in both research and policy dedicated to the promotion and strengthening of the NIH behavioral medicine agenda.

Moreover, we express our appreciation for the outstanding contributions of the members of the Conference planning committee, including Dr. Ronald Abeles of the National Institute on Aging, who also serves as Vice Chair of the NIH Health and Behavior Coordinating Committee; Dr. Andrew Baum of the U.S. Uniformed Health Services; and Dr. Norman Krasnegor of the National Institute of Child Health and Human Development. Special thanks to Dr. Stephen Weiss, a visiting scientist in the NIMH Basic Prevention and Behavioral Medicine Research Branch, for his outstanding leadership in the field and for his assistance in the organization of this conference.

I am delighted that Dr. Karen Matthews, Professor of Psychiatry and Psychology at the Western Psychiatric Institute and Clinic at the University of Pittsburgh, will join me as Co-Chair of this conference. Dr. Matthews has

a distinguished history of national leadership in behavioral medicine and will bring her considerable expertise, talents, and thoughtful insights to this meeting.

Behavioral Medicine: Scientific Futures

Behavioral medicine research has emerged as a critical area in the prevention, diagnosis, and treatment of physical disease and mental disorders, with special and important implications for the future practice of medicine. This new recognition of the importance of behavioral and social factors in the promotion of health and the etiology and prevention of disease is occurring at a fortuitous moment, a moment in which the former research institutes of the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) have been reunited with the rest of the NIH community. This merger holds great promise both for the enhancement of biomedical research and for the improvement of our health as a Nation.

The reemergence of behavioral medicine as a critical ingredient in both biomedical research and clinical care confirms what we have known since ancient times: there indeed is an intimate connection between the health of our bodies and the health of our minds, what the ancients called the soul. Socrates observed that "just as you ought not to attempt to cure eyes without head, or head without body, so you should not treat body without soul."

In more recent history, Sir William Osler, considered to be the father of modern medicine, observed that, in order to predict patient outcome in recovery from tuberculosis, "It's just as important to know what is going on in a man's head—today, we would also say a woman's—

head as in his [or her] chest." After a quiescent period, during which the body was treated without its head, the conduct of scientific inquiry over the past two decades has reaffirmed what Socrates and Osler told us years ago: the mind-body connection is too strong to be disregarded. We have seen the effects of CNS brain chemicals on the immune system; we have seen how depression can delay recovery from hip fracture. Similarly, we know that many physical illnesses can trigger certain psychological conditions. Thus, since the rise of Greek civilization, the sages and the healers recognized that psychological, behavioral, and environmental factors have a powerful impact on our lives, whether in the promotion of health or in the development and course of illness.

In our travel from ancient Athens and enlightened Europe to today's biomedical capitol of the world—the National Institutes of Health—we come full circle to witness what we hope is the end of a dualistic approach to both research and treatment. The psyche and soma are being reunited through the reintegration of the NIAAA, NIDA and NIMH into the NIH family. After almost a quarter of a century of separation, the body-oriented Institutes of the NIH experienced the return of their head; this reunion is creating a stronger and more robust institution, better equipped to address the health needs of all Americans. By bringing mental health issues back to the biomedical research community and by strengthening behavioral medicine within this context, the merger increases the likelihood of major breakthroughs in the understanding and treatment of all diseases, whether of body or mind. Moreover, the mental and addictive disorders, long stigmatized, now stand side-by-side with cancer, diabetes, AIDS, and heart disease as health concerns central to the NIH research agenda. Leading the way in education about and greater visibility for behavioral medicine is the standing NIH

Health and Behavior Coordinating Committee which has been expanded, drawing added representation from the three new Institutes as well as from the NIH Offices of Research on Women's Health, of Prevention, of Minority Health, and of Alternative Medicine.

Let us look briefly at how we came to this special moment in time.

Changing Trends in Health and Disease

As the nature and structure of society change, so do the diseases that affect us. A walk through a 19th century graveyard reveals that, at the turn of the century, people died younger and most often from infectious diseases. Public health interventions—improved sanitation, development of antibiotics and vaccines, and other advances in medical knowledge—have led to a vast reduction in the mortality and morbidity associated with infectious diseases and have extended the average human life-span by over 30 years in this century alone. In 1900, the average life expectancy was 47.3 years; by 1985, the average man was expected to live 71.2 years; the average women, 78.2 years. At the turn of the century, 3 million Americans were over the age of 65, representing but 4 percent of our population; by 1988, they numbered 30 million, 12.4 percent of the overall population. What geriatrician Robert Butler, M.D. has called the "demographic revolution"—our growing length of life and growing aging population—is the direct product of a parallel revolution in biomedical and behavioral science.

Yet, living longer does not necessarily mean living better. The acute diseases of the turn of the century to which people of all ages succumbed have given way to chronic illnesses

that slowly, inexorably affect us over the course of a longer lifetime. We no longer die of typhoid, typhus, and smallpox. In their place, our National health has been compromised by heart disease, cancer, and diabetes, and from other causes, such as homicide, suicide, and automobile accidents, all of which have been increasing rapidly and steadily. Chronic illnesses, not acute diseases, have become and will continue to be the most significant health problems in America.

Our behavior—diet, level of exercise, smoking, and substance abuse—may represent a risk factor for many of these illnesses. Behavior may influence disease progression, and it plays an important role in treatment and prevention. Behavioral factors also are a mediating factor in other salient public health problems tearing at the fabric of American society: infant mortality, teen pregnancy, homelessness, AIDS, substance abuse, and the reemergence of tuberculosis. Efforts to combat physical disease and mental illness require a dual focus on both research and on clinical intervention. Let me turn briefly to each of these important components of behavioral medicine.

The Role of Behavioral Research

Basic research in the behavioral and social sciences undergirds all of our efforts to improve the health of the American people. Basic research into the emotional, cognitive, and social processes that account for normal behavioral functioning and adaptation can advance knowledge relevant to health and illness and helps us understand such problematic deviations from healthy behavior as substance abuse, noncompliance with treatment regimens, and self-destructive behaviors. We know, for

example, that treatment success may be enhanced markedly if compliance and adherence to treatment regimens can be improved. Basic research on psychosocial and cognitive processes can be translated to increased clinical understanding of the determinants of behavior change, of the influence of individual, family, and social processes on motivation and compliance with treatment regimens, and of strategies to tailor treatments to the needs of individual patients.

Similarly, we know that many health-related behaviors are familial, strongly influenced by genetic factors. By gaining an increased understanding of the genetic determinants of behavior, we will better understand the environmental determinants with which they interact. We may learn how to "turn off" a predisposition to a particular negative health-related behavior—alcoholism, for example—or to "turn on" a positive one.

Over the past decade, research into this relationship between mind and body has yielded an entirely new field of research endeavor and opportunity: psychoneuroimmunology. Fostered first by the NIMH and more recently by activities of a trans-NIH working group, psychoneuroimmunology has been illuminating important interactions among psychological state, brain and immune functions, and health and disease. By understanding the psychobiological mechanisms underlying the production of mood, cognitive, and behavioral symptoms in physical illnesses (e.g., the depression that often predates the onset of pancreatic cancer by as much as six months, or the depression following recovery from hepatitis or mononucleosis) our understanding of the pathogenesis of physical illnesses will be greatly enlarged.

Modern Medicine: The Importance of Behavioral Medicine

When we think of modern medicine, we revel in the advent and stunning successes of new biomedical technologies and their potential for improving health. At the same time, we must recognize that these medical marvels also are forcing us, in the second half of the 20th century, to confront ethical issues we would never have dreamt of in the year 1900: new reproductive technologies, living wills, euthanasia—all questions that arise at the edges of life. We also must recognize that this fascination with and concentration on the development and operation of new medical technologies has led to the relative neglect of preventive and behavioral medicine. The behavioral and social sciences have important contributions to make to our understanding of the bases of health, functioning and well-being, as well as to our knowledge of the prevention, treatment, and cure of disease. Medicine, today, must recognize the interdependence and interactions among genetic, biologic, behavioral, and socio-cultural processes—what George Engel has termed "the biopsychosocial model of health and disease." Fortunately, that recognition is dawning in clinical care through the development and implementation of strategies to encourage people to adopt health-promoting behaviors.

As experts in the field of behavioral medicine, we all are too cognizant of the fact that simply providing information about what makes for a healthy lifestyle is necessary but insufficient in and of itself to change behavior. We know that information alone has not slimmed the obese, stamped out cigarette smoking, or substantially

influenced what we transport on that journey from dinner plate to mouth. Information alone has not encouraged enough sexually active young people to practice birth control or to protect themselves from the threat of sexually transmitted diseases. Yet, the simple fact is that improved health behaviors by every American would have a far greater impact on preventing illness, improving the quality of life, and reducing the need for medical care than any other type of invention.

As many as half of the two million deaths in the U.S. each year could be prevented if people altered the most common behavioral determinants of illness: use of tobacco, abuse of alcohol and illicit drugs, poor eating habits, failure to use seat belts, insufficient attention to immunizations and the need for medical treatment, and risky sexual practices. Were these behaviors changed, between 40 and 70 percent of all **premature** deaths could be prevented. A third of all cases of acute disability and two-thirds of all cases of chronic disability could be eliminated. Such change also would radically reduce health care costs (McGinnis and Foege 1993). In short, the key to disease prevention in this decade and beyond into the 21st century lies in the modification of our lifestyle behaviors and the environment, adopting a life-cycle approach to health that recognizes that certain important health issues are associated with specific stages of life.

The etiology, treatment, and prevention of physical illness, and mental and addictive disorders raise unique issues and challenges at each stage of the life cycle. Prevention, treatment and psychosocial adjustment to diseases such as AIDS, cancer, diabetes, and depressive illness require the development and implementation of behavioral and psychosocial interventions that are responsive to age- and gender-related differences.

The expanding scientific capacity to identify specific determinants of behavior across the lifespan—at the biochemical, psychological, and environmental levels—and the ability to tailor clinical and population-based interventions to behavioral and environmental factors argues strongly for the development of a coordinated public health approach to these problems. Through research, prevention, and treatment, the NIH is making a concerted effort to address critical issues related to behavior and health across the life cycle. This conference is a significant part of that effort. Let me now turn to the themes around which we have organized this conference.

Conference Goals and Aims

As we have discussed briefly already, behavior may

- (1) be a cause of illness or a risk factor arising through the adoption of health damaging behaviors, such as alcohol and other drug use/abuse, diet, high-risk sexual practices, or smoking;
- (2) serve as a co-factor in the progression of disease by modifying the course of illness;
- (3) be altered as a consequence of illness, with co-occurring depression, anxiety, substance abuse, and other psychosocial complications of chronic or acute illness; and
- (4) serve as a component of treatment and disease prevention.

Over the course of this 3-day conference, we will craft a behavioral medicine research agenda for the 21st century that is focused around these four key aspects of behavior as they cross the human life-span. We will grapple with issues specific to the NIH, matters that concern the

wider PHS, and issues confronting the larger biomedical and behavioral research community. We will assess the state of knowledge in behavioral medicine research across the lifespan, including a review of existing and planned NIH Institute program initiatives in the area. We will examine the broadened NIH mission to discern additional opportunities and potential pitfalls in our quest for knowledge in behavioral medicine. And, by identifying knowledge gaps and important new directions for future study, we will set forth both a comprehensive trans-NIH research agenda and a series of mechanisms through which this agenda can be moved forward.

To better focus and direct our efforts, we will seek answers to a series of specific questions that will help achieve conference goals:

- What are the pressing research questions in behavioral medicine?
- What are the gaps in current NIH research programs?
- How can behavioral and social science research across the lifespan be fostered?
- What initiatives are needed to strengthen behavioral medicine research?
- What methodological innovations are needed to facilitate research?
- What mechanisms can be identified to foster behavioral medicine research across the NIH, the PHS, and the wider academic and research communities?

By answering each of these questions, we will illustrate how the crucial connections among mind, brain, and body can be addressed more

effectively as a product of the NIH's reintegration of its own psyche and soma.

Conclusion

Research is medicine's "field of dreams." The explosion of research advances in the behavioral and neurosciences over the past two decades has already harvested advances that have improved the health of millions of Americans. It also has provided us with knowledge and tools to disclose the underlying bases of disease; to identify the basic processes of learning, memory, perception, and sensation, as well as mechanisms of behavior change. Concomitantly, our burgeoning knowledge has increased our understanding of homeostatic behaviors, including eating, sleeping, and reproductive behavior. Moreover, these research advances are revolutionizing our ability to treat—and in some cases, prevent—the onset of disease. Underlying all of these advances are vigorous efforts to develop and apply new technologies and techniques that will enable scientists to visualize and model the living brain, to repair anomalies in the nervous system, to better understand basic behavioral and physiologic processes, and to design and tailor behavioral, psychosocial, and pharmacologic interventions for the prevention and treatment of illness. It is this translation of the discoveries of basic research into treatments and preventive strategies that enables Americans to live healthier lives and provides the most complete return on our Nation's investment in the biomedical and behavioral sciences.

Our goal over the course of this conference is to chart a clear and direct course for behavioral medicine within the NIH, the PHS and the field. Madame Curie observed that "One never

notices what has been done. One only sees what remains to be done." While much has been accomplished in the area of behavioral medicine research, it is now time to turn our attention to what needs to be done to increase knowledge in the field. Let us begin to create a new vision, a strategic plan, and a fund of

human and economic resources to move our field forward into the 21st century.

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Conference Promises

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There are at least five reasons why this conference and its proceedings are timely and important to the advancement of behavioral medicine. The first is the structural impetus to the meeting: the NIMH, with its Behavioral Medicine Branch, has rejoined the NIH. With behavioral medicine activities distributed across many NIH institutes, it is a pivotal time to examine the opportunities for common and separate behavioral medicine efforts across the NIH.

Second, the NIH has increasingly recognized that behavioral factors are crucial to health promotion and disease prevention. A few examples are relevant to cite here. Prevention can be more cost effective than medical intervention in late stage disease. The best illustration of this is AIDS prevention: the only way to reduce risk of AIDS is behavior change. The widening disparity in health status according to social class suggests the importance of the social context in determining disease. Pharmacologic treatment is effective only if patients adhere to the treatment. Moreover, several clinical trials suggest that adherence to even placebo has beneficial effects on health.

Third, in recognition of the importance of behavioral factors, the NIH Health and Behavior Coordinating Committee was established to encourage and promote research in these areas. It is also recognized that exposures that impact on one system positively, may impact on another system negatively or in a neutral fashion. For example, exposure to exogenous estrogen in postmenopausal women appears to have a

favorable effect on lipids, lipoproteins, and bone, but may have a negative effect on risk for breast and endometrial cancers. In premenopausal women, exposure to exogenous estrogen, especially among smokers, leads to increased risk of stroke and myocardial infarction. In consequence, it is critical to evaluate the effects of exposures to risk/protective factors on multiple systems, in order to develop a true picture of the overall benefit and liability of risk factors and interventions. This perspective requires a multidisciplinary approach, common in the behavioral medicine community, to realize that the "whole" effect is more than the sum of its parts. Single institute research can miss the "whole" picture.

Fourth, this conference is organized according to periods in the life span, resulting in increased sensitivity to periods of change and stability among behavioral medicine researchers that have previously focussed their efforts on one life stage. Similarly, the NIH is organized by and large according to disease/system domains, with the exception of NICHD and NIA, which are focused on a given life stage. The life span development perspective thrusts to the forefront such questions as: Do processes of health and illness work the same at points of transition from one stage to the next as they do during periods of stability? Are there accumulating costs of exposure to risk that do not emerge until later life stages? Do the processes work differently at different life stages? What is a good quality of life at each life stage? Addressing these questions will enrich all of our thinking.

Finally, many of the attendees from the NIH and from the behavioral medicine community are passionately working on expanding the frontiers of knowledge within our own domain of expertise and competency. This conference gives us all an opportunity to step back, place our own work and priorities into the larger context of the full mission of the NIH, and see new opportunities for cross discipline advances and collaborations. A wonderful movie, *Turning Point*, with Anne Bancroft and Shirley MacLaine, was about two accomplished ballet dancers in the same troop as young adults, who meet in mid-life and review what had happened

to them. One went on to be a principal dancer and had a highly successful and visible career, and the other married a fellow dancer and started a dance studio for children. Their career decisions turned out to be a turning point in their life course, setting in motion a series of cascading events, which could not be stopped. Similarly, this conference, the re-joining of the NIMH into the NIH, and the activities of the NIH Health and Behavior Coordinating Committee, collectively can constitute a turning point for the NIH in shaping the future health and behavior research agenda for the nation.

Health Care Reform: Opportunities and Challenge

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Health care reform offers both opportunities and challenges for behavioral medicine research. These new directions are particularly pertinent to the proposed health care reform plan and the new era of cooperation among the NIH, NIMH, NIAAA, and NIDA.

Cooperation to Improve Health

The NIH, NIMH, NIAAA, and NIDA have come together again. The rejoining of NIMH, NIDA and NIAAA with the other institutes of the NIH promises to open up many new avenues for behavioral medicine research. The timing of this reorganization to coincide with the national movement toward health care reform further offers the behavioral science research community an opportunity to convey to the public and administration the importance of a coordinated and focused effort, which integrates biological and behavioral variables, for resolving many of the health issues facing Americans.

As has been noted several times, the separation of NIMH from NIH in the late 1960s was a turning point, an event occasioned by differences in the service delivery systems for mental and physical disorders. With the plan to invest in community mental health centers, the Health Services and Mental Health Administration was established and subsequently, the Alcohol, Drug

Abuse, and Mental Health Administration. Both were charged with responsibility for developing service systems *and* maintaining research in the mental health field.

Today, the research issues arising in different fields of study, such as pharmacology, neuroscience, and genetics, bring behavioral medicine closer to the rest of medicine, and research approaches in behavioral medicine now offer new opportunities for collaboration across subspecialties. And, as is often the case with major service delivery issues in the United States, common health service concerns, such as prevention, behavioral aspects of disease, and long-term care, require greater convergence between the systems delivering physical and mental health services. Health care reform actually provides the opportunity for a reuniting of these delivery systems much like the behavioral medicine research components have been reunited during the past year.

The Task Force on Health Care Reform has been a remarkable integrative effort involving extensive collaboration within the Department of Health and Human Services and across Federal departments. More than 500 individuals from both inside and outside the Federal Government have contributed to the work of this task force. One can expect that this national health care effort will provide a more inviting environment for cross-cutting research in behavioral medicine, with a focus on a defined,

capitated population for which prevention, early intervention in lifestyle changes, and behavioral factors and rehabilitation are given greater weight.

Major issues in the Health Care Reform Plan

The development of the Administration's health care reform plan is just the first step in a long process. The main components are: (a) managed competition between accountable health plans (AHCs), which would be supervised by health alliances (formerly known as Health Insurance Purchasing Cooperatives, or HIPCs); and (b) a standard benefits package for all plans which includes coverage of services for physical and mental disorders. The extent and cost of the benefit packages will be critical parts of the discussion between the administration, the Congress, and the public.

A number of major issues and concerns will be debated in the weeks and months to come. These include the following:

- (1) *The capacity of the current health care system to provide services to underserved areas.* As Dr. Joycelyn Elders, the U.S. Surgeon General, has noted, health care reform must include a capacity for developing and ensuring managed competition between plans in both rural and inner-city areas where health services are generally less available.
- (2) *The national capability for managing physical and mental health benefits.* As demonstrated by some of the health maintenance organizations (HMOs) and other capitated plans, it is possible to provide a much wider array of services with far less limitation on the range of benefits than would otherwise be possible if there is a capacity for determining the medical need for the benefits. A number of noted actuaries, who have reviewed much of the work of the Task Force on Health Care Reform, have questioned whether there is, in fact, a national capability at the present time to manage health benefits effectively nationwide.
- (3) *Determination of a fair price.* Related to this national capability is the need to determine what a given amount of money will actually buy in the current marketplace.
- (4) *Subsidizing the uninsured.* Another aspect is the national capability for subsidizing health premiums and service copayments for individuals and families unable to afford coverage under the current system. A driving motivation for undertaking health care reform is that, in 1990, approximately 35 million persons in the United States did not have health insurance.
- (5) *Emphasis on primary care.* The coordination of health services through a focus on primary care is being emphasized in the health care reform plan. A central feature of these discussions is the need for early screening and detection of physical and mental disorders in children.
- (6) *A national health board.* The plan includes establishment of a national health board which will set standards for benefits, guidelines for treatment, and criteria for assuring quality care. The nature of this board has yet to emerge, but, clearly, there is a need for some overall and overarching review of the entire health care system if equitable care

and coverage is to be achieved across the United States.

- (7) *Public vs. private care.* Although initially it was hoped that there would be some merger of the public and private health care systems, the current thinking is that a residual public health and public mental health delivery system will be needed which may be integrated more fully into the overall benefit plan in the future. Until there is full integration of the public and private health care systems, the mental and physical health care systems will likely continue to be separate as well—particularly in state, county, and city public health agencies.
- (8) *Public health monitoring and research.* The plan includes an infrastructure for public health monitoring and research of which the NIH would be part and which would be outside any of the benefit plans.

Behavioral Medicine and Health Care Reform: Research Needs

Two particular concerns for the participants at this conference are the relationship of behavioral medicine to physical and mental disorders and the types of behavioral research that will encourage inclusion of behavioral medicine benefits into the health care reform package. Increasingly, mental and physical disorders are each seen as having both biological and behavioral components that are similar. The emergence of a strong effort in biological psychiatry may, in fact, enable more synergistic research on the behavioral components of mental and physical disorders. It may well be, for example, that similarities in the behavioral risk factors for exacerbations of diabetes and depres-

sion will prove more significant than their differences.

Various types of behavioral research may facilitate the inclusion of behavioral medicine procedures, treatments, and benefits into health care reform. Recognizing that behavioral medicine often suffers from the same skepticism that has afflicted the mental health field in terms of the cost effectiveness of treatments, this paper is focused on identifying research that would be helpful in obtaining acceptance for the integration of benefits for mental and addictive disorders into the overall physical health care package. These areas of research, summarized below, include epidemiological studies, health services research, efficacy of treatment, health costs, treatment guidelines, and effectiveness of behavioral interventions.

Epidemiological Studies

Good epidemiological studies are needed on the conditions which are of concern to behavioral medicine. For the disorders identified, prevalence and incidence data need to be established, as well as comorbidities. The Epidemiologic Catchment Area (ECA) study has been of considerable value in bringing scientific and public attention to mental and addictive disorders [Regier *et al.*, 1993].

Another important consideration is comorbidity among the disorders of concern. In the study cited above [Regier *et al.*, 1990], 29 percent of the individuals diagnosed with mental disorders also had alcohol or drug disorders. As seen from the data, when the overall prevalence of a disorder decreases, the comorbidity increases. This type of analysis, using odds ratios and other statistical methods, is crucial for comorbidity studies of physical and mental disorders, substance abuse and physical disorders, and any behavioral medicine research.

Health Services Research

In the recent budget guidance to the NIH, Dr. Philip Lee, Assistant Secretary for Health, has requested that the NIH institutes identify their current level of effort in health services research. Previously, this research was the domain of the National Center for Health Services Research, which later became the Agency for Health Care Policy and Research (AHCPR), while the NIH and ADAMHA were unwilling to acknowledge any support for this research.

Today, the linkage of health services research to the rest of the clinical and basic research infrastructure is seen as an important new development at the NIH. This linkage is extremely useful because it allows one to chart the rate of disorders in a population against the rate at which individuals in the population seek health care treatment for these disorders.

In the overall health care system, only about 10 percent of the general population seeks care for an alcohol, drug, or mental disorder in a given year [Regier *et al.*, 1993]. About 7.5 percent seek care for respiratory conditions, and about 14 percent seek care for cardiovascular diseases [National Advisory Mental Health Council, 1993]. The discrepancy between prevalence rates and the percentage of the population seeking health care demonstrates that much pathology is not recognized by the patient as requiring treatment unless, as demonstrated, the patient develops a comorbid condition that motivates him or her to seek health care. When evaluating epidemiological data, it is important to consider these indices of severity, which determine who needs care as well as who is likely to seek care.

Efficacy of Treatment

Information is also needed on the efficacy of treatment, as assessed through controlled clinical trials. One example of the type of study required is the recent disaggregation of pharmacological and psychosocial components accomplished by Materson using data from the VA Collaborative Study [Materson *et al.*, 1993]. In his analysis, Materson reviewed the efficacy of pharmacological treatments and determined that it was possible to achieve a diastolic blood pressure of ≤ 90 mmHg in 1 year among 40 to 60 percent of the patients who were treated with various agents, compared to about 25 percent of those treated with placebo.

Similar results have been shown for long-term care of schizophrenia, bipolar, and major depression. A recent meta-analysis of the literature on the treatment of these disorders [National Advisory Mental Health Council, 1993] shows that the relapse rate for patients given a placebo is about 80 percent, compared to a rate of slightly more than 20 percent for those given active treatment.

In biobehavioral research, it is important to consider the potential for synergism in considering the relative contributions of the pharmacological agent(s) and the psychosocial agent(s) used. For example, other analyses [National Advisory Mental Health Council, 1993] demonstrate that although the relapse rates for schizophrenia can be reduced by about one-half with the use of a pharmacological agent, these rates can be further reduced by adding family skills training and other intensive training offered for the psychosocial management of schizophrenia.

Health Costs

Another important area of research is health costs—the cost of illness and the cost of treatment. In this regard, the health economic projections of NIMH's Economics Research Program, are an essential complement to data provided by AHCPR and the Health Care Financing Administration (HCFA). Clearly, the NIH will have to develop the capability for interacting effectively with these agencies in order to respond to the information needs of behavioral medicine. This information will be important in defining the benefits package and the costs involved in managing a national health care system.

Treatment Guidelines

Research is also needed to support the development of treatment guidelines by AHCPR, such as those for primary care treatment of depression. If the national health care reform package is to include coverage for treatment of insomnia, eating disorders, or sleep disorders, for example, it will be important to achieve consensus on the state of the science in these areas and on the definition of effective care.

Effectiveness of Behavioral Interventions

Finally, clinical services research is needed to evaluate the effectiveness of behavioral medicine interventions in actual clinical practice. This research will require the use of more complex, system-wide controls instead of the individual patient matching controls used in clinical efficacy studies. In order to determine the benefits that will be supported in the future health care delivery system, the National Health

Board proposed by the task force on national health care reform will be interested in studies of clinical effectiveness as well as the results of clinical trials.

Summary

Behavioral medicine is experiencing much of the same skepticism as has challenged the mental health field for some time. The field can confront these doubts by supporting high-quality basic and clinical research in behavioral medicine combined with solid epidemiological studies, health services research, health economic analyses, and assessment of the effectiveness of behavioral interventions. Questions will arise about whether prevention and intervention can truly offset the costs of illness, but, through an organized system of care, it may be possible finally to answer these questions with empirical data. The challenge of health care reform is to continue to build on the remarkable research advances made by the NIH and the larger health care community in recent years and to make the results of this research more accessible to patients and the American public.

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Mind Matters, Money Matters: The Cost-Effectiveness of Clinical Behavioral Medicine

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Introduction

In 1992, some \$838 billion was spent in the US. on health care—one of every \$7 spent on domestic goods and services. The final tab represented an increase of 14% over the year before, more than three times the 4% rate of general inflation. Even more alarming are estimates that at least 20% of the 1992 outlay for health care—some \$134 billion—was spent on unnecessary procedures and services (1992 HCFA Statistics, 1992).

Clearly, any successful, long-term reform of the health care system must include addressing the issue of cost-effectiveness. Today, more and more studies are pointing to a simple, safe and relatively inexpensive medical treatment that can dramatically improve health outcomes and reduces the need for more expensive approaches (Fig. 1).

Far from a new miracle drug or medical technology, the treatment is simply the targeted use of educational, behavioral and psychological interventions in a medical setting. These interventions include educating patients about their conditions through brochures, videos, classes, and/or individual counseling sessions, as well as a variety of strategies to encourage patients to play an active role in their own health care

Figure 1

The Bottom Line:

Reduction in frequency of treatments as a result of various clinical behavioral medicine interventions:

Total ambulatory care visits	-17%
Visits for minor illnesses	-35%
Pediatric acute illness visits	-25%
Office visits for acute asthma	-49%
Office visits by arthritis patients	-40%
Average hospital length of stay for surgical patients	-1.5 days
Cesarean sections	-56%
Epidural anesthesia during labor and delivery	-85%

(Doubilet *et al.*, 1986). Patients' psychosocial as well as medical needs are addressed through stress management techniques, psychoeducation, psychotherapy—and plain old-fashioned tender loving care.

The purpose of this paper is to highlight some of the most significant studies—to examine the growing evidence that well-designed, carefully targeted clinical behavioral medicine holds enormous promise for boosting the quality of health care in this country, at a major cost savings to everyone.

Measuring Outcomes

A number of indicators can measure the impact of behavioral interventions on health outcomes and the cost of care:

- ▶ **Health improvement** is the most important indicator, measured by decreased morbidity and mortality or increased functional status and quality of life. It is vital to remember that *the primary purpose of health care is to improve health outcomes—not to reduce costs.*
- ▶ **Behavior change** may be used as a proxy for health improvement. For example, we assume that changes in smoking behavior, diet, exercise, etc. are associated with improved health outcomes.
- ▶ **Increased satisfaction** of patients, providers, and payers may be measured.
- ▶ **Cost savings and cost-effectiveness** can be calculated directly, or sometimes inferred from decreases in hospital admissions or length of stay, number of outpatient visits, or use of drugs and surgery. The term cost-effectiveness is being used loosely here to denote potential cost savings when compared to other interventions or usual care (Doubilet *et al.*, 1986).

General Observations

The studies and statistics discussed in this paper lead to a few basic observations which may hold the keys to curbing health care costs and improving health outcomes:

- ▶ ***The true primary care providers are the people themselves.*** The average person experiences some kind of physical dis-

comfort or symptom about once every three days. Between 70% and 90% of these symptoms are self-diagnosed and self-treated without the help of health professionals. On top of this, at least 25% of physician office visits are for problems that patients could treat themselves (Vickery *et al.*, 1983). These percentages point to an enormous opportunity to reduce health care costs simply by helping patients better care for themselves—knowing when to seek professional advice and when and how to use self-care. A vital function of the health care system is to help equip people for safe, effective self-care—the value of which is born out in the studies reviewed here.

- ▶ ***A significant portion of health-care costs are from treatment of health problems with psychosocial roots.*** What goes on in our heads—our thoughts, feeling and moods, can have a dramatic effect on the onset of some diseases, the course of many, and the management of nearly all (Ornstein & Sobel, 1987). Nearly a third of patients visiting a doctor develop bodily symptoms as an expression of psychological distress. Another third have medical conditions which result from behavioral choices such as smoking, alcohol and drug abuse, poor diets, etc. And even in the remaining patients with medical disease such as arthritis, heart failure or pneumonia, the course of their illness is often strongly influenced by their mood, coping skills, and social support.

Failure of the usual medical response to address these needs leads to frustration, ineffectiveness, and a gross waste of vital health care resources. These studies show that psychological and behavioral interven-

tions can be developed to help patients more directly address their distress and, in the process, help them become less dependent upon costly medical care.

- ▶ ***Increasing a person's sense of control and optimism improves health outcomes and decreases health care costs.*** Virtually all the clinical behavioral interventions in these studies included elements which directly or indirectly boost self-confidence and reduce vulnerability to stress, depression, and physical illness. There is a biology of self-confidence. Engendering a positive feeling of success and control may be more important to health than the specific methods and strategies used in the various behavioral medicine interventions (Ornstein & Sobel, 1989).
- ▶ ***Group and social support is often an important component of effective health education and behavioral interventions.*** Many of the most effective and efficient interventions in these studies were delivered in small groups. At least one study proved the benefit by comparing the same interventions in group and individual settings. It would appear that social support itself is good medicine—and cost-effective too.
- ▶ ***Changes in behavior and established patterns of healthcare utilization may take years to show their full effect on health and costs.*** Many of these studies measure results over extended periods of time. Effective clinical behavioral medicine involves a basic attitude change away from expecting/demanding a quick fix to a willingness to invest effort and money in long-term change—on the part of both patients and providers.

Scope of Paper

This paper focuses on clinical behavioral medicine interventions. Not discussed is evidence on cost-effectiveness of community interventions such as worksite health promotion, or preventive services such as screening, immunizations, and lifestyle risk reduction. The studies included here are drawn from a growing body of research demonstrating the health/cost benefits of patient education and emotional support in dealing with these specific conditions:

- ▶ Minor and acute illnesses
- ▶ Psychosomatic complaints and stress-related disorders
- ▶ Chronic pain
- ▶ Diabetes
- ▶ Asthma
- ▶ Arthritis
- ▶ Surgery
- ▶ Childbirth

Minor and Acute Illnesses

Self-care education reduces costly doctor visits by as much as one-third.

To evaluate whether self-care education affects how patients use medical services, the Rhode Island Group Health Association—a health maintenance organization (HMO)—conducted a large, prospective, randomized, controlled trial (Vickery *et al.*, 1983). Patients were offered written materials, a telephone information service, and individual counseling by a trained nurse. Though the telephone information

service was hardly used, the program as a whole reduced visits for minor illness by 35% and reduced the total use of ambulatory care by 17%. There was no evidence that the health of patients suffered as a result of following self-care information and visiting the doctor less often. Overall, the program saved \$2.50 in medical costs for every \$1 spent on education.

Fever, or high temperature was the most common reason for acute pediatric visits to Kaiser Permanente in Southern California, accounting for 20% to 25% of all pediatric complaints. This HMO conducted a study to determine whether an office health education program designed to increase knowledge about fever in children could affect how parents use medical care (Robinson *et al.*, 1989). In this study, 500 families who visited the doctor with a feverish child under 13 years old were divided into two groups. Only one group was shown a 10-minute slide presentation on fever. Participants in both groups were seen individually by a physician. All were given a pamphlet covering all the major points of the slide presentation and had the opportunity to ask questions triggered by the pamphlet. After seven months, the group that watched the slide presentation made 35% fewer visits for fever than the group that only received a pamphlet. After eight months, the slide group made 25% fewer visits for all acute illnesses. Clearly, informing and reassuring parents with an innovative audiovisual approach had a significant impact.

Psychosomatic Complaints and Stress-Related Disorders

Addressing the psychosocial roots of illness delivers better outcomes at a lower cost.

Physical discomfort resulting from psychological distress is one of the most common reasons

people seek medical care. A 20-year study at Kaiser Permanente concluded that more than 60% of all medical visits were by the "worried well" with no diagnosable disorder (Cummings & VandenBos, 1981). Other studies estimate that 25-50% of visits to doctors are for problems with psychosocial origins.

Many people develop physical symptoms ranging from headaches to sleep disorders to gastrointestinal disturbances as expressions of psychological distress. Several key studies prove that addressing the root causes of these symptoms pays off. In a review of the literature on the cost-effectiveness of biofeedback and behavioral medicine treatments for stress-related disorders, the cost/benefit ratios of some of these treatments suggested savings four times greater than costs (Schneider, 1987).

One study at the Harvard Community Health Plan in Boston focused on high utilizing primary care patients who experienced physical symptoms with significant psychosocial components (Hellman *et al.*, 1990). The study investigated the effectiveness of two interventions aimed at helping patients change behavior. Both interventions focused on the mind/body relationship and offered patients educational materials, relaxation-response training, and awareness training. Both included cognitive restructuring—special techniques for recognizing and changing distorted thought patterns. The two groups were compared with a group receiving only information about stress management. The behavioral medicine groups met once a week for six weeks in 90-minute sessions. The information-only group held just two 90-minute sessions, two weeks apart.

Researchers looked at physical symptoms, levels of psychological distress and the number of visits to the HMO before and after treatment. Patients in the information-only group experi-

enced no significant changes. But the patients in the behavioral medicine groups after six months reported less physical and psychological discomfort and each had nearly two fewer visits to the health plan than the patients in the control group. The estimated net savings to the HMO above the cost of the intervention for the 46 behavioral medicine patients was \$3,900 in the first six months alone. If 25–50% of all physician visits are by psychologically distressed patients, the long-term cost savings from targeted behavioral medicine interventions could be remarkable.

Another study examined data on 235 inpatients referred for stress-related disorders to the Department of Behavioral Medicine at Hohf Clinic and Hospital in Victoria, Texas (Gonik *et al.*, 1981). The department's inpatient treatment program averaged 11 days and included medical management, biofeedback training, structured in-room self-study and self-management activities, as well as psychotherapy with outpatient follow-up. In the 5 years prior to the intervention the patients averaged 26 hospital days per year. In the two years post-intervention, average hospital days plummeted 68% to 7.3 days per year. And these figures *include* the 11 days of hospitalization for the inpatient behavioral medicine treatment program. The program resulted in at least \$3 saved in the first two years for each dollar invested—including the cost of the inpatient and outpatient behavioral treatment.

A meta-analysis—quantitative review of the literature—combined results from 58 controlled studies of the impact of mental health treatments on medical utilization and costs. In 85% of the studies, after brief psychotherapy, medical utilization decreased from 10–33%. Hospital length of stay was down on average by 1.5 days (Mumford *et al.*, 1984). The costs of the mental health treatment were more

than offset by the savings in medical care utilization.

One study measured the effect of mental health treatment on patients with one of four chronic diseases—chronic lung disease, diabetes, ischemic heart disease, and hypertension. By the third year following diagnosis, those who had seven or more outpatient mental health visits a year beginning within 12 months of their diagnosis had overall lower cost for medical services—specifically inpatient services (Schlesinger *et al.*, 1983).

Chronic Pain

Behavioral group shown to help chronic pain sufferers and lower cost of care.

Every year, thousands of people in chronic pain make thousands of visits to doctors, driving up health care costs and rarely finding relief. Why? Most likely because the psychosocial needs of people in constant pain are not adequately addressed.

At least one study indicates that a systematic behavioral group program designed to help people cope with the physical and psychological stress of chronic pain can make a difference—at a fraction of the cost of the unproductive medical visits. One study focused on the effects of a group intervention with 109 patients who had been living with chronic pain for an average of 6.5 years (Caudill *et al.*, 1991). Their pain conditions included headaches, backaches, stomachaches, and neck pain. The patients attending a 90-minute group meetings led by a physician and psychologist once a week for 10 weeks.

During the 10 sessions, patients learned about the physiology of pain, medical and behavioral

treatment approaches, the relaxation response, yoga exercises, communication skills, goal-setting strategies, problem-solving skills, and cognitive restructuring. Homework entailed keeping daily pain diaries, assessing medication use, practicing the relaxation response, listening to a relaxation audio tape, and scheduling pleasurable activities.

In reviewing patients' status and clinic visits one year before the program and one to two years after, it became apparent that behavioral intervention did not make the pain go away but did decrease negative psychological symptoms such as anxiety, depression, and hostility. Furthermore, clinic visits decreased by 36% in the first year after the program and continued to decline in the second year. The program cost about \$1,000 per group, or \$11,000 for all 109 patients. However, the net savings in clinic visits alone was estimated to be at least \$12,000 in the first year and \$23,000 more in the second. And these estimates do not include savings from reductions in prescription drugs and "reassuring" diagnostic tests. Projecting these results, it appears that effective behavioral intervention for chronic pain sufferers could net our struggling health care system at least \$35,000 in savings every two years for each 100 patients served.

Diabetes

Teaching self-management skills keeps diabetics out of the hospital.

About 11 million Americans—or one in 20—have diabetes, and almost half of these cases are undiagnosed (Somers, 1990). Diabetes is the number one cause of new blindness in people between the ages of 20 and 74 and contributes to at least 7% of all deaths in this country (*Diabetes Output Education*, 1986).

Furthermore, diabetics are about 2.3 times more likely to be hospitalized than the rest of the population, and between 6% and 9% of all diabetic pregnancies result in serious congenital malformations of the fetus (Scheffler *et al.*, 1992).

The treatment of diabetes depends on appropriate self-care. Diabetics need training in how to manage their condition. They must learn to balance diet and exercise requirements with drug therapy (insulin or oral agents). They need to be able to monitor their own blood glucose. Numerous studies have proven the cost-effectiveness of an integrated program of diabetes outpatient education and care. For example:

- ▶ At the Los Angeles County-University of Southern California Medical Center, an integrated diabetes education program and care decreased the rate of hospitalization for 6,000 patients by 73% and the average length of stay by 78%—for an estimated savings of \$2,319 per patient each year (Miller & Goldstein, 1972; Miller *et al.*, 1981).
- ▶ At the Grady Memorial Hospital in Atlanta, Georgia, diabetes outpatient education and care reduced the incidence of severe diabetic ketoacidosis by 65% and the number of lower extremity amputations by 49% in a group of 12,950 patients—for an estimated savings of \$437,500 per year (Davidson *et al.*, 1979; Davidson, 1983).
- ▶ In Dusseldorf, Germany, a five-day intensive outpatient education program given to 212 patients over three years cut the number of days spent in the hospital from 16.7 days per year to 6.3 days (Assal *et al.*, 1985; Muhlhauser *et al.*, 1983).

- ▶ An audit of hospital records of 898 people with diabetes in Maine revealed that inadequate self-management contributed to one of every six hospitalizations. One of every 10 patients had their hospital stay extended for teaching purposes only. In another study of patients admitted to a community hospital, a specific educational deficit was considered to be responsible for 27% of admissions (Sinnock).

Comprehensive diabetes management is also effective with children. In 1978, Children's Hospital Medical Center in Cincinnati introduced a treatment program supervised by two full-time pediatric endocrinologists that included structured education by a diabetes nurse educator and a dietitian, and social and psychiatric support services (Drozka *et al.*, 1990). Initial interventions were geared to the child's developmental level, family attitudes, and health values and were followed up by patient/family education sessions. Round-the-clock telephone support was also made available.

Examination of admission records of 798 diabetic children between 1973 and 1987 revealed that the program saved the hospital about \$342,000 per year—savings were mainly derived from an average reduction of 1.2 days in the length of stay among children with diabetic ketoacidosis—a life-threatening complication of diabetes.

Aggressive diabetes management has also been shown to benefit pregnant women and lower medical costs of both mothers and babies (Scheffler *et al.*, 1992). The California Diabetes and Pregnancy Program (CDAPP), also known as the "Sweet Success" program, recruits diabetic women either before or soon after they become pregnant. The program provides comprehensive prenatal care, including nutrition,

education, and support services specifically developed for pregnant diabetics.

A comparison of CDAPP participants at three hospitals—Children's Hospital of San Francisco, Sutter Memorial Hospital, and Loma Linda University Medical Center—with a control group of diabetic deliveries at five hospital sites in California showed that the CDAPP group incurred 30.3% fewer charges, mostly due to shorter lengths of stay and healthier babies. The program returns more than \$5 for every dollar spent.

Asthma

Education in small groups helps asthma patients and reduces acute medical visits.

At least 6% of the population has at some time been told by a doctor that they had asthma, and 3% report they currently have it. Of those, 21% report that asthma has placed long-term limitations on their usual activities and 18% report five or more doctor office visits during a year (Wilson *et al.*, 1993). Mortality from asthma, considered to be largely preventable, has been rising in recent years and also increases with age.

To better understand the impact of different interventions, American Institutes for Research and Kaiser Permanente in Northern California followed 323 adult patients with moderate to severe asthma. Participants were randomly assigned to one of four groups. One test group received small-group education and another individual teaching. One control group received written information only in the form of a workbook, and the other got usual care with no formal asthma education. The study compared changes in knowledge, self-management

behaviors, symptoms, functional status, and use of medical services. Data were collected from patients by questionnaire, diary, physical examination, laboratory testing, and examination of medical records from one year prior to two years after the program.

Those receiving small-group education—and to a lesser degree, those receiving individual instruction—knew more about asthma, had more symptom-free days and were bothered less by asthma symptoms. Individual teaching was linked with improvements in medication compliance and in patient-physician communication, but only those in the small group program demonstrated physical activity improvements and significantly fewer medical visits for acute exacerbations over the long haul.

All groups had 30% fewer acute visits in the two years following treatment than in the baseline year. In the first follow-up year, there were no differences in the change in acute visits among the treatment and control groups. But by the second follow-up year, the group program participants reduced acute visits below baseline by 49%—nearly twice that of the usual care control patients.

These results clearly demonstrate the value of educating patients about their disease and favor small groups as the most effective means. The findings also demonstrate that it takes time—as long as two years—to realize the full benefits of this type of intervention.

Arthritis

Learning to self-manage the symptoms of arthritis can decrease the pain of the pocket-book as well as joints.

Approximately one-fifth of all Americans under age 65, and half of those over 65, have some kind of painful condition of the muscles, bones or joints that requires medical attention. Many of these conditions are minor and quickly get better on their own. But for many, the pain and disability of chronic arthritis are daily companions that must be managed.

A study was conducted at Stanford University to evaluate the impact of the Arthritis Self-Management Program (ASMP) on 401 chronic arthritis sufferers. This 12-hour health education class meets once a week for six weeks in a two-hour session under the direction of two trained lay leaders, one of whom usually has arthritis (Lorig *et al.*, 1993).

After four years, although physical disability was almost 9% greater, pain was reduced by 20%, visits to physicians by 43%, and perceived self-efficacy was significantly higher. Akin to confidence, self-efficacy is a person's perception or belief in one's ability to perform a specific behavior or act. Self-efficacy reflects the control people seek to exercise over the conditions that influence their lives. It determines to a great extent their actions, their motivation, their perseverance, and their vulnerability to stress and depression.

The cost of the intervention was \$54 per person. Based on the reduced physician visit rates, adjusted four-year health care savings were \$648 per person with rheumatoid arthritis and \$189 per person with osteoarthritis. Given these figures, if only 1% of the patients in the United States with moderate-to-severe osteoarthritis of the hand (103,000) and only 1% of the patients with classical or definite rheumatoid arthritis (21,000) participated in the ASMP, total discounted savings over four years would

equal \$19.5 million for osteoarthritis and \$13.6 million for rheumatoid arthritis.

Surgery

Surgical patients recover faster with preoperative education and psychological support.

Americans are the most operated upon people in the world. Each year over 25 million patients undergo surgery. The speed of recovery and length of hospital stay is influenced by many factors including how well the patient is prepared to deal with the psychological impact of surgery.

A meta-analysis was done on 191 studies conducted between 1963 and 1989 of the effects of psychoeducational interventions on the recovery, postsurgical pain, and psychological distress of adult surgical patients (Devine, 1992). The operations in these studies were both minor and major, including abdominal (gall bladder, bowel, or gastric) and thoracic (heart and lung). The interventions were in three broad categories: 1) health care information—details about what would be done before and after surgery, timing of the various procedures and activities, and the functions and roles of various health care providers. 2) skill-building exercises for coughing, breathing and relaxation. 3) psychosocial support—identifying and attempting to alleviate patient concerns, providing reassurance, encouraging patients to ask questions throughout hospitalization and shaping specific expectations of recovery.

Most of the studies—from 79% to 84%—indicated beneficial effects from the interventions. Length of stay was decreased by an average of 1.5 days even in the studies conducted during the late-1980s when changes in hospital reim-

bursement had already increased the pressure to shorten hospital length of stay. Assuming a very conservative \$200 savings in hospital expenses and \$20 in educational costs, this yields \$10 in savings for every dollar invested in patient education.

Another review compiled results of 13 studies using hospital days post-surgery or post-heart attack as outcome indicators. This meta-analysis showed that psychological intervention reduced hospitalization approximately two days below the control group's average of 9.92 days (Mumford *et al.*, 1982).

A study at Mount Sinai Medical Center in New York and Northwestern Memorial Hospital in Chicago evaluated psychiatric screening and consultation for 452 patients 65 years or older admitted for surgical repair of fractured hips. These interventions led to early detection of psychiatric problems, better psychiatric care, earlier discharge, and substantial cost savings. The psychiatric interventions cost each hospital about \$20,000. Yet, Mount Sinai saved about \$167,000 by reducing the mean length of hospital stay by 2.2 days while at Northwestern the savings exceeded \$97,000 due to shortening hospital stays by 1.7 days (Strain *et al.*, 1991).

Childbirth

Emotional support in labor reduces C-sections and shortens labor.

Cesarean section is the most common surgical procedure performed in the United States, affecting about one in every five deliveries. Delivery by C-section extends the hospital stay of mother and child and increases the risk of maternal infection and other complications.

Five studies conducted in Guatemala, Canada, the United States, and South Africa have confirmed that the continuous presence of a supportive female during labor and delivery can reduce the need for C-section, shorten labor and delivery, and reduce perinatal problems (Klaus *et al.*, 1992). In all cases, the mothers were healthy women with a normal pregnancy giving birth for the first time. The intervention was a *doula*—a trained lay person who provided emotional support consisting of praise, reassurance, physical contact (such as rubbing the mother's back or holding her), explanations of what was happening, and a continuous presence. Though far from ideal, in these studies the women in labor met their *doulas* for the first time only after they were admitted to the hospital.

One of these studies took place at Jefferson Davis Hospital in Houston, Texas. Participants were divided into three groups: a control group, an observed group to measure the potential supportive effects of a passive observer, and a group actively supported by *doulas* (Kennel *et al.*, 1991). Of the 204 patients in the control group, 18% had C-sections and of the 212 in the group supported by *doulas*, 8% had C-sections—a reduction of 56%. The presence of a *doula* also resulted in other benefits. Epidural anesthesia was reduced by 85%. Labor was an average of 2 hours shorter. And only half as many babies required more than 48 hours hospitalization because of neonatal problems.

A meta-analysis of all five studies showed that the presence of the *doula* reduce the length of labor by 25%; the odds of having a C-section between 34% and 67%; and the odds of needing analgesia between 1% and 47%, oxytocin between 43% and 68%, and forceps between 35% and 82%. This, in turn, reduced the length of hospital stay and the rate of complica-

tions among newborns. Meanwhile, the average cost of the *doula* was \$200. Based on these findings, if every woman in the United States had a supportive woman with her continuously throughout labor, maternity health care costs might be reduced by as much as \$2 billion per year.

The beneficial effects of physical contact and massage are as apparent with newborns as with laboring women. A randomized clinical trial at Jackson Memorial Hospital in Florida showed that premature babies who received body stroking and passive movements of the limbs for 15 minutes three times a day for 10 days averaged a 47% greater weight gain per day despite equivalent caloric intake. The massaged babies were more active and alert, and were discharged from the hospital six days earlier than their counterparts. The savings on hospital costs alone were \$3,000 per infant (Field *et al.*, 1986).

Summary

Evidence is mounting that addressing the psychological and educational needs of patients makes economic and health sense. All these studies remind us that health care providers should not simply treat patients as disordered machines to be fixed with physical or chemical interventions. By providing information, emotional support, and skill training, people can be encouraged to participate as active partners in health care. The result appears to be healthier patients, and often, lower health care costs.

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Behavioral Medicine Over the Life Span

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A life span approach to behavioral medicine is necessary for five reasons. First, the salience of risk variables to physical health changes over time. Second, the strong association noted between SES variables and physical morbidity is often an illusion due to the fact that some other antecedent variable has affected both health and SES. Third, due to its complexity and due to superstition and sentiment, research in behavioral medicine is often distorted by observer bias and prejudice. Much of this bias can be averted by studying the same sample from a number of different disciplinary perspectives over time, for life time prospective study removes many prejudices. Fourth, health behaviors are far more important to physical morbidity than are stress, defense and conflict. The effect of poor health behaviors and self-care on physical health is slow but steady. To appreciate the magnitude of these effects requires prolonged follow-up. Lastly, "stress" which is often invoked as an important variable in behavioral medicine often proves to be relatively unimportant if the individual is carefully studied over time.

Let us take these points one at a time. First, behavioral variables affecting physical morbidity change with the passage of time. Many years ago I noted a strong correlation of good mental health and warm childhood with the physical health of 50 year old men (Vaillant 1979). When the men were 65, (Vaillant 1991) the effects of a warm childhood environment and mental health before age 50 had become less salient and disappeared if one controlled for affective disorder. In contrast, the influ-

ence of heavy cigarette smoking and of alcohol abuse before age 50 proved very significant indeed. Elevated adolescent blood pressure was powerfully associated with poor health at age 50 largely because it predicted essential hypertension. By age 70 some men had outgrown hypertension, some men had controlled it effectively through treatment; and thus, by age 70 the association between adolescent hypertension and general physical morbidity had disappeared.

Second, social class, which is powerfully associated with physical health, probably usually works by proxies. However, to determine whether social class is a causal variable often requires multigenerational study. For example, schizophrenia was believed associated with social class until longitudinal studies showed that the parents of schizophrenics did not differ from the parents of controls in social class. Rather, schizophrenia causes downward social mobility. Similarly, alcoholism is often seen as a result of unemployment, poor education, bad living conditions and disrupted childhood homes. However, prospective multigenerational study reveals that alcoholism is the cause, not the result of these conditions (Vaillant 1983).

Of course, in other instances there are direct links between social class and physical morbidity; but even then the relationship is often not due to stress or anomie or impaired morale but due to some direct health behavior or self-care variable that is affected by social class. Two obvious examples are the fact that in recent years smoking cessation is much more common

among the highly educated and second, among women smoking initiation is more common among the less well educated. Both of these factors result in poor health in the socio-economically disadvantaged. Again, unhealthy eating habits and limited access to medical care are much more common among the American poor than among the rich. Both lead to physical morbidity.

Third, there is a need for interdisciplinary study. Behavioral medicine by its very nature tends to attract nontraditional approaches to biological illness. Studies by psychologists and sociologists often outnumber those by geneticists and biologists. In addition, nontraditional, humanistic approaches often lead to sentimental and superstitious approaches to problems that were previously thought of in too concrete a fashion. Scientific safeguards are needed. Such safeguards can be supplied by an interdisciplinary team or by investigators of different persuasions studying the same sample. Put differently, behavioral medicine does not need a national institute of social medicine as much as it need projects like the Stanford Heart Study where social scientists expert in communication like Nathan Maccoby team up with internists like Jack Farquahar to help study peoples' compliance toward the selfcare of heart disease.

Studies of alcoholism provide frequent examples where the failure of interdisciplinary study has lead to erroneous conclusions. For example, the Rand report, which was carried out by sociologists, considered people who died as "lost" from study rather than the source of important and interesting results. In the Albany and Framingham Studies of heart disease, alcohol abuse was not recognized as a risk factor in heart disease because alcohol abuse was incorrectly measured by using quantity/frequency measures rather than problem drinking measures like the "CAGE".

The fourth reason why a life span approach is needed, is to remind investigators that stress, immature defenses and conflict do not lead to physical morbidity as much as do poor self-care and poor health behaviors. Let me offer two familiar examples. It was noted that widowers often died of heart disease shortly after losing their wives. It was hypothesized that grief, perhaps operating through the hypothalamic-pituitary axis was helping to "break the hearts" of the widowers. More careful research revealed that widowers died of heart disease when bereaved only if they had preexisting heart disease. Thus, the most likely explanation of their increased mortality was poor compliance with cardiac care. Again, depression has often been linked with cancer suggesting perhaps the effect of stress and depression on the hypothalamic-pituitary axis affected immune mechanisms. Careful research has repeatedly shown that depression probably does not cause sufficient alteration in immune mechanisms to lead to cancer; and, indeed, the link between depression and cancer is rather weak (Zonderman *et al.*, 1989). Rather, the most likely way that depression is linked with cancer is that people who are depressed are more likely to drink heavily and smoke heavily, both of which habits can more than double the incidence of cancer.

Finally, the whole concept of "stress" is misleading. Too seldom do investigators consider what are the risk factors that mediate increased perception of stress and that also lead to poor health—e.g. depression and alcoholism. Alcohol abuse and depression are both disorders that are significantly influenced by genetic factors and that often do not manifest themselves until adult life. Both alcohol abuse and depression dramatically increase individuals' sensitivity to stress. Both alcoholism and depression induce individuals to use less adaptive defense mechanisms (Vaillant, 1993). Without a life span

approach it becomes easy to blame the individual's increased physical morbidity on either poor coping styles or on increased stress. But if one takes the long range view, it is possible to appreciate both that the correlation between high scores on the Holmes-Rahe Life Events stress score and morbidity are actually rather modest and that, to my knowledge, none of these studies effectively controlled for alcohol abuse, a robust primary cause of both physical morbidity and stressful life events.

Table 1 illustrates the relationship between depression and poor physical health. People who are depressed report more stress but also drink more and smoke more. In addition, people who are alcoholic are much more likely to have secondary depression. Thus, it would seem a great mistake to invest a great deal of research in the effect of stress on physical health without controlling for premorbid alcohol abuse and depression.

Table 1
Association Between Affective Disorder Prior to Age 50,
Self-Care and Physical Morbidity in 183
70 Year Old College Men

	Not Impaired		Psychosocially Impaired	
	Mentally Most Healthy (n=50)	Intermediate (n=84)	Personality Disorder- or Alcoholism (n=24)	Affective Disorder (n=25)
Depression and Habits				
Cigarette use>40 pack-y	2%	18%	38%	40%
100+ psychiatric visits	0%	2%	2%	25%
Alcohol abuse	0%	13%	17%	44%
Depression (NEO)>17 (n=131)	5%	5%	19%	62%
Physical Health				
Subject dead<70 years	2%	14%	25%	36%
Subject chronically ill or dead<66 years	22%	36%	54%	79%

(Vaillant et al 1992)

To conclude, I think there are three important points that NIH should keep in mind in assigning funding to behavioral medicine. First, to

favor interdisciplinary studies, especially interdisciplinary studies that take a life span approach. Second, to appreciate that while cata-

strophic stress plays an enormously important etiologic role in PTSD type disorders, they are relatively uncommon. Similarly, SES plays an etiologic role as related to sources of physical morbidity such as abuse of crack cocaine, lead poisoning, impaired morale due to discrimination and poor access to medical care. But more often elevated stress and poor SES are merely proxies for other more salient variables.

Behavioral medicine should favor studies that directly link primary behaviors to health or at least try to control for them. For example, the association of poverty and physical morbidity has probably much more to do with substance abuse than to despair over a minimum wage. The disruptive, disorganized inner-city family has much more to do with causing teenage pregnancy than does lack of education which is often a result of early pregnancy. In short, we need studies that keep cause and effect relationships straight.

Lastly, we need as much research in understanding compliance as we do in understanding stress. Disorders of compliance lead directly to complications in COPD, in diabetes, and in obesity—disorders that themselves cause stress and elevated scores on life events scales.

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An Overview of NIH Behavioral Medicine Research Programs

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This paper presents an overview of behavioral medicine research programs sponsored by the National Institutes of Health (NIH). The study of behavioral and social factors is a critical component of the effort to achieve a comprehensive understanding of the foundations of good health, and the prevention, onset, progression of, and rehabilitation from disease. The Institute of Medicine's seminal report of a decade ago, *Health and Behavior*, (Hamburg et al. 1982) and the more recent *Healthy People 2000: National Health Promotion and Disease Prevention Objectives* (U.S. Department of Health and Human Services 1991), have led the scientific community and the public to recognize more clearly that lifestyle and behavioral factors are significant causal agents in the Nation's rates of morbidity and mortality, contributing to all 10 of the leading causes of death in America. Moreover, behavioral, social, and cultural processes interact with biological processes (e.g., endocrine, immune, and central nervous systems) to influence health and disease.

The study of human behavior, then, is an essential component of the Nation's research capacity to address a large number of crucial health needs, including the discovery of improved approaches to the prevention and treatment of physical and mental disorders. The health of virtually the entire population could be improved through changes in specific behaviors; cost savings in terms of decreased human

suffering and health care costs are potentially enormous. Reductions in behavioral risk factors are linked to decreases in disease; similarly, behavior changes and psychosocial interventions can influence the course and treatment of illness. To that end, health and behavior issues represent a critical part of the mission of each of the Institutes within the National Institutes of Health.

This paper discusses the history of NIH's involvement in behavioral medicine research, including the NIH's conceptualization of this field of investigation. This presentation will examine the NIH's programmatic activities in behavioral medicine, including particular areas of emphasis. The paper will conclude with a discussion of the challenges to and opportunities for strengthening the behavioral medicine research agenda as the result of the merger of the former research institutes of the Alcohol, Drug Abuse, and Mental Health Administration (the National Institute of Mental Health, National Institute on Drug Abuse, and the National Institute on Alcoholism and Alcohol Abuse) into the NIH community.

Over the next three days, our efforts to formulate a research agenda for behavioral medicine in this decade and beyond into the 21st century will serve to illustrate how the crucial connections among mind, brain, and body can be addressed more effectively through the reintegration of the NIH's own psyche and soma. In

addition, we will forge linkages between the fields of behavioral medicine and consultation/liaison research by adopting both a multidisciplinary and a life span approach to some of the most important health problems facing our Nation.

History of Behavioral Medicine in the United States

Despite the long-standing recognition that behavioral factors affect both health and the inception and course of illness, only in the past 25 years has serious attention been focused on understanding how behavioral factors can be harnessed by the field of preventive and behavioral medicine in the treatment and prevention of physical disease. The National Institute of Mental Health has played and continues to play a major role in generating such attention. Since its inception in 1946, the NIMH has advanced its primary mission—understanding, treating, and preventing mental and behavioral disorders—by supporting basic, clinical, and epidemiologic research on mental disorders. Additionally, NIMH-supported research and programs have sought to understand and explicate the biological processes that underlie both normal and disturbed behavior, as well as the behavioral, social, and environmental variables that affect human health and disease. In the late 1940s, Alexander and others conducted pioneering studies of psychosomatic medicine, examining personality and psychodynamic factors in the etiology of "psychosomatic disorders" such as ulcers, asthma, and migraines. The historical interest of the NIMH in behavioral factors affecting physical health dates to the first grant awarded in 1948, supporting a study of the relationship between psychological variables and cardiovascular physiology. However, it was not until the 1950s, following the

establishment of the American Board of Preventive Medicine in 1948 and the American College of Preventive Medicine in 1954, that research and clinical inquiry was focused directly on preventive health care. The decade of the 1950s marked the beginning of the systematic study of the psychophysiology of physical and mental disorders; by the next decade, investigators began to study genetic and biological factors and mechanisms, and their interactions with environmental processes.

It was not until the 1970s, with the publication of the Lalonde Report in Canada (Lalonde 1974) the U.S. Surgeon General's report on smoking and health (U.S. Department of Health, Education and Welfare 1979) and the Institute of Medicine's reports on stress and human health (1981) that widespread credibility was given to the role of biobehavioral and environmental factors in the maintenance of health and prevention of illness. In 1977, a conference, convened and co-sponsored by the NIH and Yale University, highlighted the need for better integration of the biomedical and behavioral sciences in research designed to increase our understanding of health and disease. In the same year, the National Heart, Lung, and Blood Institute (NHLBI) established a Behavioral Medicine Research Branch, the first of its kind at the NIH (Krasnegor 1990). It was also in the late 1970s that the Academy of Behavioral Medicine Research and the Society of Behavioral Medicine were founded in a focused attempt to stimulate further research and clinical work in this field (Krasnegor 1990).

By the first half of the 1980s, the field of behavioral medicine had taken flight; momentum grew over the course of the decade, both within the National Institutes of Health and the Alcohol, Drug Abuse and Mental Health Administration. In 1980, a joint ADAMHA/NIH Interagency Committee planned and convened

a series of six conferences to clarify the behavioral aspects of selected major public health problems and to help strengthen health and behavior research both within the Public Health Service and in the wider research community. The Committee also provided Federal input to the Institute of Medicine (IOM) on a seminal review of the state-of-the-art in health and behavior. The final IOM report, published in 1982, has become a classic in the field (Hamberg et al. 1982).

In the same year that it established the Interagency Committee with the ADAMHA, the NIH established an Ad Hoc Institutional Review Group (IRG) to review and evaluate extramural research applications in behavioral medicine. Momentum continued. An NIH Working Group on Health and Behavior Research was set in place in 1981; at congressional direction four years later, the NIH established the Office of Disease Prevention within the Office of the NIH Director. This growing emphasis on disease prevention was reflected in the publication of the Public Health Service's (PHS) report, *Healthy People 2000* (U.S. Department of Health and Human Services 1991), a volume that, as observed earlier, outlines objectives and strategies for achieving a healthier American population by the next millennium.

During the decade of the 1980s, individual NIH and ADAMHA Institutes initiated activities targeted toward behavior and health. The NHLBI convened a series of conferences on biobehavioral aspects of cardiovascular and pulmonary disease research; the American College of Preventive Medicine developed guidelines for a national effort in preventive medicine. From these initiatives emerged both growing research emphasis on the relationship of biobehavioral factors in the pathogenesis of medical illnesses and clinical interest in the

phenomenon that health could be enhanced either by eliminating behavioral risk factors such as smoking or by developing health-promoting behaviors such as proper diet, exercise, and adherence to treatment regimens.

In a parallel development, the NIMH, then part of the Alcohol, Drug Abuse and Mental Health Administration, began to support clinical training opportunities in the area of consultation/liaison psychiatry. This 50-year-old discipline emphasizes the diagnosis, treatment, and prevention of psychiatric morbidity among physically ill and somatizing patients, coupled with the provision of mental health consultation, liaison, and training in a variety of medical settings to clinicians outside the field of mental health. In the latter part of the 1980s, the Institute sponsored a series of workshops to promote both research and research careers in consultation/liaison psychiatry; it also established a program in health services research designed to examine how health outcomes and health care cost are affected by the provision of mental health services in medical and surgical settings.

During the same period, the NIMH established the Health and Behavior Research Branch, the Office of Disease Prevention, and the Office of AIDS Research Programs. In 1983, the larger ADAMHA launched a series of programs to stem the epidemic of AIDS, a disease currently without cure or vaccine that is transmitted primarily by high-risk sexual and drug-abusing behavior. Researchers and clinicians alike became painfully aware how little we knew about effective behavior change methodologies. In 1987, an AIDS Institutional Review Group and an Office on AIDS were established within the Office of the Director of the NIMH to stimulate research on behavior change related to AIDS, and on the neuropsychiatric and psychoneuroimmunologic aspects of this disease.

In 1988, the NIMH undertook a critical review of its programs in health and behavior research. As a consequence of its evaluation, the Institute broadened the mission of the Health and Behavior Branch to include programs on basic prevention and behavior change strategies. As part of a wide-scale NIMH reorganization undertaken in 1992, the broadened and renamed Branch—the Basic Prevention and Behavioral Medicine Research Branch—was relocated from the Division of Basic Brain and Behavioral Research to the Division of Epidemiology and Services Research, better aligning the Branch with related consultation/liaison and health services research programs already underway in the Epidemiology and Services Research Division. Concomitantly, the NIMH established a Health Behavior and Prevention Grant Review Committee to centralize the review of grant applications in health and behavior research, a process that previously had involved more than fourteen separate review committees. Plans are now underway to develop an NIMH Health and Behavior Consortium to improve coordination of research across all of the NIMH research branches, divisions, and offices.

At the NIH, in 1992, an Office of Alternative Medicine was established within the Office of the NIH Director in order to evaluate unconventional therapies—such as acupuncture, visualization, meditation, massage, and certain nutritional interventions to treat or prevent illness. The same year witnessed the reintegration of the NIMH, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Institute on Drug Abuse (NIDA) into the NIH family.

To facilitate this merger, the NIH Director established the NIH Reunion Task Force, discussed in greater detail later in this paper. With representation from each NIH institute, center, and division, and from the Office of the

NIH Director, the Task Force highlighted ways in which the expanded mission of the NIH can increase our understanding of health and disease. In further recognition of the enhanced mission of the NIH, the Director chartered the previously established Working Group on Health and Behavior as a standing NIH Research Coordinating Committee. The working group, including representatives from the majority of the Institutes, centers, and division (ICDs) of the NIH, has a specific mandate to advance the field of behavioral medicine within the intramural and extramural programs of the NIH Institutes. Perhaps as a product of the Coordinating Committee's semiannual NIH Health and Behavior Report to Congress, the House and Senate asked the NIH to intensify its efforts in health and behavior still further. Indeed, congressional interest in the field led to a mandate that the NIH establish an Office of Behavioral and Social Sciences within the Office of the Director, NIH, to coordinate research across the Institutes and to give this research prominent focus within the NIH.

The specific activities of both the Reunion Task Force and the Health and Behavior Coordinating Committee will be discussed in greater detail later, in the context of ongoing NIH activities in the field. First, however, it is important to clarify how the NIH defines the field of behavioral medicine.

Behavioral Medicine: Towards a New Definition

As we have seen, while the concept of behavioral medicine grew out of psychosomatic studies of the 1940s, it is today much more than studies of psychophysiology. It draws upon aspects of mental health research, consultation/liaison psychiatry, psychology, social

science inquiry regarding human behavior, and biomedical inquiry. As in many fields, a definition requires more than the addition of the apparent parts of the whole. Numerous definitions for behavioral medicine have been proposed, yielding greater smoke than clarity, complicating both conceptualization of the field of inquiry and coordination of public and private sector research and clinical activities in the field.

One definition is drawn from the 1977 NIH/Yale behavioral medicine conference and emphasizes "the development and integration of biobehavioral and biomedical scientific knowledge and techniques relevant to health and illness and the application of this knowledge and these techniques to prevention, diagnosis, treatment and rehabilitation. The goal of health and behavior research is to seek through both basic and clinical research to understand the relationship between behavior and illness in order to find ways to maximize healthy behaviors and minimize health-damaging behaviors in all populations." The hallmark of biobehavioral medicine is the capacity to foster connections among basic, clinical, and applied sciences, and to translate this knowledge into improved patient care.

The definition describes the conceptual outlines of the field of health and behavior research, explaining the goals and applications of such research. Unfortunately, the definition is not sufficiently "user friendly" either to help inform program development or to track program activities or budgets. In direct response to these identified difficulties, the NIH Health and Behavior Coordinating Committee developed a new, more operational definition of behavioral medicine. By restricting the definition to *health-related* behavioral and social sciences research, the Coordinating Committee acknowledged that behavioral medicine is but one part

of the larger body of behavioral and social sciences research conducted and supported by the NIH. Further, with the reunion of the NIMH, NIAAA and NIDA into the NIH family, the Health and Behavior Coordinating Committee reexamined the meaning of the terms "health," "well-being," "functioning," "disease," and "illness" as they relate to conditions of both mental and physical etiology.

The definition was conceived as a five-part series of categories, each of which falls within the rubric of health and behavior research. They include: biobehavioral mechanisms (processes through which behavior, health and illness interact); identification and distribution of psychosocial risk and protective factors (factors that lead to or safeguard against illness or substance abuse); development, maintenance, and change of health-related behaviors; behaviors resulting from a disease or treatment; and behavioral and social interventions to prevent and treat illness or to promote health. The use of this functional definition both will improve both how policy in the field is conceived and how programs in health and behavior research are identified at the NIH. And with this new definition in hand, we turn to a review of the current NIH portfolio of health and behavior research.

NIH Programs in Health and Behavior Research

Thus far in the decade, behavioral medicine issues have been receiving unprecedented attention at the NIH. All of the NIH Institutes and centers support health and behavior research; many Institutes now have Behavioral Medicine research branches. Today, the NIH supports \$835.2 million in health and behavior research, roughly 8 percent of the \$10 billion total NIH

research budget up from \$446.5 in FY 92. The ADAMHA Institutes' health and behavior research portfolio represent a considerable proportion of the increase, with FY 1993 NIMH expenditures at \$95 million alone.

A wide range of NIH-supported studies on the role of behavioral and social factors in health and illness fall within the new definition of health and behavior research of the Health and Behavior Coordinating Committee described earlier in this paper. Moreover, the research crosscuts virtually all of the NIH Institutes, ranging from studies of behavioral factors that affect the triggering of myocardial infarction, to evaluation of the neural bases of eating behavior. NIH Institutes are supporting research to identify and manage behavioral risk factors for high-risk sexual behaviors, HIV infection, and for unintentional injuries in children. Yet another focus of health and behavior research seeks to modify alcohol-related risk-taking behaviors, such as driving under the influence of alcohol. Equally important is ongoing research designed to promote adherence to treatment regimens. NIH-supported research has found not only that psychosocial and educational interventions for asthma sufferers help reduce its occurrence, but also that such interventions are cost-effective means of lowering acute care hospital visits. These represent but a few examples of a panoply of research areas of current interest to the NIH Institutes, a matter to which we will turn in a few moments.

Crosscutting NIH Activities

Responding to Congressional Directive. Congress emphasized the importance it placed on health and behavior issues in 1992 when it directed the NIH to double its efforts in health and behavior over the following three years and to develop a ten-year implementation plan

outlining precise health and behavior initiatives to be undertaken across all of the Institutes. The Office of Disease Prevention in the Office of the Director in consultation with the Health and Behavior Coordinating Committee, has coordinated preparation of this implementation plan. To intensify NIH's efforts in biobehavioral research still further, Congress in 1993 directed the NIH to establish an Office of Behavioral and Social Sciences within the office of the NIH Director.

Health and Behavior Coordinating Committee. The NIH's Health and Behavior Coordinating Committee (HBCC) has played a major role in promoting biobehavioral research throughout the NIH. First established as a working group in 1981 and chartered formally in 1993, the HBCC is charged with (1) facilitating the exchange of programmatic and scientific information on health and behavior across NIH Institutes and offices; (2) providing a forum for considering new program initiatives; (3) serving as a contact point for other governmental, private, professional, and scientific organizations concerned with health and behavior research; (4) responding to information requests about NIH health and behavior activities; and (5) making recommendations for research needs and future directions to the NIH Director.

To that end, the HBCC and its members from each of the NIH's ICDs have engaged in a variety of activities. Working with the Office of Disease Prevention, Office of the Director, NIH, the HBCC participated in the development of the previously mentioned congressionally mandated NIH Health and Behavior Implementation Plan, designed to develop initiatives to increase the level of support for health and behavior research and programmatic activities at the NIH. The HBCC further maintains active liaison with relevant professional associations and has fostered close working relationships

with NIH ICDs, Offices, and the NIH Reunion Task Force. The HBCC also has undertaken a number of specific initiatives, including:

- (1) conduct of a seminar series on women's health and behavior issues, cosponsored by the NIH Office of Women's Health Research;
- (2) development of a seminar series on behavioral and social factors in tuberculosis to help stimulate ICD initiatives at the interface of physical and behavioral health issues;
- (3) submission of recommendations to the Director, NIH, concerning expansion of quality-of-life research at the NIH, urging that resources be provided for the design, implementation, and evaluation of health-related quality-of-life indicators in NIH-supported clinical trials;
- (4) sponsorship of a trans-NIH conference on pain research that evaluated current knowledge concerning biobehavioral aspects of pain, to identify research needs, and to initiate greater interdisciplinary and interagency collaboration in pain research, leading ultimately to a trans-NIH program announcement in the area. In large measure as a product of the high profile provided to health and behavior research by the HBCC, the plenary sessions of the 1992 NIH Research Festival featured specific sessions on biobehavioral issues—a first in the history of the Festival; and
- (5) co-sponsorship with the NIMH of this NIH-wide National Working Conference on New Research Frontiers in Behavioral Medicine to foster coordination and expansion of behavioral medicine research within and across NIH Institutes' mandate.

NIH Reunion Task Force. The NIH reorganization has broadened and enriched the NIH mandate and has provided exciting new opportunities for its scientific enterprise. As already briefly mentioned (see p. XXX), the reintegration of the NIAAA, NIDA, and NIMH into the NIH prompted the NIH Director to establish the NIH Reunion Task Force in 1992. The Task Force, with 33 members drawn from the senior-level ranks of each of the Institutes, offices, and centers of the NIH, serves to foster scientific collaboration, enhance interdisciplinary coordination of programs, give the behavioral sciences and neurosciences prominent scientific focus within the NIH, and to place the study of mental and addictive disorders at the heart of the NIH's research agenda.

To that end, the Task Force convened a number of working groups: AIDS risk behaviors, eating disorders, psychoneuroimmunology, compliance/adherence behaviors, the interface of neuroscience and behavior, and family roles in health and illness. The membership of these working groups included both intramural and extramural NIH professionals across several Institutes and offices with a common interest in the specific area of working group focus. The goal of these working groups was to better coordinate research in these crosscutting areas, to identify research gaps, to work toward collective NIH-wide solutions, and to organize conferences and workshops.

The NIH Reunion Task Force's working groups convened a series of conferences and workshops that addressed key research issues, including:

- (1) a major symposium for primary care physicians that translated research advances into clinical practice recommen-

dations, providing a forum for health care professionals to learn more about the interrelationship of mental and physical illness;

- (2) a symposium focused on social and behavioral sciences methodology and AIDS risk behavior;
- (3) seminars for NIH staff on the importance of compliance and adherence in clinical trials of treatments for chronic disease, infectious diseases, and addictive disorders;
- (4) a public forum on mind-body interactions in health and disease, addressing how psychological factors affect biological mechanisms such as the neuroendocrine system, immune function and health outcomes, followed by a scientific workshop examining the state-of-the-art in psychoneuroimmunology;
- (5) a public day-long program on "Understanding and Healing the Human Brain" to educate policy makers and the public to issues in neuroscience and behavior research, and
- (6) a special seminar, *Research Opportunities at NIH*, at the annual meeting of the National Council on Family Relations.

Thus, the Task Force is highlighting ways in which the expanded mission of the NIH will increase our understanding of health and disease. The success of these activities depends upon receptivity to and creativity in our crafting of new opportunities for collaboration and in discovering ways in which scientists and consumer groups can be brought together to solve some of the critical health problems facing our Nation. Whether the discussion is about AIDS, teen pregnancy, heart disease, violence, cancer, the re-emergence of tuberculosis, substance abuse or depression—to name but a few public health issues facing our country today—behav-

ior is a key variable in both understanding the causes of the problem and in developing effective prevention and treatment strategies.

NIH Behavioral Medicine Initiatives

In 1991, former Surgeon General Dr. C. Everett Koop observed that "if the goal of education in public health is to change behavior, then we, as public health educators, have a lot to learn." To achieve that goal—by increasing our overall understanding of human behavior—each of the NIH Institutes, Centers and Divisions (ICDs) increasingly has fostered research in behavioral aspects of health and illness within its individual research mandate.

As noted elsewhere in this presentation, the rededication of the NIH to the field of health and behavior is but one part of a PHS-wide effort. With the publication of *Healthy People 2000* (U.S. Public Health Service 1991) which set out objectives for improving the health of the American people and relied to a great extent on better understanding how to change risk-taking behaviors and enhance health-related protective behaviors, the issue of behavioral medicine was placed squarely on the Nation's health research agenda. That volume, coupled with Dr. Koop's injunction to the field, challenged the Federal research community to place increasing emphasis on health-enhancing changes in behavior to improve the quality of life and to reduce the incidence of disease.

The renewed interest in the field moved forward with even greater urgency, when in direct response to the Congressional mandate, the NIH's Institutes, Centers and Divisions set forth a behavioral research plan to take the field into

Table 1
National Institutes of Health
Health and Behavioral Research
(in thousands of dollars)

	1991 Actual	1992 Actual	1993 Actual	1994 Estimate	1995 Estimate	Percent Change
NCI*	\$71,172	\$80,173	\$118,914	\$131,000	\$144,000	9.92
NHLBI	54,692	67,929	79,225	83,000	86,500	3.72
NIDR	5,841	6,261	6,142	6,539	6,781	3.70
NIDDK	16,000	16,600	16,900	17,600	18,400	4.55
NINDS	34,580	40,337	34,421	35,955	37,298	3.74
NIAID	7,579	6,314	8,340	8,179	8,441	3.28
NIGMS	3,262	4,313	4,313	4,313	4,313	0.00
NICHD	51,900	56,000	58,194	59,300	61,500	3.71
NEI	4,900	6,484	9,142	9,617	9,969	3.66
NIEHS	3,292	7,022	9,800	9,883	10,150	2.68
NIA	60,775	61,029	65,051	67,000	69,000	2.99
NIAMS	8,431	6,604	5,805	6,195	6,442	3.99
NIDCD	6,674	7,725	10,560	11,041	11,347	2.77
NIMH	156,962	163,433	156,638	167,824	176,015	4.88
NIAAA	---	33,027	34,000	34,000	34,000	0.00
NIDA	---	168,472	164,210	174,800	180,970	3.53
NCRR	26,823	22,982	24,069	24,888	26,010	4.53
NINR	17,755	20,376	21,377	22,500	23,400	4.00
FIG	655	697	568	885	942	6.44
NLM	2,443	2,650	6,544	6,333	6,500	2.64
TOTAL	533,738	778,448	835,213	881,242	921,978	4.52

* In FY 1993-1995, NCI had a large increase due to the ASSIST Program and the Anti-Smoking Behavioral Program

NOTE: NINDS figures were revised to reflect a definition change at that Institute.

the next millennium, describing the current range of health and behavior research within each Institute, Center and Division (ICD), and setting forth new research directions for the field on an ICD by ICD basis.

Before describing the current portfolio and directions for behavioral medicine research at the NIH, it is important to recognize that our ability to "count" the amount of research that has been ongoing has been severely hampered. Until the NIH Health and Behavior Coordinating Committee developed its operational definition of behavioral medicine, no uniformity of definition existed across the NIH ICDs. The result has been that reporting of expenditures for such studies has been idiosyncratic and not readily translatable from Institute to Institute. The new operational definition of biobehavioral medicine, as described earlier, will help the NIH achieve greater uniformity in reporting.

Notwithstanding these problems of counting and labeling behavioral medicine research, today, each of the ICDs support health and behavior research; many of the Institutes have behavioral medicine research branches. The research focuses on behavior influencing prevention and treatment, and on professional and public education. The current ongoing and future proposed health and behavior research activities of the various NIH ICDs are described briefly, in turn.

National Institute on Aging: The NIA is charged with the mandate to conduct and support biomedical, social and behavioral research and research training related to the aging process and the diseases and other special problems and needs of the aged. Clearly, social and behavioral factors play a key role in health and functioning as people age; they play an equal role in the prevention and treatment of disorders that manifest in aging. To that end, the NIA

supports research on health behaviors not linked to any specific disease or disability as well as on promoting behaviors related to preventing or coping with illnesses. High priority initiatives have been undertaken in the area of Alzheimer's disease (AD), focusing on behavioral techniques to manage the symptoms of AD, such as wandering and disruptive behaviors, and on ways to safeguard the physical and mental health of caregivers (interventions to lessen so-called caregiver burden). The search for means of safeguarding and prolonging independence in old age also include behavioral research, in such areas as improving and sustaining cognitive function, avoiding injuries (e.g., falls), promoting healthy diets and exercise, slowing the tendency toward frailty (e.g., osteoporosis), and enhancing self-care capacity. Over the course of the next few years, the NIA plans to continue to expand its research programs on the nature, determinants and consequences of health behaviors and lifestyles in the middle and later years of life.

National Institute on Alcohol Abuse and Alcoholism: The NIAAA supports research on the etiology, prevention and treatment of alcohol abuse and alcoholism. As such, it has a significant portfolio and interest in behavior and health, from investigation of risks for alcohol abuse among different population groups to the development and evaluation of mechanisms for prevention, intervention and treatment. Over the coming years, the Institute will continue to emphasize four particular areas either related directly to or touching on aspects of behavioral medicine: community-based prevention, treatment effectiveness, genetic susceptibility to alcoholism, and changing the environment of alcohol use as a preventive tool. In the quest for interventions to treat alcoholism, the NIAAA also will be looking at issues of compliance behaviors, whether to pharmacological regimens or to non-somatic interventions.

Studies seeking a genetic basis for alcoholism may provide mechanisms through which behavioral intervention may prevent the disorder in those predisposed to alcoholism. Finally, public health mechanisms, such as pricing, age restrictions and warning labels, are being evaluated as potentially valuable strategies through which the environment of alcohol use may be altered, leading to improved efforts to prevent the disorder.

National Institute of Allergy and Infectious Diseases: The control and prevention of allergic, infectious and immunologic disease is the foremost mission of the NIAID. Whether in AIDS, asthma, hospital acquired infection, STDs, hepatitis B, or other disease and disorder research under the Institute's purview, the NIAID has included specific language in its research announcements and initiatives to encourage study of: behavioral risk factors associated with disease acquisition, transmission, or progression; interventions to change risk-associated behaviors; measures of disease outcome that include quality-of-life indicators; and strategies to improve compliance behavior. In addition, the Institute has sought mechanisms through which the behavioral factors leading to high drop-out rates in clinical trials may be mediated or eliminated, thereby helping to safeguard the quality, reliability and validity of study findings. With an adequate funding base, the NIAID has indicated its desire to broaden its behavioral research initiatives on HIV and STDs by encouraging research to increase health-seeking behaviors associated with early diagnosis and compliance with treatment, and to alter risk-associated behavior.

National Institute of Arthritis and Musculoskeletal and Skin Diseases: The NIAMS supports research in behavioral medicine in a variety of areas of interest, grouped, as is the case with most of the NIH Institutes, around

specific diseases or disorders. With about \$6.3 million in health and behavior research—one of the NIH's smaller portfolios, the Institute has some important areas of emphasis, including behavioral factors (diet, alcohol, exercise) associated with osteoporosis, Lyme disease, sports injuries, pain management, and sun-induced damage. In some cases where identifiable behavioral risk factors play a major role, the Institute supports research into effective means of reducing the risk factors for these disorders. Thus, for example, the NIAMS supports research into the efficacy of exercise and diet in increasing peak bone mass to counteract the later effects of osteoporosis; has undertaken educational efforts regarding the potential damages to the skin from too much sun; and has developed strategies to prevent exposure to ticks responsible for Lyme disease. In other cases, such as the Institute's involvement in research on lupus and rheumatoid arthritis, the emphasis of behavioral interventions is on patient assistance, including the reduction of health-impairing lifestyles that may complicate such conditions. Other areas of interest include the behavioral and neuropsychiatric manifestations of autoimmune disorders and psychosocial issues related to these illnesses.

National Cancer Institute: Research over the decades has amply demonstrated that only a small percentage of the cancers that affect Americans are a product of genetic factors that are not now preventable. Rather, lifestyle factors—tobacco and alcohol use, diet, environmental hazards including excessive exposure to sunlight, sexual behavior, and failure to use available screening and diagnostic tools now available—are significant causal factors in and preventable behaviors leading to the development of cancer in all U.S. population groups. The NCI has dedicated a significant portion of its portfolio to initiatives in this area and to

biobehavioral aspects of cancer treatment. Through a broad range of traditional research support mechanisms, the NCI supports research targeting prevention initiatives through behavioral interventions in breast cancer (screening, relationship to other lifestyle activities such as alcohol ingestion and smoking), lung cancer (reducing and, ultimately eliminating tobacco use), colorectal cancer (issues of diet and screening), cervical cancer (early sexual activity, multiple sex partners, use of screening procedures), skin cancer (excessive exposure to UV radiation, self-examination), and AIDS-related cancers. The Institute also focuses substantial research on issues of screening and detection, behaviors that are influenced through education. Moreover, issues of the quality-of-life for cancer patients are another important behavioral focus, ranging from questions of adherence and compliance to treatment regimens to psychosocial issues arising for cancer patients, to overall patient education. Additionally, the evaluation of psychosocial interventions, such as support groups, in the treatment of cancer is being explored. Over the next few years, the NCI will continue to emphasize behavioral research to learn more about the causes of cancer, barriers and access to care, on behavior change as a preventive tool, on adherence/compliance issues, and on adjunctive psychosocial treatment interventions.

National Institute of Child Health and Human Development: Like the NIA, the NICHD does not take a disease-specific approach to research. Rather, its research focuses on childhood health and mortality, nutrition, women's health, and on reproductive health and well-being. A wide range of research areas in behavioral medicine are supported, some looking at behavioral effects on maternal health, others at child and adolescent well-being. Among the initiatives being undertaken by the Institute in the area of

behavioral medicine are investigations of the linkage between behavioral and biological factors in successful reproduction. This also includes questions of adherence and compliance to health-promoting behaviors during pregnancy. Corollary to these studies are investigations designed to promote healthy lifestyles and behaviors in children and adolescents, including the identification of risk factors for eating disorders, behavioral issues in the use of anabolic steroids, and methods to reduce risk-taking behaviors, such as early sexual activity, and injurious behavior. The NICHD has a particular interest in many of these issues as they relate to minority populations.

National Institute on Deafness and other Communication Disorders: Communication disorders—predominantly deafness—may be of genetic etiology, may arise as the product of disease, or may occur as the result of environmental insults that often are controllable. The NIDCD's behavioral research portfolio places greatest emphasis on this last category. Noise—whether a rock concert attended by teens, or the use of "play" musical instruments by toddlers or just a product of the accumulation of exposure over the course of years—can induce hearing loss. A behavioral intervention, exposure to conditioning noise, may help make the auditory system more resistant to the effects of loud noise. At the same time, education about hearing loss and hearing conservation, through prevention research, has been initiated as another means of combating this problem. Similarly, research regarding the health consequences of exposure to noise pollution has suggested a number of behavioral interventions targeted toward prevention. Another aspect of NIDCD's behavior research portfolio is focusing on early detection and treatment of hearing impairment, childhood language impairment, and sensory disorders. The behavioral implica

tions of undiagnosed disorders of these types are profound; behavioral interventions to help those with such disorders are being sought.

National Institute of Dental Research: Dental research over the past two decades has focused on prevention-related research and information dissemination to the public and to dental professionals. As a testament to its success, oral health, particularly that of children and adolescents has improved markedly. Nonetheless, other populations continue to show high levels of disease. To that end, the NIDR is expanding its research portfolio in an effort to identify behavioral predictors of oral disease and enhance disease-prevention strategies.

National Institute of Diabetes and Digestive and Kidney Diseases: While diabetes has not found to be caused solely by behavioral factors, certain health-related behaviors may make its inception more or less likely and its course more or less severe. The NIDDK is supporting research to evaluate significant behavior-related aspects of diabetes, among them obesity, the role of diet and exercise, related depression, and compliance with treatment. The Institute also is investigating metabolic aspects of osteoporosis, most notably strategies to ensure sufficient dietary calcium is ingested at all stages of life. Yet other areas of behavioral medicine research are in approaches to the treatment of renal disease, including questions of diet and, perhaps most important, quality-of-life, in both chronic and end-stage renal disease, and on the psychosocial and psychophysiologic aspects of colon disease, including irritable bowel syndrome.

National Institute on Drug Abuse: The NIDA maintains a significant and diverse prevention and epidemiology research program targeted toward the elimination of substance abuse. Not surprisingly, the five key focal areas of investigation are (1) risk factor research; (2) interven-

tion research; (3) clinical epidemiological research; (4) research on the consequences of use and abuse; and (5) public and professional education. Risk factor research is seeking to identify causal patterns and factors leading to drug abuse, including the progression from initiation of use through dependency. Clearly, behavioral factors—peer pressure, availability, membership in high-risk subpopulations—affect initiation of drug use, but research is needed to ascertain how to prevent such behaviors from being initiated. Intervention research seeks to identify specific preventive practices and programs for populations at risk; clinical epidemiological research will ascertain whether such interventions are able to alter the risk of drug dependence in larger populations of at-risk persons.

National Institute of Environmental Health Sciences: The NIEHS conducts and supports studies to prevent and control environmental illnesses (such as result from lead poisoning and exposure to environmental toxins) and to evaluate the role of environmental exposure in the development of other illnesses such as cancer and reproductive disorders. While the vast majority of the research is at the basic and clinical levels, some behavioral research is ongoing at the Institute. For example, the NIEHS was focal in the deployment of a nationwide campaign to screen for and to prevent lead poisoning in young children. Ongoing research is intended to develop strategies for prevention and counseling of high-risk groups, such as pregnant women, newborns and infants, and inner city minority populations. Other critical behavioral research is related to both individual and societal risk factors for toxic poisoning in high-risk populations, such as migrant workers, minority and low-income groups, women of childbearing age, infants, children, and the elderly. Such investigations include the placement of hazardous waste sites,

prevention strategies for persons working in hazardous waste management or in industries that use high concentrations of toxic chemicals (e.g., migrant workers, chemical and pharmaceutical manufacturers, among others.) With a better understanding of the risk factors, educational interventions to prevent or reduce exposure can be developed.

National Eye Institute: The NEI's focus is on the prevention, diagnosis, and treatment of diseases that affect vision. Many of its research projects attempt to identify lifestyle and behavioral risk factors, assess intervention strategies to prevent eye disease, or improve patient eye care or compliance with medication regimens. Among those behaviors being investigated are diet and nutrition, smoking, ultraviolet light exposure, hygiene, early detection, and compliance with rehabilitation. Prevention, as a first line of defense, targets education about diabetic eye disease, about lifestyle-related causes of cataracts (e.g., smoking, drugs UV radiation, diet), and about screening to prevent amblyopia. When vision becomes impaired, compliance strategies are needed to help assure behaviors work toward the goals of vision therapy. Finally, rehabilitation research includes the identification of motivational, social, and economic determinants to encourage successful rehabilitation for those who have lost sight or retain only partial sight.

National Heart, Lung and Blood Institute: Historically, the NHLBI has taken a leadership role in the conduct of behavioral medicine research at the NIH; indeed, it was the first Institute to establish a Behavioral Medicine Research Branch to examine these issues. Cardiopulmonary and hematological research form the focus of the NHLBI, with substantial behavioral research turned toward the risk factors functioning in coronary heart disease, cardiovascular disease, asthma, stroke, myocar-

dial infarction, hypertension, and other disorders of the cardiac, pulmonary, and hematological systems. Lifestyle factors, not surprisingly, are being studied extensively: smoking, exercise, stress, diet, among others, with an eye not only toward behavior change in those who have already been diagnosed with cardiac or pulmonary disease, but also toward primary prevention. The NHLBI has supported research related to the role of behavioral factors in triggering and surviving myocardial infarction, among others. Further, a vast amount of the educational literature on heart and pulmonary disease that has been developed for consumer and health care provider alike has been the product of the NHLBI working in collaboration with organizations in the private sector. Another example of such educational activity that is now ongoing is in the area of asthma. Building upon an increasingly successful educational campaign targeted toward childhood asthma, the NHLBI has begun to evaluate how best to enhance behavior-related lifestyle change in asthmatic adults. Through this research initiative, the NHLBI hopes to develop a campaign that will help alter behavioral factors affecting adult asthma such as smoking, avoidable allergens (e.g., pets) and inadequate attention to treatment regimens.

National Institute of Neurological Disorders and Stroke: The neurological and neuromuscular systems form the focus of the NINDS research portfolio and initiatives. The Institute supports a varied and wide-ranging set of programs directed toward gaining new understanding of the biological basis of behavior and on behavioral interventions in the treatment of neurological disorder. The NINDS is also supporting studies of cognitive processes, providing clues for the development of behavioral interventions designed to alter cognition. The NINDS is also exploring the role of behavioral factors in neurological disorders such as

stroke, epilepsy and narcolepsy, a sleep-related neurological disorder. The goal of behavioral research at this stage is to educate to the risk factors. For example, in the case of stroke, hypertension, diet, and stress are among the areas to be addressed in interventions to lower the incidence of stroke. Similarly, psychosocial interventions are being evaluated in neurological rehabilitation from stroke and brain tumor.

National Institute of Mental Health: The NIMH, perhaps more than any other Institute, places a major emphasis on behavioral medicine. Over 20% of the NIH's support of \$835.2 million for behavioral medicine research is from the NIMH portfolio. In contrast to the traditional NIH disease-specific orientation found in many of the Institutes, the NIMH fosters research on mechanisms, models, and issues of co-morbidity of physical and mental illness, and theory-driven intervention research that cross diseases. The NIMH also supports research on homeostatic behaviors and disorders, including cognitive behaviors, sleep, ingestive, and reproductive behavior. Specifically, the NIMH focuses investigation on: (1) genetic approaches to health damaging behaviors; (2) psychological and biobehavioral aspects of AIDS; (3) psychoneuroimmunology; (4) compliance-adherence to treatment regimens; (5) psychological and biobehavioral factors and mechanisms in physical illness; (6) co-morbidity of physical and mental disorders; (7) psychosocial treatment and prevention interventions for physical disorders; (8) development and testing of diagnostic assessment instruments; (9) consultation/liaison and health services research; and (10) risk-taking and health-damaging behaviors.

Each of the three research-related divisions of the NIMH supports some aspect of behavioral medicine research. The Division of Basic Brain and Behavioral Sciences supports research through the programs of the Personality and

Social Processes Research Branch, the Basic Behavioral and Cognitive Sciences Branch, and the Cognition and Behavioral Neurosciences Research Branch. The Division of Clinical Research's Child and Adolescent Disorders Research Branch and its Mood, Anxiety and Personality Disorders Research Branch both focus on behavioral research. Primary in this Division's portfolio of behavioral medicine research are studies looking at risk factors for and behavioral interventions in eating and sleep disorders, and the behavioral implications of comorbidities of mental and physical disorders.

The Division of Epidemiology and Services Research forms the primary focus for the NIMH's involvement in behavioral medicine research. Housed within that Division is the Basic Prevention and Behavioral Medicine Research Branch. The Branch supports research, research training and career development awards, sponsors workshops and conferences, supports research grants and contracts, and publishes information regarding research on a wide range of prevention and behavioral medicine topics.

National Institute for Nursing Research: Unique in its focus on a health discipline rather than on a body system or a segment of the human life span, the National Institute for Nursing Research supports a wide range of behavioral medicine research. With nearly 50% of its FY 1993 budget dedicated to health and behavior research, the NINR has sought to identify psychosocial risk factors associated with health and disease, looking particularly at the close interdependence of social, biological and behavioral mechanisms in the preservation of health or the development of illness. With its focus on nursing, the Institute has evaluated behavioral medicine from the perspective of the nursing intervention. NINR-supported research spans the full breadth of the definition of

Table 2

Major Area of Interest
Basic Prevention and
Behavioral Medicine
Research Branch
Division of Epidemiology and
Services Research
National Institute of Mental Health

- Nutrition, ingestive behaviors and eating disorders
 - Circadian rhythms, sleep and its disorders
 - Sexual and reproductive behavior
 - Biopsychosocial aspects of medical illness
 - Psychoneuroimmunology and health
 - Prevention and behavior change
 - Compliance/adherence to treatment regimens
 - Health-related practices and attitudes
-

behavioral research crafted by the Health and Behavior Coordinating Committee, encompassing biobehavioral mechanisms; identification and distribution of psychosocial risk and protective factors; development, maintenance, and change of health-related behaviors; behaviors resulting from a disease or treatment; and behavioral and social interventions to prevent and treat illness or to promote health. Thus, the NINR has supported research on successful pregnancy outcomes, addressing psychosocial risk factors that affect fetal development (e.g., smoking, substance abuse, diet) and behaviorally modulated aspects of neonatal development that may have an effect on growth and maturation, such as feeding and handling by the mother.

The NINR has sought to further research risk-factor related research throughout the life span, not merely during pregnancy. Indeed, because

nurses are among those in most direct contact with children and adolescents (both in physicians offices and at schools), research is ongoing to evaluate a full range of preventive interventions to promote healthy lifestyles, at the level of the individual, the social environment (including the school), and the wider community, crossing ethnic and racial groups with targeted messages. Messages include issues of high-risk sexual activity and AIDS, substance and alcohol abuse, smoking, and other risk-taking behaviors.

At the same time, the NINR focuses upon ways in which behavioral interventions by nurses may affect the prevention of disease, the maintenance of health and the rehabilitation from illness. The Institute has worked with other NIH Institutes to help improve the overall quality of life for those with chronic illness by studying ways to improve motivation, expectations, and to ensure adherence compliance behavior with treatment regimens. (Recent research, for example, has sought to help mediate the effects of chemotherapy-induced nausea on treatment compliance.) The research focuses not only on the individual with the chronic disorder (such as Alzheimer's disease, diabetes, ESRD, among others, but also on the nurse-patient relationship and the relationship between the patient and any informal caregivers (such as family). The NINR places emphasis not only on the patient, but also in the caregiver, supporting research on psychosocial aspects of caregiver burnout and stress.

NIH Office of Research on Women's Health: The Office of Research on Women's Health was established specifically to respond to a significant gap in biomedical and behavioral medicine research. For the most part, women have not been research subjects in studies of other than specified "women's disorders." As described in its mandate, the ORWH serves as

a focal point for women's health research at the NIH, setting and monitoring policy, promoting and directing research, and enhancing scientific career development. The Office works collaboratively with the NIH ICDs to bring women's health research to the mainstream of all extramural and intramural research conducted or supported by the NIH.

Following a ground-breaking report—*Opportunities for Research on Women's Health*—the ORWH identified 14 areas of research interest that currently suffer from significant gaps in knowledge applicable to women. Each has significant behavioral medicine components, ranging from preventive activities, through adherence-compliance questions for those already diagnosed with the particular diseases or disorders in question. Among the current areas of particular focus in the ORWH are depression, behavioral and cultural disease risks and interventions, alcohol and drug use and abuse, sexual behavior (including both reproductive health and STDs), abuse and violence, lung cancer, occupational disease and disability, and cardiovascular disease. The ORWH is specifically targeting both social and behavioral research in these areas. The goal is to help elucidate the social and psychological context within which women adopt behaviors and make decisions that put them at risk of disease or promote their health and well-being. In addition, the ORWH is working with the Office of Disease Prevention, Office of the Director, NIH, in the oversight and conduct of the Women's Health Initiative, described in greater detail below.

NIH Office of Minority Health: Part of the Office of the Director, NIH, the Office of Minority Health fosters research on diseases and conditions that are unique or that disproportionately affect ethnic and racial minority populations. Behavioral issues (e.g.,

diet, smoking, substance abuse), some of which may be culturally mediated, and other barriers, such as discrimination have caused minority populations to be at greater risk of morbidity and mortality from certain diseases. The Office works with each of the NIH ICDs to promote inclusion of minority populations in both biomedical and behavioral research studies and to foster the recruitment, retention, and promotion of minority investigators.

Office of Disease Prevention: The Office of Disease Prevention (ODP), within the Office of the Director of the NIH is responsible for advising the NIH Director regarding disease prevention, and providing overall guidance to the research Institutes on biomedical and behavioral research programs that seek to improve the Nation's health through research, research training, and the exchange of knowledge as these activities relate to disease prevention. To that end, the Office coordinates and facilitates the systematic identification of research activities pertinent to disease prevention, including identification of behavioral and environmental risk factors for disease and the identification of behavioral interventions. The Office further encourages adoption of behavior change as warranted to prevent disease. Working with the ICDs of the NIH, the Office helps establish grant announcements that will enhance disease prevention, including behavioral intervention design, assessment, and implementation. This coordinative function also includes the role of linking the disease prevention and health promotion activities across the larger DHHS and the job of monitoring the effectiveness and progress of disease prevention and health promotion activities across the NIH. The Office further has the responsibility of undertaking the 10 year implementation plan for health and behavior as mandated by Congress, and shares responsibility with the Office of Research on Women's Health, NIH, for the coordination and

oversight of the Women's health Initiative (described below).

Women's Health Initiative: Coordinated by both the Office of Disease Prevention and the Office of Research on Women's Health, Office of the Director, NIH, the Women's Health Initiative, announced in the spring of 1991, is the largest prevention study ever to be undertaken in the United States. Each of the three components of the Initiative has important behavioral components as it examines methodologies to reduce the risks of cardiovascular disease, breast and colorectal cancer, and osteoporosis in postmenopausal women. The first component—a clinical trial—will examine a variety of approaches to reducing the risk of these diseases, including attention to such behavioral factors as smoking, inattention to screening opportunities, absence of exercise, and inadequate or inappropriate diet. The second aspect—an observational study—is designed to determine both biological markers and predictors (including behavioral predictors) for disease. A community prevention study, the final component, will test preventive strategies—including various behavior change methodologies—to achieve the adoption of healthful behaviors. This major undertaking provides the opportunity for the integration of biomedical and behavioral medicine research across a wide spectrum of disease and behavior.

The Future of Behavioral Medicine Research

The NIH Health and Behavior Coordinating Committee has sponsored this national working conference on new Frontiers in Behavioral Medicine. The report that will be produced from this conference is intended to chart a course for behavioral medicine into the 21st

century. But how do we foster growth of the NIH behavioral medicine research programs? The answer lies in a coordinated and collaborative effort that emphasizes not just research of excellence, but researchers of excellence as well.

What is key, now, is the development of an NIH Strategic Plan in Health and Behavior that will articulate the mechanisms through which NIH behavioral and social science research may be better coordinated across ICDs. With such a plan in place, we must develop the mechanisms to better coordinate overall NIH Behavioral Medicine Research. Our new definition marks a start in that direction; and improved computerized tracking system for awards made in behavioral medicine would also help. Establishment of trans-NIH work groups on health and behavior topics that crosscut ICDs is yet another possible mechanism. This greater degree of coordination, in turn, can and should lead to growing collaborations across NIH ICDs, increasing the number of collaborative program announcements and RFAs, heightening interest and involvement of the NIH Intramural research laboratories, and, ultimately advancing science in this field across the NIH. The institution of an overarching PHS Interagency Health and Behavior Coordinating Committee would broaden the scope of involvement in behavioral medicine to other PHS agencies beyond the NIH.

Beyond NIH, however, additional work needs to be done to enhance and strengthen the field. A host of issues related directly to research need to be resolved. Many disorders are a product of multiple contributory factors, among them, behavioral factors. Indeed, many behaviors (whether protective or damaging) themselves are multifactorial in nature. This interface of biology and behavior is a focal area ripe for investigation; and that investigation requires

a multidisciplinary approach that crosscuts basic, clinical, social, and psychological aspects of research. Longitudinal and prospective studies also are called for.

Even before these exciting new areas of behavioral medicine research can be plumbed, a wide range of methodological issues must be addressed. For example, reliable, valid and, perhaps most important, standardized research measures—particularly, but not solely in the area of health quality-of-life—must be developed to enable research to be replicated. Only through consensus on research measures and diagnostic instruments can comparisons of data be made across institutions and across research activities. Only through the development of solid measures can we be certain that the research findings we disclose are robust enough to lead to clinical application. Moreover, we must determine how case control studies in behavioral medicine are to be undertaken, clarifying methods through which confounding variables in the area of behavior may be controlled without "contaminating" the test or control groups. One mechanism through which much may be gained is by identifying, evaluating and, if appropriate, applying strategies and methods that have been tried and found successful in other areas of investigation.

With collaboration in place, with instruments and methodologies that are solid in their reliability and validity, the field will be ripe for sizable growth and exploration. To that end, we must be able to deploy significant resources, predominantly research resources. I am speaking not only about standard investigator-initiated research awards. Rather I am speaking about the development of program projects, collaborative multi-site research programs, and research centers of excellence in behavioral medicine research.

Yet even research centers of excellence, program projects and collaborative multi-site research programs fail in the absence of investigators to populate them, to conduct the growing body of research that advance the field and that will contribute to the font of clinical knowledge drawn upon by the clinician in day-to-day work with patients.. We must begin to develop and support a growing, cadre of young investigators in the field. Using already proven building blocks—summer institutes, FIRST awards, intramural and extramural research training fellowships, among others—a growing number of investigators will be drawn to the field. Some will move from other fields of investigation; others will come to the behavioral medicine research field as new young investigators.

By providing the role-models, the training, and the incentive of a flourishing research field, the next generation of researchers will be well-prepared to meet the challenge of science. The importance of behavioral medicine research cannot be denied, from its role in the etiology of disease through its ability to aid or hinder clinical treatment regimens.

I have provided but a few suggestions about research needs and directions for the field of behavioral medicine research, mostly related to the activities of the NIH in forwarding the field. I look forward to hearing the thoughts and ideas that are being set forth in this Conference. Our work here and our recommendations will form the cornerstone of our field's future directions.

Conclusion

Our Nation's investment in biomedical and behavioral research has already yielded benefits for every American citizen. Research, above all, is an investment in the future. By investing today in research to improve the health of those

who will play an increasingly important role in our society tomorrow, we secure the health of our Nation's economic and social fabric in the 21st century.

Research on health and behavior, the study of interactions of biological, behavioral, environmental factors in health and disease and behavioral and psychosocial interventions to prevent and treat illness and to promote good health is a critical part of our national health care agenda.

In conclusion, let me invoke President Franklin D. Roosevelt's words from 1940—"we cannot be a strong Nation economically unless we are a healthy Nation." Roosevelt's definition of domestic national security is as relevant today as it was then. Essential to this effort to improve the health of all of our citizens, is the development and implementation of a comprehensive behavioral medicine research agenda. Our work together over the next three days is an important step toward this goal.

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DISEASE PROCESSES

Behavioral, Biological, and Environmental Interactions in Disease Processes

Andrew Baum, Ph.D.

Investigation of psychological influences in disease processes has been a cornerstone of behavioral medicine since its inception. The notion that biological, behavioral, and environmental factors interact to shape the pathogenesis of modern disease has proven useful in understanding and treating heart disease, cancer, HIV disease, and a variety of other medical problems. Behavioral factors have emerged as key mediators of pathogenesis and even a cursory review of the evidence suggests that behavior, by itself or as it interacts with biological processes and environmental variables, is a major determinant of health and disease. This paper highlights important research accomplishments in these areas to stimulate consideration of promising areas for future research.

These interactions include genetic factors/predispositions, subject variables (including age, gender, socioeconomic status, race, developmental stage, and personality), social factors such as social support, environmental factors (e.g., chemical/toxic exposures, sanitation, health care availability) and biological factors

related to both genetic and environmental influences. The confluence of these variables represents a number of complex processes, one of which is stress. Because stress has been considered to be a primary mediator by which environmental and social events are translated into psychological and biological changes likely to affect disease processes, stress will be used as an example of these interactions.

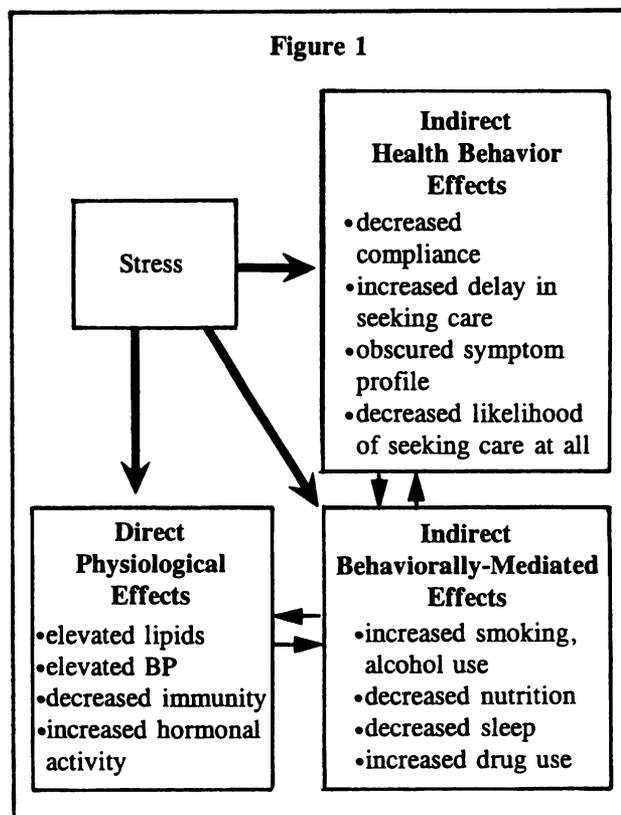
Stress is best thought of as an affective state characterized by psychological arousal and by threat perception or recognition of environmental demand. Some have described stress as a process, unfolding as a stressor is recognized and appraised, distress and arousal increase, and attempts to cope are applied to the situation (e.g., Lazarus & Folkman, 1984). As such, the evaluation of an environmental event or other stimulus as being stressful initiates a series of cognitive, emotional, and biological changes that both motivate and prepare the individual to respond effectively (e.g., Baum, Cohen, & Hall, 1993). It is most likely as a direct or indirect result of these changes that disease processes

are affected; the study of these interactions has occupied a considerable amount of attention in behavioral medicine.

The role of stress and other biopsychosocial phenomena in disease processes may be examined by considering any number of illnesses, but for this paper, heart disease, cancer, and HIV disease will be used as illustrations. As three major diseases in the U.S., they accounted for nearly one million deaths in 1989 (NCHS, 1992). They are all chronic diseases and include several forms of pathogenesis and dysfunction. They all also have sufficiently different causes and courses of progression that they provide a broad selection of disease processes that might be affected by behavioral variables.

Stress and Health

As depicted in figure 1, stress appears to affect health in three basic ways (Krantz, Grunberg, & Baum, 1985). First, stress can cause physiological and biochemical changes that directly influence pathogenesis or alter physiological equilibrium. Increases in blood pressure and endocrine status, as well as increases in lipid levels, damage to blood vessel walls, alteration in platelet function, and a variety of other physiological changes are associated with stress and have been linked to the development of heart disease and hypertension (e.g., Krantz, *et al.* 1985; Krantz & Manuck, 1984; Patterson *et al.*, 1994; Schneiderman, 1983). Stress-linked changes in immune function and changes in susceptibility to illness have been identified and linked to viral infection (e.g., Cohen & Williamson, 1991), and some have described stress as a contributor to the initiation and progression of cancer and HIV disease (e.g., Baum & Temoshok, 1990; Kiecolt-Glaser *et al.*, 1985; Sklar & Anisman, 1981).



A second pathway by which stress affects health is through behavioral changes that affect physiological systems in ways that change disease vulnerability. One of the best examples of this is smoking, which has effects on bodily systems that contribute to cancer and heart disease. Stress appears to increase health-impairing behaviors such as smoking and drug use, and decrease health-protective behaviors such as good diet, exercise, and sleep (e.g., Cella, Mahon, & Donovan, 1990; Epstein & Perkins, 1988; Grunberg & Baum, 1985). In addition, stress may affect behavior when one is already ill. Stress and anxiety from treatment procedures alone may affect disease processes (e.g., Andersen, Karlsson, Anderson, & Tewfik, 1984) and, by delaying help-seeking, increasing relapse from smoking or drug use cessation, interfering with compliance with medical regimens, and/or obscuring or masking symptoms

or otherwise making accurate diagnoses difficult stress may contribute to disease progression. Such effects on health behaviors represent a third way in which stress may contribute to the development of disease.

Stress and Disease Processes

Disease processes are often complicated and highly variable, but can be understood in two or three major stages. Pathogenesis begins with an event or events that initiate the development of a particular disease. For heart disease, such an initiating event might be original vascular injury or plaque formation in the coronary arteries, while for cancer it might be a mutation or stimulation of protooncogenes, and for HIV disease it would be initial infection by the disease-causing virus. Following this, progression of the disease may be characterized broadly as a single stage or as a variable sequence of stages culminating in end-stage disease. In heart disease and cancer, the progression of coronary artery occlusion or tumor growth appears to vary considerably, and end-stage disease is probably not as readily identifiable as is AIDS, the final stage of HIV disease.

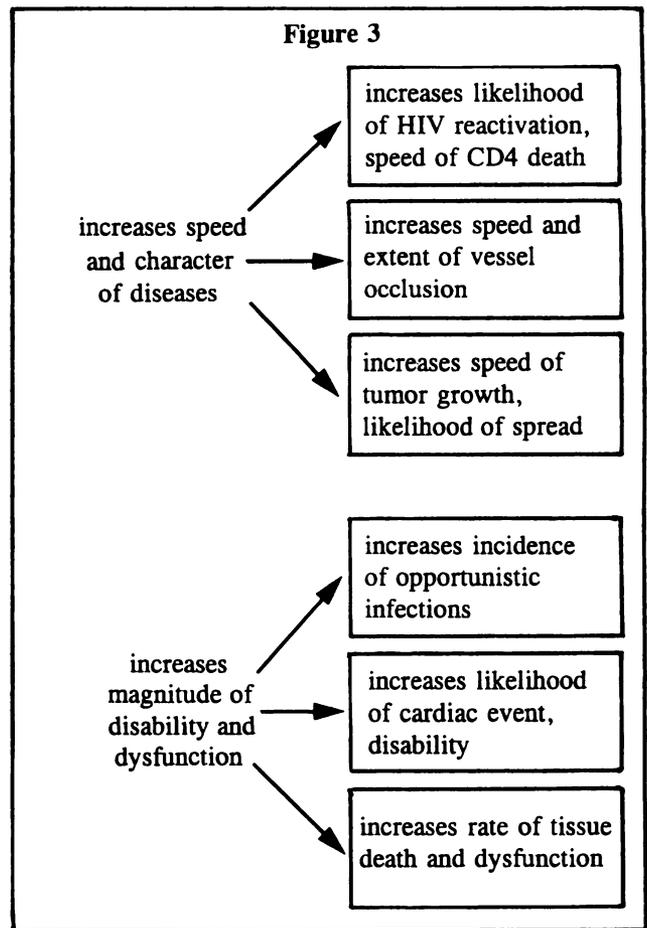
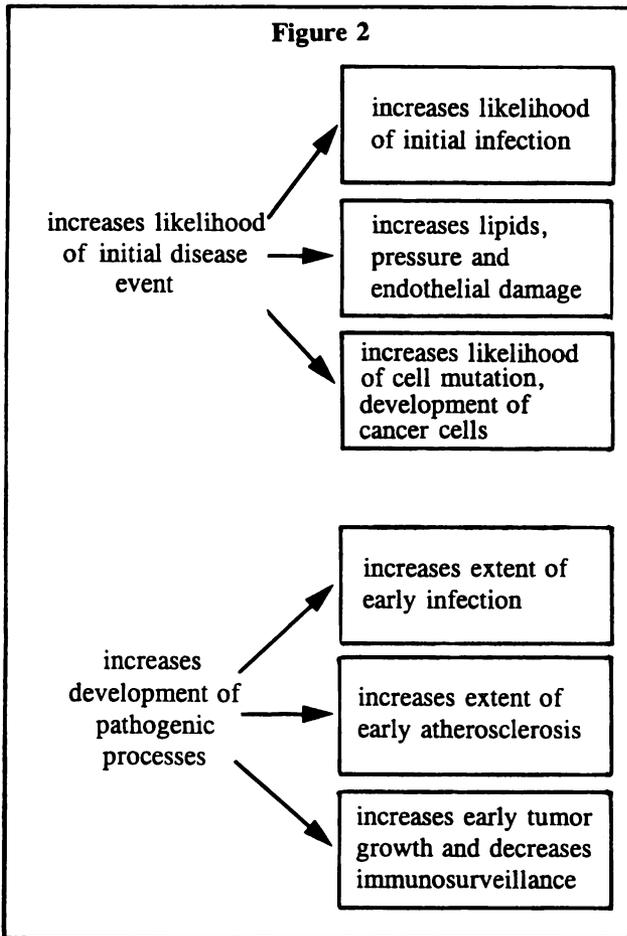
This same general framework can be used for any illness, including colds and upper respiratory infections. Initial exposure to the causing virus may be followed by infection and the course of the illness, with increasing and waning symptoms. Unlike these minor illnesses, CHD, cancer, and HIV disease ordinarily do not show any tendency to abate and, without major medical intervention, are typically lethal.

As variable and complex as these disease processes are, it is not surprising to find a relationship between biobehavioral variables such as stress and disease progression. Stress

is an influential player in events leading up to and including myocardial infarction and sudden death (e.g., Schneiderman, 1983; Krantz *et al.*, 1993). This occurs in at least two basic ways. Stress can affect the development of atherosclerosis; behaviors such as diet, drug and alcohol use, exercise, compliance with prevention or treatment regimens, and smoking affect the course and outcomes of heart disease (e.g., Krantz *et al.*, 1985). Similarly, stress appears to have immunosuppressive effects that could reduce immunosurveillance and decrease the likelihood that tumors or irregular cells would be detected and eliminated.

Stress also may affect immune status and immunosurveillance through behavioral changes such as increased drug use, poor sleep, lack of exercise, or dietary changes. Finally, stress could affect the likelihood of HIV infection, by increasing drug use, interfering with intentions to minimize risks posed by unprotected sex or multiple partners, and by decreasing adherence to protective advice.

There is now sufficient evidence to support many of these implicit and explicit mechanisms by which stress may affect disease processes. However, systematized investigation of biobehavioral interactions has not yet specified all of these links or even provided unequivocal evidence of some of the more basic connections between stress and illness. A number of important questions remain, including those that are specific to each illness or group of illnesses and also cross-cutting issues reflecting the similarity of mechanisms underlying stress effects. For each of a series of basic questions, one can formulate a variety of research questions and investigations. One can study the effects of stress and behavioral variables on the likelihood of initial disease events, on early development of pathogenic processes and bodily resistance to



pathology, on increases in the speed of progression of the disease or in the magnitude of its symptoms, or on increases in the magnitude of disability and dysfunction or in death. At each of these points, important questions and issues concerning mechanisms and environmental mediation can be identified.

Levels of Influence

Of the many questions that can be addressed, some apply to different points in the disease process. The effect of stress can be examined or conceptualized at almost any point beginning with the likelihood of initial disease events. It is fairly clear now that stress is related to disease at some level, but the many different

ways in which stress affects disease development and progression are not well understood. Consequently, the possibility that stress and behavioral variables are among several interacting causes of disease, has not been fully and systematically analyzed. In part this is due to the inherent difficulties in studying initial events or causes of diseases that may develop over years or decades and are hard to detect for many years. The selection of a single initiating event may often be arbitrary and may reflect a consequence of an earlier event. For HIV disease, detection of infection is more readily available for study than are initial events in cancer and heart disease, and examination of behavioral influence on initial infection is relatively more developed. However, potentially important questions about etiological mecha-

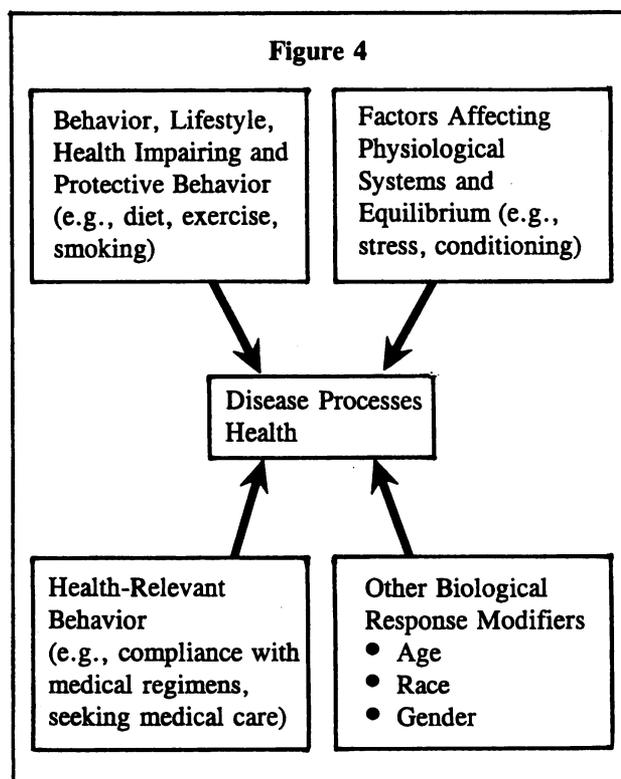
nisms and application to disease prevention can be asked about all of these diseases.

The kinds of research issues that emerge are depicted in Figure 2. Initial events, including selective rejection of HIV upon exposure, ways in which stress reduces likelihood of detection can be examined in cases of HIV disease, while the relationship of stress to genetic and growth factor changes and subsequent cell mutation or irregular growth emerge from research on cancer. Behavioral factors, including diet and exercise, should be exemplified by questions about stress and endothelial damage that could lead to coronary heart disease (modified, one would expect, by diet, smoking, exercise, hostility, and a number of other variables).

Stress and behavioral influences may also be important determinants of early disease progression once infection or damage has been accomplished. The early course of HIV disease, (e.g., how quickly it becomes latent; intensity of symptoms, extent of early viral replication) is variable and stress could be involved in these manifestations of disease. For cancer, the extent to which stress or behavioral variables affect early tumor growth, tumor resistance to bodily surveillance, strength and efficacy of surveillance, and the mechanisms underlying these links are relevant, reasonable questions. While research on heart disease has established a number of mechanisms by which stress and behavior affect early heart disease, more remains to be learned about influences on early atherosclerosis, changes in blood pressure, and factors such as lipid and platelet levels.

The extent to which stress or behavior affects the speed and character of disease and whether (and how) these processes influence the magnitude of dysfunction, disability, and death are also of interest. Findings from studies of HIV

disease have not provided much evidence of behavioral influences on the rate of progression of the disease, but possible effects on latency and viral reactivation and on cognitive and mental health outcomes of the disease are important.



The course of cancer is affected by a number of variables and it can become more benign or more threatening during its progression. Tumor growth and metastasis appear to be sensitive to stress and psychological variables such as control, as noted in animal studies. Reoccurrence and spread of the disease have been linked to stress, stressful life changes, symptom distress, and immune changes occurring as a result of stress (e.g., Levy *et al.*, 1985; Levy *et al.*, 1991; Munkres *et al.*, 1992; Ramirez *et al.*, 1989). Coping variables have also been tied to progression of cancer (Dean & Surtees, 1989).

In heart disease, stress and behavioral influences also have effects on the later stages of disease development. Even after atherosclerotic lesions have become established, stress, diet, drug use, and similar health-related behaviors continue to affect the rate and degree of vessel occlusion. At this stage of disease one is often receiving treatment; compliance with treatment regimen also emerges as an important determinant of disease course.

The effects of biobehavioral processes on the final stages of these chronic illnesses are also important, though the degrees of freedom available for intervention may be fewer due to the overwhelmingly predominant effects of the established pathology. A patient with AIDS, for example, may continue to lead a reasonably normal life much of the time and may survive with AIDS for many years, but the likelihood of successful intervention to affect disease course at this stage may be diminished by the advanced stage of pathogenesis. Regardless, a variety of important issues derive from this level of analysis. The length of time patients survive and their quality of life are the most important outcomes, but the latter variable has yet to be fully integrated into research and treatment of chronic, life threatening illnesses.

The course of HIV disease in end-stage AIDS is focused largely on the patient's resistance to opportunistic infections that may prove fatal because of the immunocompromise generated by the disease. The likelihood that one is exposed to, develops, and/or resists such infections may be related to a number of variables, including stress and compliance. Disability, psychiatric and intellectual sequelae, and quality of life are likely to vary as a function of biobehavioral variables as well.

Survival among cancer patients has been associated with stressful life changes, expressive

activities and emotion, and coping (Funch & Mettlin, 1982; Hislop *et al.*, 1987; Greer *et al.*, 1979; and Pettingale *et al.*, 1985). Further study of the interactions of biobehavioral and environmental variables as they affect quality of life, disability, organ dysfunction, and other aspects of cancer survival or death is important.

Similarly, a range of coronary events, from angina and silent ischemia to myocardial infarction and sudden death appears to be linked to stress and behavioral variables (Falkner & Ragonesi, 1986; Krantz *et al.*, 1988; Kamarck & Jennings, 1991). Rehabilitation, quality of life after one has experienced a coronary event or life threatening dysfunction, recovery or relapse, and a variety of other outcomes associated with heart disease or other cardiovascular diseases need to be better understood. Systematic investigation of these issues will not simply provide more information about "mind-body" interactions and about how the body or disease work; it will provide critical information for prevention and treatment of disease by providing a more detailed and complete picture of how these diseases start and how they progress.

Gender, Minority Status and Developmental Stage

One of the underlying themes of the conference is the applicability or extension of this research to women and minorities and the need to consider gender, minority status, and age in studies or evaluations of the causes and course of disease. At a very superficial level, these variables influence prevalence of certain diseases within subpopulations, e.g., men do not develop cervical cancer or ovarian cancer for obvious reasons, and for the same reasons, women do not develop prostate cancer. Sickle cell anemia principally affects African-Americans, and other illnesses appear to be restricted

to specific ethnic or racial groups. However, these basic differences in genetic or physiological make up do not readily explain why African-American men are more likely to die of heart disease or cancer than white men, why women do not show comparable vulnerability to heart disease as compared to men, or why African-Americans and Hispanics are disproportionately represented in cases of HIV disease and AIDS.

Such differences are more likely related to differences in environment, including stress experience or responsiveness, limited resources and access to health care, and the interaction of these and other behavioral factors for which race and gender may be surrogates. Anderson (1993) has suggested that the environments in which minorities in the U.S. are likely to live are inherently more stressful and toxic than are those in which others live. With fewer resources, a greater likelihood of living in high crime areas or poor areas, discrimination, and frequently poorer job status, it should come as no surprise that health problems in these populations may be more prevalent and more severe.

This same logic can be applied to gender and age-related differences in stress and disease. Are differences in rates, types, or age of onset of heart disease between men and women genetically determined? Are they a function of biological differences between men and women, or are they due to interactions of these variables with stress, socialized patterns of coping and use of social support, and a range of other biobehavioral variables? The growing literature on gender and stress suggests that there are a number of differences and complicating factors involved in this interaction (e.g., Baum & Grunberg, 1991; Polefrone & Manuck, 1987; Saab *et al.*, 1989; Stoney *et al.*, 1987). Answers to questions about differential vulnerability to illnesses such as autoimmune diseases

will also provide guidance on important issues in treatment and prevention.

Age and developmental stage are also important because little consideration has traditionally been paid to age differences or maturational influences on stress and disease processes. We know relatively little about stress among children, the unique interactions of stress and the pressures of adolescence, or the relationship between stress and aging. The fact that different ages, minorities, or gender are over- or underrepresented in diseases for which there are no readily available reasons for selective vulnerability suggest that Anderson's (1993) analysis is pertinent to these issues. That is not to say that these differences are all due to chronic stress. Rather, it is suggested that the *experience* of being a minority group member or being young or old or being male or female in our society is critical in understanding the differential rates of illnesses that we have observed. Often in research we control variables such as socioeconomic status and gender in order to explain the effects of one or another variable of interest. By doing so, however, we remove part of what it means to be poor or a man or woman and, consequently, lose some of our ability to predict processes or outcomes affecting health status. Understanding the psychological relevance or impact of poverty, gender, age, or minority status is an important goal in itself as well as a critical factor in understanding disease processes and biobehavioral influences on health.

Conclusions

The approach advocated here involves a complex model of disease processes that includes traditional, behavioral and biologically oriented risk factors, but focuses particular attention on environmental-behavioral-biological **interac-**

tions (see Figure 3). For example, by viewing heart disease in terms of biobehavioral processes that contribute to death and disability, by viewing cancer and HIV disease as a function of stress, immunosurveillance, health impairing and protective behaviors, mood, age, gender, minority status, and other variables as well as viral activity or genetically-linked immune or molecular cell-based changes, we can better explain the outcomes of many of the major diseases of our time. This is not to deny the importance of biological factors that have traditionally been incorporated into models of disease, but rather to suggest that a more comprehensive approach which includes behavioral variables and biobehavioral interaction among all of these factors will provide a more useful model for understanding the complex issues associated with etiology, treatment and prevention of chronic disease.

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Prenatal/Infant/Child

Overview

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At no other time in the history of the biomedical and behavioral sciences has either the need been so great or the opportunities so promising for understanding the basic biological and behavioral processes of health and disease. The health and medical sciences have evolved to the point where it is recognized that no single gene, solitary bacteria, or environmental event can account for the onset and progression of a specific disease. The etiology of diseases now is most often attributed to a complex array of biological, behavioral, and environmental circumstances acting in a reciprocal fashion to cause a disease or affect its trajectory. The challenge, in the next decade, is to determine mechanisms whereby these biological, behavioral, and environmental processes act in concert to bring about health and disease.

The discussion of the task group on basic processes framed these challenges in initiatives that focused on the interaction of genetic propensities and the expression of these propensities in different types of environments. The emphasis in the initiatives is not on genotypes and phenotypes but on larger issues of development, health and disease. For instance, one initiative examines the earliest of environments affecting health and disease, that is, the quality of the prenatal environment (A-1-4). Although a fetus begins to develop with a certain genetic

endowment, the prenatal environment influences how genes are expressed. Healthy fetal development provides the foundation for all of subsequent development but there are few models for understanding the intricate interactions between development of the fetus and the health, life style, and behavior of the mother. Animal and human models for understand and improving fetal development are greatly needed.

Advances in molecular biology have enabled us to identify genes that are risks for specific diseases and to diagnose disease in the fetus (A-1-1). This new knowledge inevitably will lead to new stressors in families and the children so identified. Even in the presence of a known genetic defect, disease expression may vary with environmental circumstances that are subject to modification. The health care system has new responsibilities to help families and children deal with these stressors. Guidance is needed to design interventions to prevent disease expression and on how and when to tell children about their risk for developing a disease. There also is the need to determine how the disease risk affects cognitive and emotional development of the affected child.

Given that some children **will** develop chronic disease, we need to examine the interface between a normal developmental trajectory and

the onset and course of chronic diseases (A-1-2). Recent research indicates that both genetic and experiential/environmental factors interact to influence the onset and trajectory of childhood disease but there is minimal data on the etiology of many chronic diseases. Specifically lacking are data on the interaction of the individual developmental, familial, and environmental factors that precipitate the expression and influence the trajectory of chronic disorders in genetically predisposed children.

The impact on cognitive, behavioral, social, emotional and familial processes of disease and disability in childhood is in need of much further elaboration (A-1-3). Specifically, childhood diseases and disabilities have implications not only for the involved child, but for the family as well. At diagnosis, parents are often confronted with difficult decisions regarding medical interventions and even decisions regarding the balance between longevity and quality of life. The health of parents of children with chronic diseases is adversely affected as well. Finally, medical interventions may have long-term side effects on the cognitive, emotional, and social development of the affected child. Understanding the impact of childhood disease and disability on the child and family may improve the family's decision-making process, improve ability to cope, and reduce the co-morbidity with other physical and psychological disorders.

Implications for Research Strategies

The initiatives described by the Basic Processes Task Group mandates an interdisciplinary research approach. No one discipline possesses the collective wisdom to confront the challenges of combining genetic, behavioral, and environmental perspectives to develop testable theories and hypotheses regarding the onset and progression of both states of health and disease. Cross-institute collaboration is essential for solving these complex health problems.

Although not specifically stated in the initiatives, the importance of measuring biological substances as well as behavioral and environmental factors is understood. Indices of immune, endocrine, autonomic nervous system, hematological, genetic, and other biological processes are essential to incorporate into research designs that examine health-behavior interactions.

The Task Group initiatives strongly endorses a developmental perspective to disease processes. Developmental changes within children, their families, and their environment affect both the onset and progression of acute and chronic disorders. To explain the developmental processes involved, a longitudinal research perspective is essential.

Task Group Initiatives

✓ *Developing Behavioral Strategies to Cope with Genetic Risks and Modify Genetic Disease Expression (A-1-1)*

Need and Justification

Advances in genetic science have led to the need for behavioral research in related areas. The Human Genome Project will permit us to identify genes that are risks for specific diseases and to diagnose specific disease in the fetus. This knowledge will lead to new stressors for individuals affected. More families will be faced with caring for children who have genetic liabilities for disease. Even in the presence of a known genetic defect, disease expression may vary with environmental circumstances that are subject to modification. For example, when genetic markers for hyperlipidemia are present, lifetime dietary modifications may reduce clinical expression of the condition. It is important to help families deal with stressors unique to genetic diseases (e.g. guilt), and to develop behavioral interventions to reduce morbidity from these diseases. More guidance is needed with respect to when children are told about their condition, and how information provided to children should vary with developmental stages and/or cognitive abilities. Important research questions evolving from these issues include:

1. How can environmental variables, particularly those related to behavior, be addressed effectively in order to prevent

or reduce expression of a genetic defect? Examples of conditions for which this information is needed include diabetes, juvenile migraine, mental health disorders and hyperlipidemia.

2. How do families react to and cope with an identified genetic risk factor in a child? What are the best ways to help families cope? What are the effects of support groups on affected children and on their families? How do restrictions on diet and activities impact on children and on their families?
3. Given a child's awareness of an identified genetic disease, how does this impact on the child's neurocognitive development and behavior?

Research Approach/Methodology

These research questions require a multi-disciplinary approach involving experts in molecular and behavioral genetics, child development, and health care specialists in the specific disease/condition to be studied. A longitudinal design over a decade is a desired research approach. Research initiatives should be sensitive to ethnic, cross cultural, and gender issues.

✓ **Genesis and Trajectory of Childhood Disease and Disorders (A-1-2)**

Need and Justification

Recent estimates based on data from the National Health Interview Survey indicate that 31% of children in the United States are affected by a chronic disorder. Little is known, however, about the relation of a normal developmental trajectory to the onset and course of many of these disorders including asthma, migraine headaches, hyperactivity, childhood cancer, juvenile rheumatoid arthritis, insulin dependent diabetes, diabetes mellitus, attention deficit disorders, dyslexia and stuttering. Data indicate that both genetic and experiential/environmental factors interact to influence the onset and trajectory of these childhood disorders, but minimal data exist regarding etiology.

In the future, the monogenic disorders (single gene anomalies), including the muscular dystrophies and inborn errors of metabolism may be

amenable to genetic engineering and targeted gene therapy. In the multifactorial/polygenic disorders, however, the interaction with experiential/environmental precipitators is critical and not well understood. Lacking are data on the interaction of the individual developmental, familial, and environmental factors that precipitate the expression and influence the trajectory of chronic disorders in genetically predisposed children.

Research Approach/Methodology

Multidisciplinary, longitudinal studies, a combination of "Behavioral Framingham" and the "Manhattan Project," are needed to substantively address these health problems. Emphasis should focus on both interindividual and intra-individual differences in health, behavioral and developmental outcomes.

✓ **The Cognitive, Behavioral, Social, Emotional and Familial Impact of Disease and Disability in Childhood (A-1-3)**

Need and Justification

Childhood diseases and disabilities have implications not only for the involved child, but for the family as well. At diagnosis, parents are often confronted with a number of difficult decisions. If the child is severely compromised, the parents may need to first make decisions regarding the nature and extent of medical interventions. The disease process and its treatment may also affect the child's cognitive, behavioral, and social development. For example, some cancer treatments may be associated with CNS changes. Subtle neuropsychological effects have been documented in childhood diabetes, especially in youngsters diagnosed before five years.

For most chronic disorders, the decision-making process continues throughout the child's life. Decisions may surround difficult choices between potential longevity and quality of life. Both the seriousness and the repetitive nature of the decision-making process can present real and complex challenges for every member of the family. Further, for many chronic conditions, caregiving demands can tax psychological, financial, and social family resources. There is evidence that mothers of these children suffer more anxiety, depression and psychosomatic symptoms than mothers of healthy children. However, these effects have not been carefully evaluated. Further, the effects on siblings and fathers have received even less attention.

Although caring for a child with a chronic disease or disability can be stressful, it is also feasible that there are positive effects of these disease-induced close family relationships. For example, families may become better problem-solvers or siblings may have greater empathy as a consequence of living with a child who has a chronic condition. Understanding the impact of childhood disease and disabilities on the child and family may improve the family's decision-making process, may improve the child's and family's ability to cope with the condition successfully, and may reduce the child's and family's comorbidity with other physical and psychological disorders.

Research Approach/Methodology

Research methods should be sensitive to both the developmental stages of the child and the developmental stage of the disease. For example, disease/disability effects may be different depending upon the age of the child, and different stages in the disease (e.g., diagnosis, remission, relapse) can place different demands on child and family. Although some research tools exist to assess child and family psychosocial functioning, the development of new measurement tools and strategies is encouraged where no reliable and valid measures exist. In addition to the assessment of deficits and or dysfunction, measures of positive adaptation should be included.

✓ **Fetal Environment: Normative and Pathological Developmental Consequences (A-1-4)**

Need and Justification

Research on early development is usually focused upon the neonatal and infancy periods. However, recent advances have begun to clarify important aspects of the biobehavioral development of the fetus and the consequences of in-utero ontogenesis for post-natal behavior and physiology. The compelling nature of this research area has been brought into sharp focus because of the advances made by neonatologists to sustain premature babies at a development stage that would formerly have been untenable. Clearly a greater understanding of the natural processes of fetal maturation and the interaction between the fetus and the uterine environment is essential for appropriate medical delivery to the premature infant as well as to the normal, full-term child. There is also an important need for a greater understanding of the relationship between prenatal processes and postnatal processes that can have effects across the life span. Some examples of this research domain include fetal chronobiology and its relationship to SIDS, fetal learning, fetal sensory development, sexual differentiation and its subsequent effects on the later expression of gender differences, and the biobehavioral sequelae of in utero exposure to environmental toxicants. In addition, there is a continuing research need to refine the analysis of how the behavior, cognitive and affective state, and physiology of the pregnant woman impacts the health and well-being of her developing fetus and child.

Some recommended research goals include:

- ▶ Design of the appropriate environment for the premature infant that takes into account sensory factors (e.g., noise) and light/dark cycles for setting circadian patterns,
- ▶ Develop new technologies to help predict disease vulnerability in childhood from knowledge of fetal status,
- ▶ Identify fetal events that determine status of the neonate at birth,
- ▶ Examine effects of maternal age, race and ethnicity on prenatal care and subsequent child development,
- ▶ Design studies of the behavioral pharmacology of obstetric drugs in the fetus and neonate.

Research Approach/Methodology

- ▶ Establish inter-disciplinary research teams including physicians and other health-care providers, behavioral and biological scientists to study fetal psychobiological development.
- ▶ Undertake longitudinal studies that include demographic and environmental variables on fetal well-being prior to conception.

- ▶ Design normative studies of basic fetal physiology and behavior employing animal models and, where possible, studies of developing humans.
- ▶ Undertake research to develop new and reliable measurement tools for assessing fetal biobehavioral development.
- ▶ Establish valid animal models of biobehavioral development of the fetus, which would facilitate testing of the long-term effects of perturbations during pregnancy.
- ▶ Develop new imaging techniques to systematically assess fetal behavior, physical maturation and physiology.
- ▶ Undertake research to refine endocrine and immune assay methods for evaluating the fetus.
- ▶ Develop methods for assessing physical and behavioral well-being before and after fetal therapy.
- ▶ Develop better methods for measuring fetal distress.

Adolescent/Young Adult

Overview

Redford Williams, M.D.

The Adolescent/Young Adult group identified the development of health-damaging behaviors during this critical life period as a key focus for research aimed at increasing our understanding of and ability to intervene on disease processes.

The first initiative (A-2-1) takes as its starting point the well-documented effects of low socio-economic status (SES) on health and disease. It proposes longitudinal studies to evaluate the influence of factors in several domains—physical environment, sociocultural environment, individual neurobiology, and individual psychology—upon the adoption and maintenance of health damaging behaviors (e.g., smoking, alcohol and drug use, psychophysiological hyperreactivity) across the adolescent years.

The second initiative (A-2-2) takes a key developmental milestone during this period—puberty—as the focus of proposed studies of the interaction of biological, psychological, and social responses to puberty as they influence short- and long-term changes in health-relevant behaviors.

The third initiative (A-2-3) proposes studies to increase understanding of the underlying neurobiological processes at work during adolescence and early adulthood whereby the experience of stress/distress can lead to adverse health outcomes.

The final initiative (A-2-4) takes as its focus the major cause of death and disability in adolescence and young adulthood—violent events and accidents. The research proposed under this initiative would attempt to increase understanding of the basic underlying processes—including biopsychosocial characteristics and health behaviors—that lead to behaviors that predispose to injury events.

By seeking to determine the factors involved in the development of biological and behavioral characteristics that potentiate disease processes, the initiatives proposed can lead to identification of targets for interventions to prevent or ameliorate the development of these health-damaging characteristics.

Task Group Initiatives

✓ **Socioeconomic Status and the Development of Health-Damaging Behaviors and Risk of Adverse Health Outcomes in Adolescents (A-2-1)**

Need and Justification

Socioeconomic status (SES) is a strong and consistent predictor of morbidity and premature mortality from all causes. This association is found with each of the key components of SES: education, income, and occupational status. Efforts to explain this association have been unsuccessful. The primary focus of research has been on the impact of poverty and its correlates but these do not adequately explain the observed SES-health association which exists throughout the SES hierarchy. Other explanations have focused on smoking, diet and physical activity which are associated with risk factors such as elevated lipids, excess weight, and high blood pressure. Both these behaviors and the associated risk factors show a linear relationship with SES and may be one pathway by which SES influences health. However, like poverty, these variables do not explain the SES-health association. Other potential pathways that may act independently or interact with health behaviors include differential exposure to physical and social environments that may damage health or promote risk behavior, personality characteristics such as resilience and hostility, or individual differences in physiological reactivity to stress.

The period of adolescence is a critical time during which behaviors are established and

social environments are accordingly selected which influence SES. The period of adolescence is also a critical time during which many health risk behaviors (e.g., tobacco, alcohol and drug use, sexual risk behaviors, obesity and eating disorders) are initiated and established, and individual differences in psychological (e.g., hostility) and neurobiological characteristics (e.g., excessive adrenergic arousal to stress) are observed. Therefore, adolescents provide an optimal population for studies of the process by which social class is related to the development of health-related behaviors, and to adverse health outcomes. This initiative is designed to encourage these studies. It is anticipated that the processes involved are likely to be multifactorial, reflecting the influence of variables from a number of domains including:

- ▶ *Physical environment*—e.g., crowding, toxic exposure, crime, poverty
- ▶ *Sociocultural environment*—e.g., life events, social support, peer norms, family resources, chronic stress
- ▶ *Individual neurobiological characteristics*—e.g., excessive adrenergic reactivity to stress, neurotransmitter levels
- ▶ *Individual psychological characteristics*—e.g., hostility, psychopathology, coping, health perceptions

For example, various studies confirm that lower social class and fewer years of education are associated with greater exposure to life events, greater social isolation, higher levels of hostility, and cigarette smoking. Ultimately, the success of efforts in the areas of primary prevention and risk reduction will depend on a clear understanding of the processes by which such variables as these from each of these domains interact in the acquisition and maintenance of health-related behaviors. Given that adolescence is the time that the SES-health trajectory may be set, this initiative calls for research on the processes underlying the SES-health association during adolescence and young adulthood.

Research Approach/Methodology

Research designs should emphasize intermediate prospective studies which can capture developmental patterns that encompass the transitions from late childhood through the pubertal period, to young adulthood.

Multiple studies should be funded to span the SES and ethnic spectra. Different applicant institutions should focus on key samples to characterize specific sub-populations.

✓ ***Influence of Early Adolescent Development on Immediate and Long Term Processes (A-2-2)***

Need and Justification

A life span perspective on health and illness requires an emphasis on the role of human development. Understanding the biological, social, and psychological changes occurring in early adolescence is critical to identifying: (a) factors crucial to the development of health-related behaviors and processes in early adolescence that persist into adulthood; (b) factors that influence the health of adolescents; and (c) factors that influence later adult health, independent of adult health practices. Research initiatives are needed to identify the *interactions* of key factors in the biological, social, and psychological changes that occur in early adolescence and the effects of those interactions on health and disease processes.

Although enormous progress has been made in understanding the persistence of health behaviors and some biological processes in adolescence into young adulthood, too little information is available on fundamental aspects of adolescent development to specify why adolescents are at risk for certain health problems, either immediately or in later adult life. Certain adolescent factors (e.g., adolescent obesity) appear to be related to adulthood health, independent of adult level of the factor in question (e.g., adult weight). Basic knowledge on the interaction of biological, social, and psychologic changes in early adolescence necessary to understanding disease processes and to develop prevention and treatment strategies has not been adequately developed. Taking an interactive systems approach to early adolescent development should permit advances in understanding

how to prevent further risk factor development and to promote good health in early adolescence and later adult years.

Research Approach/Methodology

We recommend that both cross-sectional and longitudinal prospective designs be employed to investigate the variability in the onset and progression of puberty; the biological (e.g., reproductive hormones, neurobiological changes), psychological (e.g., self-concept and identity) and social (e.g., peer group identification) responses to the variability, and the relationship of the interaction of these systems to short-term and long-term changes in health-relevant behaviors or processes. Candidate outcome variables for study include weight, body image, central body fat, psychophysiologic responses to stress, insulin and glucose metabolism, lipid levels, immune function, substance abuse, and reproductive behaviors. We recommend that candidate outcomes not be studied in isolation, but in appropriate subsets, depending on the mission of NIH agency involved.

The cross-sectional approach would provide estimates of the extent of variability, while the longitudinal design would allow assessment of the temporal sequencing of the interactions. The cross-sectional studies could focus on small samples intensively studied, perhaps using the new ambulatory techniques for monitoring on line ongoing behavioral and biological processes. It is anticipated that large samples will be needed to assure representation of diverse groups of adolescents and that follow-up should

continue at least through young adulthood. Furthermore, it is likely that the onset and progression of the pubertal transition and responses to puberty are affected by secular trends so a sequential cohort design may be

most appropriate. Because the pubertal transition may start in some children between the ages of 8 to 10, it is recommended that pre-pubertal children prior to the age of 10 be enrolled in the longitudinal aspects of the study.

✓ **Neuroscience and Behavior (A-2-3)**

Need and Justification

Several decades of research have presented well documented evidence of the interaction between neurobiological processes and the pathophysiology of disease. There is extensive literature which demonstrates that the experience of distress results in neurobiological changes that can have adverse health outcomes. These outcomes involve changes in neuropeptides, immune responses, hormones, and sympathetic activation which are associated with specific disease outcomes such as: infectious diseases, multiple sclerosis, diabetes, heart disease, gastrointestinal diseases, malignancies, and pain.

In adolescence and early adulthood there are a number of concomitant changes which occur. Profound changes associated with puberty provide a psychological and physiological susceptibility to behaviors and stressors that can have deleterious immediate or long term effects. Since many of the biobehavioral processes associated with acute and chronic disease are initiated at this age, a deeper understanding of the underlying mechanisms linking neuroscience and behavior is important for prevention, clinical management, and disease intervention.

Research Approach/Methodology

There is an overriding need for multi-disciplinary research to address these problems. To

accomplish this, basic scientists and behavioral scientists must join forces to address specific disease entities, some of which are elucidated below:

- ▶ Animal models have shown a relationship between chronic psychological stress, menstrual cycle dysfunction and acceleration of atherosclerotic disease. These models now need to be investigated in women.
- ▶ The data on reactivation of latent herpes viruses such as genital herpes (HSV-2) and Epstein Barr Virus in relation to behavioral stress need to be further investigated. Similar studies need to be performed on latent HIV.
- ▶ Experimental autoimmune encephalomyelitis (EAE) in animals is being used as a model to study multiple sclerosis. Preliminary evidence suggests that EAE pathology can be modulated by stress; this need to be further explored to determine if there is relevance for human diseases processes.
- ▶ Juvenile diabetes is a major health concern for young adults and has a broad spectrum of negative physiological outcomes, e.g., impact on the immune system. Behavioral studies to improve treatment compliance could have significant impact on clinical outcome and therefore on patient care costs.

✓ **Adolescent Liability for Injury and Violent Events (ALIVE) (A-2-4)**

Need and Justification

Injury events, including homicide, suicide and accidents are the leading cause of death among young adults in the United States. These injury events as well as physical assault are major contributors to morbidity and loss of social capital. Not only do these events effect health at the level of the individual, but they impact the health-damaging capacity of micro (family, neighborhood) and macro (community) environments.

The basic underlying processes that lead to behaviors which, in turn, predispose to or protect against injury events are poorly understood. Predisposing conditions, as well as risk-protecting variables need to be understood at multiple levels of biobehavioral organization including the physical and social environments, interpersonal processes, individual characteristics (e.g., behavioral, psychophysiological and biochemical factors), health behaviors (e.g., alcohol, drugs, and smoking) and interaction with the health care system.

Research Approach/Methodology

The problem of injury events is so pervasive in adolescents and young adults today that a broad

range of research responses should be encouraged. Each proposed study should encompass methods that integrate the multiple components contributing to vulnerability to injury events. Accordingly, analytic strategies need to emphasize multivariate modeling. Innovative strategies are needed to integrate qualitative and quantitative data and to analyze clusters of related variables.

Research designs could include laboratory studies, clinical investigations, and large-scale cohort studies that would facilitate understanding the incidence and prevalence of injury events in the sociocultural context in which they occur. Accidental as well as intentional injuries could be included in this research. Research teams to carry out this research should be interdisciplinary.

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Midlife Adult

Overview

Neil Schneiderman, Ph.D.

The group working on disease processes in the midlife adult has proposed four initiatives:

- 1) Psychosocial Effects on Disease Progression: Endocrine and Immune Mediation (A-3-1)
- 2) Co-Morbidity of Psychiatric and Somatic Disorders (A-3-2)
- 3) Behavioral Sequelae of Disease and Its Treatment (A-3-3)
- 4) Social, Economic and Cultural Factors that Affect Disease Progression: Investigation of Underlying Processes (A-3-4)

The first initiative would look at endocrine and immune parameters as potential mediators of psychosocial effects on disease progression. Recent evidence has indicated that psychosocial factors may influence the course of such disorders as AIDS, cancer and coronary heart disease. While endocrine and/or immune variables have been implicated as putative mediators of these relationships, the exact manner by which particular endocrine and immune changes mediate relationships between specific psychosocial variables and variations in disease outcome remain to be elucidated. More specifically, the group felt that controlled psychosocial

interventions provide a potential method for experimentally manipulating psychosocial variables in such a way as to clarify the mediating roles that endocrine and/or immune variables may play in influencing disease outcome.

The second initiative proposed by the group would examine the co-morbidity of psychiatric and somatic disorders. Thus, for example, persons who are depressed have a greater risk of suffering coronary events and show a poorer prognosis following an event than people who are not depressed. The group felt that several research approaches could be used to explicate the association between psychiatric illness and physical disease. These could include: (a) epidemiological and case control studies to detect prevalence and specific relationships of co-morbid states; (b) animal studies to determine if behavioral and/or pharmacologically induced models of psychological disorders lead to somatic disturbances and vice versa; (c) treatment studies using pharmacologic and behavioral interventions for somatic disease to examine their effects on psychological states; (d) treatment studies of psychological disorders to determine their impact on somatic states; and (e) studies examining potential common genetic determinants of somatic and psychological symptoms.

The third initiative deals with the behavioral sequelae of disease and treatment. Thus, for example, arterial hypertension among middle-aged adults is accompanied by deficits in neuropsychological functioning. Likewise, different antihypertensive therapies have been shown to affect, either favorably or adversely, cognitive and behavioral performance. In order to deal with these issues as they relate to common chronic disease, it is proposed that 1) clinical studies of the behavioral correlates of common chronic diseases and therapeutic interventions be undertaken, and 2) behavioral evaluations be added to ongoing and planned clinical trials. The scope of measurement would include neuropsychological assessment as well as measures of mood, personality and quality of life. Physiological measures, such as changes in cerebral blood flow would also be appropriate.

The fourth and last initiative suggested by the group involved the development of studies to

identify the sociocultural and psychosocial factors that best explain the relationships of sociodemographic, gender and ethnic variables to disease progression.

Because the four initiatives each deal with multiple diseases, they should be considered within the framework of trans-NIH activities. It was also felt that while research into such disorders as obesity, dyslipidemia and Type II diabetes have traditionally been supported by different Institutes, evidence suggests that the underlying psychosocial, biobehavioral and biomedical mechanisms have more in common across disease states than was previously supposed. Thus, the disease state orientation of some institutes at the NIH may inadvertently have led to the advantages of a more coordinated approach being overlooked. Trans NIH coordination and support of studies examining disease processes in the midlife adult would therefore appear to be clearly warranted.

Task Group Initiatives

✓ **Psychosocial Effects on Disease Progression: Endocrine and Immune Mediation (A-3-1)**

Need and Justification

A growing body of research indicates a variety of relationships between social support, stress, personality and coping variables with disease progression. Such relationships have been documented in illnesses such as cancer, AIDS, and cardiovascular disease.

Recent research provides growing evidence for a causal influence of social relationships on health (House *et al.*, 1988). In a classic animal study using virally induced mammary tumors in mice, Riley (1975, 1981) showed that tumor incidence could be reduced from more than two-thirds to less than ten percent by placing the animals in low-stress conditions by reducing crowding. This effect is mediated by changes in the immune system (Ben-Eliyahu *et al.*, 1991).

Cancer relapse has been found to be associated with severe social stress (Ramirez *et al.*, 1989), while decreased survival in humans has been found to be associated with poor coping styles (Greer *et al.*, 1990) and low quantity or quality of social support (Rodin, 1986; Funch & Marshall, 1983; Goodwin *et al.*, 1987; Joffres *et al.*, 1985; Ganster & Victor, 1988; Kennedy *et al.*, 1988).

Even when possible differences in health habits are controlled in the data analysis, social rela-

tionships affect survival rates. In a prospective study of the effect of social ties on mortality, Berkman and Syme (1979) followed 6,928 adults for 9 years and found that individuals with many social ties had lower mortality rates than individuals who had fewer such ties. A similar study by House *et al.* (1982) among 2,754 adults followed for 10 years replicated these results and supplied further validation by using data from physical examination rather than self-reports of health.

The provision of a social support intervention for isolated individuals under stress has been related to improved health outcome (Ganster & Victor, 1988; Rodin, 1980, 1986; Raphael, 1977; Spiegel *et al.*, 1989; Turner, 1981). Social support has been shown to be an important factor in mediating individuals' ability to cope with stress. One particularly clear example is the finding that higher mortality rates are often reported during the first year after the loss of a spouse and that married cancer patients survive longer than unmarried persons (Goodwin *et al.*, 1987).

Possible mechanisms of the positive effect of social support on health include: 1) better treatment compliance, diet and activity levels (Stones *et al.*, 1989); 2) stress-reducing effects of social support which are thought to influence response to disease via hypothalamic control of protein metabolism, glucocorticoid and prolactin

secretion (Bovard, 1985; Bovbjerg, 1989; Levine *et al.*, 1989; Malarkey *et al.*, 1983; Spiegel, 1993); and 3) stress and support-mediated effects on immune function (Ader *et al.*, 1990; Antoni *et al.*, 1990; Cohen *et al.*, 1991; Fawzy *et al.*, 1990; Glaser & Kiecolt-Glaser, 1985; Herberman, 1985; Kemeny *et al.*, 1987; Kennedy *et al.*, 1988; Levy *et al.*, 1987; 1991).

Current evidence suggests that psychosocial stressors can affect catecholamine and cortisol responses, which in turn appear to be associated with decreases in immune function (Schneiderman, *in press*). Similarly environmental stressors (e.g., Glaser *et al.*, 1987) and affective disturbances (e.g., Calabisis, Kling, & Gold, 1987) have been shown to impact negatively on immune function. Conversely, relaxation training has been shown to reduce markers of sympathetic nervous system activity (Hoffman *et al.*, 1982) and urinary and plasma cortisol levels (McGrady *et al.*, 1987). Relaxation training has also been shown to reduce distress and enhance immune function measures such as natural killer cell cytotoxicity and mitosis responsiveness in geriatric subjects (Kiecolt-Glaser *et al.*, 1985).

More recently, Antoni *et al.* (1991) and Esterling *et al.* (1992) provided evidence that combined cognitive behavioral stress management and relaxation training reduced the affective distress and the adverse immunologic and virologic effects associated with notification of HIV-1 seropositivity. Findings from these studies raise the question of whether psychosocial stressors and/or psychosocial interventions can influence HIV-1 disease progression via changes in endocrine and immune mediation.

Although studies that have restricted themselves to examination of CD4 and/or CD8 number

have provided inconsistent results concerning the relationship between psychosocial factors and immune markers in HIV-1 spectrum disease, studies that have used additional measures of immune status have reported positive results. Thus, measures such as the *in vitro* lymphocyte response to phyto-hemagglutinin have been able to relate psychological and/or immune changes to disease progression (Ironson *et al.*, 1994) and have been able to differentiate disease progressors from nonprogressors in HIV-1 seropositive subjects (Schellekens *et al.*, 1990). The existing data suggest that in order for psychological factors to be related to immune markers and disease progression in HIV-infected individuals, it is necessary to control for: (a) heterogeneity in the source of infection and disease stage of subjects at the point of study entry; (b) heterogeneity of study subjects in terms of gender, ethnicity, age and drug use; (c) too limited a selection of immune markers; and (d) failure to assess individual differences in transactional variables such as coping strategies.

The proposed program will clarify relationships between psychosocial variables, disease progression and disease outcome. It will also help to identify psychophysiological endocrine and immune processes which underlie these relationships. These findings will enable us to develop specific interventions which can help individuals to modify the relationship between psychological and social environment and disease progression. Psychosocial interventions have the potential for substantial cost savings of invasive medical procedures by providing enhanced social support. They may also help elucidate physiological mechanisms of psychosocial influences on health, increasing research communication between psychosocial and biomedical investigators.

Research Approach/Methodology

Proposals should involve systematic study of the relationships across three domains:

- 1) psychological and social variables, including social support, social stressors, coping styles, personality variables, quality of life, and SES;
- 2) endocrine and/or immune function, measured in vivo or in vitro;
- 3) disease progression, e.g. cancer recurrence or mortality; HIV progression to AIDS or mortality.

Designs with well-defined clinical populations; systematic assessment of all variables; controlled interventions; comparison among relevant populations, including study of gender, social class, ethnicity, and other variables are encouraged. Proposals may be broad and generic or be targeted to specific diseases.

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✓ **Co-morbidity of Psychiatric and Somatic Disorders** **(A-3-2)**

Need and Justification

There is a growing literature suggesting an association between psychiatric illness and physical disease. For example, the prevalence of non-insulin dependent diabetes is 5% in the general population but over 25% in adults who have been diagnosed with major affective disorders. People who are depressed have a greater risk of coronary events and show a poorer prognosis following an event that patients without depression. Anxiety disorders are more common in people with mitral valve prolapse and irritable bowel syndrome. Conversely, many chronic diseases appear to lead to depression. Depression is often first discovered following the diagnosis of coronary artery disease, cancer, HIV infection, diabetes and other chronic illnesses.

The importance of these co-morbid states is reflected at a number of levels: 1) The co-existence of psychological or psychiatric disorders may interfere with preventative and therapeutic interventions of both disorders, thereby compromising clinical outcome and dramatically increasing treatment costs; 2) co-morbidity of

psychiatric and somatic disease may complicate accurate diagnosis of either condition; 3) common CNS mechanisms of psychiatric and somatic disease may exist, leading to a greater understanding of pathophysiology; 4) co-morbidity of psychiatric and somatic disease may lead to an exacerbation of both problems.

Research Approach/Methodology

A) Epidemiological and case control studies to detect prevalence and specific relationships of co-morbid states; B) animal studies to determine if behavioral and/or pharmacologically-induced models of psychological disorders lead to somatic disturbance and vice versa; C) treatment studies using both pharmacologic and behavioral interventions for somatic disease to examine their effects on psychological states, and treatment studies using pharmacologic and behavioral interventions for psychological disorders to examine their effects on somatic states; D) studies examining potential common genetic determinants of somatic and psychological symptoms.

✓ **Behavioral Sequelae of Disease and Its Treatment (A-3-3)**

Need and Justification

Aside from overt psychiatric manifestations of neurobiological disease, very little is known regarding the effects that common physical diseases may have on normative, adult behavioral functioning. Similarly unstudied are the neurobehavioral and "quality of life" sequelae of interventions aimed at the amelioration or prevention of disease. The latter gap in knowledge is particularly notable, due to the widespread prescription of medications having known or probable effects on the central nervous system.

In the few instances where behavioral consequences of disease and treatment have been evaluated, however, potentially important associations have been documented. For instance, arterial hypertension among middle-aged adults is accompanied by deficits in neuropsychological functioning (e.g., in attentional, mnemonic and perceptual-motor skills) that approximate those of normotensive, elderly individuals. Likewise, antihypertensive therapies variably influence cognitive and behavioral performance, in some cases restoring hypertension-associated deficits, at other times having little or no manifest effect on behavior, and occasionally, introducing new areas of deficit. In turn, possible real-life implications of such effects are numerous, including influences on occupational performance, mood and interpersonal relationships, as well as on patients' readiness or ability to adhere to medical regimens. In the latter sense, the behavioral consequences of disorders and their treatment may affect the course of disease itself.

It is proposed that broad-based research be conducted into the behavioral sequelae of chronic diseases and their various pharmacologic and surgical interventions. The range of phenomena to be studied would include the components of human information processing (e.g., attention, memory, learning ability, psychomotor speed and coordination, executive skills), affect and its regulation, personality, and more generally, perceived quality of life. Specific questions to be addressed concern: (a) what common behavioral effects are associated with specific diseases and treatments; (b) how these effects may vary between individuals and the determinants of such interindividual variability; (c) how the behavioral sequelae of disease and treatment influence activities of daily life; (d) what physiologic mechanisms underlie any behavioral changes observed; and (e) what prognostic implications these changes have for the course of disorder and its therapy. The public health significance of this area of research is manifold, particularly in enhancing our understanding of the costs of physical disease and interventions. By mapping the behavioral correlates—and where indicated, toxicity—of common therapeutic agents, such research may also generate guidelines (in addition to efficacy and mechanisms of action) for the rational selection of treatment.

Research Approach/Methodology

It is proposed that two types of research be supported: (a) clinical studies of the behavioral correlates of common chronic diseases and therapeutic interventions; and (b) addition of

sensitive behavioral evaluations to ongoing and planned clinical trials. The scope of measurement should include neuropsychological assessment; measures of mood, personality, and

quality of life; and where mechanistic hypotheses are indicated, appropriate physiologic measurements (e.g., CBF measurements in studies of cognitive declines associated with hypertension).

✓ **Social, Economic and Cultural Factors that Affect Disease Progression: Investigation of Underlying Processes (A-3-4)**

Need and Justification

Sociodemographic, economic and cultural factors have long been implicated as important determinants of disease risk and progression (Antonovsky, 1967; Kitagawa & Hauser, 1973; Williams, 1990). Socioeconomic status is one of the most robust predictors of mortality and disease progression across a number of different diseases, including cardiovascular disease (Rose & Marmot, 1981), cancer (Dayal *et al.*, 1982), and AIDS (Peterson & Marin, 1988). Furthermore, even controlling for SES and the presence of behavioral risk factors, certain groups, such as African Americans and women experience a worse prognosis following diagnosis of and treatment for coronary heart disease, diabetes, some cancers, AIDS, and other chronic diseases (Haan & Kaplan, 1985).

Despite the clear evidence linking economic and social factors to disease progression, few studies have focused on identifying the underlying psychological, social, and structural processes that account for these relationships. Membership in a sub-group based on one's ethnicity, income, education, occupation and/or gender carries with it a myriad of psychological and social experiences that increase risk and can accelerate disease progression. These include exposure to chronic stress; the effects of discrimination; depression, anxiety and other psychological responses; the absence of social support; limited access to medical care, and use of less effective or ineffective coping methods, including substance abuse. Studies are needed

to identify the underlying psychosocial factors that best explain the relationship of sociodemographic, gender and ethnic variables to disease risk and progression. The ultimate goal is the design of interventions to favorably alter these underlying processes, decreasing incidence and impeding the progression of disease.

Research Approach/Methodology

Because so little is known about the specific psychological and social factors underlying the relationship between sociodemographic variables and health outcomes either for healthy populations or different patient sub-groups, studies utilizing a variety of approaches, including multimodal approaches, are needed. These methods include:

- ▶ large scale, prospective studies of healthy individuals, individuals at high risk for disease and patients with chronic diseases such as CVD, AIDS, cancer, which attempt to link psychosocial factors such as stress, coping modes and social support with health outcomes, such as morbidity, mortality and health-related quality of life.
- ▶ small-scale case studies using ethnographic and case-history approaches
- ▶ case control studies
- ▶ pilot focused intervention studies

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Senior Adult

Overview

Janice Kiecolt Glaser, Ph.D.

A variety of behavioral and psychosocial factors have been identified as relevant to the health of the elderly. There is an emerging body of evidence that supports an important role for behavioral and sociocultural factors in the incidence, progression, and consequences of disease in the elderly. While more work needs to be done in this broad area, there is also a need for investigation of potential common mechanisms which may underlie the impact of behavioral and sociocultural factors, and ethnicity. The initiatives contained in this section are targeted at examining potential common pathways, understanding the extent to which disease processes may reflect more distal versus more recent or proximal effects, and the importance of minimizing 'disease'-related disabilities and maximizing function.

Common disease mechanisms discussed related to cumulative oxidative damage, down-regulated immune function, and sympathetic hyper-reactivity to stress. As one example, recent evidence highlights the importance of longitudinal studies of personal relationships: convergent evidence from several laboratories suggests that social support may interact with chronic stressors to produce differences in sympathetic nervous system (SNS) reactivity, neuropeptide release, and immune function. For example, family caregivers of Alzheimer's disease (AD)

victims who were high in social support displayed different patterns of age-related heart rate reactivity and blood pressure than caregivers who were low in social support (Uchino *et al.*, 1992).

Earlier data from the spousal caregivers in this same sample showed that caregivers had poorer immune function than controls, and low social support was associated with greater declines in immune function over the course of a year (Kiecolt-Glaser *et al.*, 1992); importantly, spousal caregivers had more prolonged infectious illness episodes (primarily respiratory tract infections) than controls. Similarly, Irwin *et al.* (1992) found higher levels of neuropeptide Y (NPY) in AD caregivers compared to controls; levels of NPY, a sympathetic neurotransmitter released during emotional stress, were inversely correlated with NK cell activity.

Consistent with these data, chronic stress has also been implicated as a factor in enhanced cardiovascular reactivity as well as higher levels of urinary catecholamines in two studies from Baum's laboratory (Fleming *et al.*, 1987; McKinnon *et al.*, 1989); they also reported that cardiovascular measures took longer to return to baseline levels in chronically stressed, compared to unstressed subjects (see, also, Pardine & Napoli, 1983).

Recent studies of the immunological consequences of brief experimental stressors have provided preliminary evidence that individuals who exhibit the largest "sympathetically mediated" increases in cardiovascular reactivity also show the largest catecholaminergic actions and immune changes (reviewed in Kiecolt-Glaser *et al.*, 1992). If sympathetic activation is a marker or determinant of immune function, then the cardiovascular, endocrine, and immune changes evoked by brief experimental stressors may help to illuminate the nature of the interactions among these physiological systems. For example, Crary *et al.* (1983a, 1983b) demonstrated that epinephrine (EPI) injections resulted in increased NK cell numbers, decreased blastogenic responses to three mitogens, and decreased CD4 cell numbers. These EPI induced changes, which reflect short-term rather than chronic sympathetic activity, are thought to reflect transient alterations in lymphocyte migration from lymphoid organs and peripheral blood mediated through adrenergic receptors on lymphocytes or via the sympathetic innervation of lymphoid organs (Ottaway & Husband, 1992). Importantly, leukocytes incubated with substantially larger EPI concentrations than levels expected in vivo did not affect mitogen stimulation (Crary *et al.*, 1983a), suggesting that EPI per se is not sufficient to produce these immunological changes and underscoring the potential importance of analyses of the interrelationships between autonomic and immune responses.

The age-related loss of beta adrenergic receptor sensitivity in the face of maintenance of alpha-1 adrenergic receptor sensitivity also highlights the importance of age-related changes in cardiovascular reactivity and their relationship to endocrine and immune function (Lakatta, 1987), particularly in view of evidence that SNS activity can inhibit antigen processing and presentation (Heilig *et al.*, 1993). Longitudinal

studies that evaluate the relationships among social support, SNS activity and reactivity, stress-related immune and endocrine changes, and longer-term changes in health are clearly warranted to determine whether extrapolations from cross-sectional data on acute events to chronic and longitudinal effects are warranted.

It has also been suggested that narrowing of physiological capacity and ability to maintain homeostasis may be involved in disease processes in the elderly. However, little is known about these changes, including whether they help to explain behavioral and sociocultural influences on disease. "Frailty" may reflect more generalized failure across multiple systems.

For example, immunological changes may also reflect changes in other systems. Evaluation of the blastogenic response in 403 older adults with a mean age of 86 showed that the lymphocytes of 18% of the sample did not proliferate in response to three mitogens (Murasko *et al.*, 1988). While the overall mortality of the population for a two-year period was 15%, negative responders had twice the mortality of positive responders.

The major cause of death in both groups was sudden death or a diagnosable cardiovascular-related disease. The authors suggest that decrements in cellular immunity may reflect changes in other systems as well, and may provide one marker of physiological aging. Similarly, a 16-year longitudinal study of 105 healthy elderly men showed that declines in the absolute number of peripheral blood leukocytes (PBLs) were associated with subsequent mortality within three years of death when compared with 5 or 10 years before death (Bender *et al.*, 1986). There was no association between the decrease in lymphocyte numbers and age at death, smoking status, or prior cardiac illness. Moreover, a

20-year longitudinal study of 273 healthy adults over 60 showed that poorer skin-test responses were associated with subsequent morbidity and mortality (Wayne *et al.*, 1990). While these are provocative studies, research that takes such a broad view of morbidity and mortality has been the rare exception, not the rule, and psychosocial factors have been only considered infrequently, despite evidence of their growing importance.

Convergent evidence from psychosocial and immunological domains suggests that the links among depression, personal relationships, and immunity could be stronger and could have more potent health consequences for older adults than younger adults. The number of relationships diminishes as people age, and the quality of close relationships becomes more salient (Carstensen, 1992). Thus, troubled relationships could have a greater impact on older adults because of their smaller social networks (Levenson *et al.*, 1993). In addition, immune function declines with age, particularly functional aspects of the cellular immune response (Murasko *et al.*, 1988; Wayne *et al.*, 1990). Finally, age and distress may interact to promote immune down-regulation: older adults show greater immunological impairments related to depression than young adults (Schleifer *et al.*, 1989). Thus, the increased distress associated with poorer or fewer close relationships could have a greater physiological impact in older adults compared to younger adults, a process that clearly deserves further study.

Moreover, alterations in social support that result in increased depressive symptoms have important implications for functioning and well-being. Wells *et al.* (1989), reporting on 11,242 outpatients from the Medical Outcomes Study, showed that patients with either a current depressive disorder or depressive symptoms in the absence of disorder had worse physical,

social, and role function, worse perceived current health, and greater bodily pain than patients with no chronic conditions. In particular, they noted that the poorer functioning that was uniquely associated with depressive symptoms was comparable or even worse than that uniquely associated with the eight chronic medical conditions they studied.

Depression interacted with these medical conditions in an additive fashion; for instance, among patients who had current advanced coronary artery disease and depressive symptoms, they found twice the reduction in social functioning associated with either of the conditions alone. Among the chronic conditions they studied (hypertension, diabetes, current coronary artery disease, current angina, current arthritis, current GI problem, current lung problems, or current back problems), the only chronic condition associated with greater functional problems than depression was current heart conditions. The authors emphasized that depressive symptoms even in the absence of depressive disorder were associated with considerably poorer functioning and had clear clinical significance. Since the chronic conditions studied by Wells *et al.* (1989) are all associated with increasing age, assessment and treatment of depression would seem important in minimizing the loss of function and disease-related disability.

Understanding possible common pathways is complicated by the unknown extent to which various disease processes in older adults reflect more distant versus more recent or proximal effects; for example, the extent to which the current health status of individuals who stopped smoking some years earlier continues to reflect residual risks or damage. Data from animal models suggest greater plasticity and recovery following chronic stressors in younger animals compared to older animals (Ackerman *et al.*,

1991). Thus, age may also interact with recency of disease processes to influence risk.

As outlined above, older adults represent an important population for whom the maintenance of function and minimization of disability are paramount. The enhanced understanding of common psychosocial and physiological links and pathways could lead to the development of more cost-effective interventions.

Longitudinal, population-based, studies with multi-modal assessments, e.g., psychosocial, neuromuscular, sensory, cardiovascular, metabolic, immunological measures, etc., are clearly needed. Also needed—a broad-based variety of behavioral and sociocultural factors to assess the role of co-morbidities in this population.

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Task Group Initiatives

✓ **Common Physiological Pathways Underlying Behavioral and Sociocultural Determinants of Health and Disease in the Elderly (A-4-1)**

Need and Justification

A variety of behavioral and psychosocial factors have been identified as relevant to the health of the elderly. There is an emerging body of evidence that indicates that behavioral and sociocultural factors play an important role in the incidence, progression, and consequences of disease in the elderly. While more work needs to be done in this broad area, there is also a need for investigation of potential common mechanisms which may underlie the impact of behavioral and sociocultural factors on the aging process. This initiative is targeted at examining potential common pathways. For example, mechanisms related to cumulative oxidative damage, down-regulated immune function, and sympathetic hyperactivity to stress have been suggested.

As one example, recent evidence highlights the importance of longitudinal studies of personal relationships. Convergent evidence from several laboratories suggests that social support may interact with chronic stressors to produce differences in sympathetic nervous system (SNS) reactivity, neuropeptide release, and immune function. Family caregivers of Alzheimer's disease (AD) victims who were high in social support displayed different patterns of age-related heart rate reactivity and blood pressure than caregivers who were low in social support (Uchino *et al.*, 1992). Earlier data from the

spousal caregivers in this same sample showed that caregivers had poorer immune function than controls, and low social support was associated with greater declines in immune function over the course of a year (Kiecolt-Glaser *et al.*, 1992); importantly, spousal caregivers had more prolonged infectious illness episodes (primarily respiratory tract infections) than controls. Similarly, Irwin *et al.* (1992) found higher levels of neuropeptide Y (NPY) in AD caregivers compared to controls; levels of NPY, a sympathetic neurotransmitter released during emotional stress, were inversely correlated with NK cell activity.

Consistent with these data, chronic stress has also been implicated as a factor in enhanced cardiovascular reactivity as well as higher levels of urinary catecholamines in two studies from Baum's laboratory (Fleming *et al.*, 1987; McKinnon *et al.*, 1989); they also reported that cardiovascular measures took longer to return to baseline levels in chronically stressed, compared to unstressed, subjects (see, also, Pardine & Napoli, 1983).

Recent studies of the immunological consequences of brief experimental stressors have provided preliminary evidence that individuals who exhibit the largest "sympathetically mediated" increases in cardiovascular reactivity also show the largest catecholaminergic actions and immune changes (reviewed in Kiecolt-Glaser *et*

al., 1992). If sympathetic activation is a marker or determinant of immune function, then the cardiovascular, endocrine, and immune changes evoked by brief experimental stressors may help to illuminate the nature of the interactions among these physiological systems. For example, Crary *et al.* (1983a, 1983b) demonstrated that epinephrine (EPI) injections resulted in increased NK cell numbers, decreased blastogenic responses to three mitogens, and decreased CD4 cell numbers. These EPI induced changes, which reflect short-term rather than chronic sympathetic activity, are thought to reflect transient alterations in lymphocyte migration from lymphoid organs and peripheral blood mediated through adrenergic receptors on lymphocytes or via the sympathetic innervation of lymphoid organs (Ottaway & Husband, 1992). Importantly, leukocytes incubated with substantially larger EPI concentrations than levels expected in vivo did not affect mitogen stimulation (Crary *et al.*, 1983a), suggesting that EPI per se is not sufficient to produce these immunological changes and underscoring the potential importance of analyses of the interrelationships between autonomic and immune responses. The age-related loss of beta adrenergic receptor sensitivity in the face of maintenance of alpha-1 adrenergic receptor sensitivity also highlights the importance of age-related changes in cardiovascular reactivity and their relationship to endocrine and immune function (Lakatta, 1987), particularly in view of evidence that SNS activity can inhibit antigen processing and presentation (Heilig *et al.*, 1993). Longitudinal studies that evaluate the relationships among personal relationships, SNS activity and reactivity, stress-related immune and endocrine changes, and longer-term changes in health are clearly warranted to determine whether extrapolations from cross-sectional data on acute events to chronic and longitudinal effects are warranted.

It has also been suggested that narrowing of physiological capacity and ability to maintain

homeostasis may be involved in disease processes in the elderly. However, little is known about these changes, including whether they help to explain behavioral and sociocultural influences on disease. "Frailty" may reflect more generalized failure across multiple systems. Identification of common pathways could lead to the development of more cost-effective interventions.

Methodologies

Longitudinal, population-based, studies with multi-modal assessments, e.g., psychosocial, neuromuscular, sensory, cardiovascular, metabolic, immunological measures, etc. are clearly needed. Also needed — a broad-based variety of behavioral and sociocultural factors to assess the role of co-morbidities.

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✓ **Minimizing Loss of Function: The Identification of Individuals or Circumstances that Minimize Disability with Progressing Age and that Promote Function (A-4-2)**

Need and Justification

This initiative would examine the various socio-cultural, personal and environmental factors that affect the course of disability. Focus would be on identifying factors that facilitate continued coping and independence despite irreversible illness. Efforts should be made to identify the most cost-effective levels of intervention to promote continued function.

Two broad types of studies should be considered:

- ▶ Contrasting individuals with the same disease—focus on differential decline in function and risk factors;
- ▶ Identifying individuals who "age" well—who have the "function of a 50 year old at 70"—sustained global health rather than focusing on a single disease.

Research Approach/Methodology

Studies can be at level of:

- ▶ epidemiology — longitudinal studies
- ▶ intervention studies
 - at disease level
 - at person level
 - at household level (e.g., household structure, social supports)
 - at societal level (stigma, environmental barriers)
 - in terms of health services utilization

A widely accepted measure assessing "activities of daily living" or "absence of loss of function" would be particularly useful in comparing results across such studies.

✓ ***The Role of Distal and Proximal (In Time and Space) Psychosocial Factors in Disease and Aging Processes (A-4-3)***

Need and Justification

Aging and the development of chronic diseases are long-term, often life long, processes which take place within a broad and changing socio-cultural environment. Most existing research, however, focuses on a relatively narrow and limited context. Epidemiologic and etiologic studies often analyze the effects of single or small numbers of risk factors assessed at a single point in time. Studies of disease and disease processes are also limited in their scope in terms of time and space. Research is needed which considers how the patterning of exposures to risk factors over time and space influence their impact on health and aging. Studies are also needed of the impact of disease course and treatment on broader psychosocial functioning at a given point in time and over longer periods of time.

For example, health behaviors and lifestyles such as smoking and drinking are known to have important effects on health. However, much less is known about how and why these effects may vary over the life course, and how important are the effects of diet and smoking history in earlier life as compared to current diet and smoking practices. Similarly, what are the effects of socioeconomic circumstances at different points in the life span. Recently we have seen people survive or recover for long periods from formerly fatal diseases (e.g. many cancers and CHD), but we know less about the longer-term effects of experiencing the disease

and treatment process, especially on psychosocial outcomes.

Studying those issues is crucial to understanding the consequences across the life cycle, especially in older age, of exposure to risk factors and the experience of disease at different points in the life course. It is also essential to understanding the potential impact of risk factor interventions or disease treatment at a given point in the context of earlier experience.

This requires current research to be broadened in scope and length to encompass long-term longitudinal studies, and assessment of a broad array of psychosocial risk factors on medical outcome.

Research Approach/Methodology

The major need is for data on risk factor exposure and disease outcomes over as much of the life cycle as possible. Such data can initially be obtained more easily from existing longitudinal studies, which contain repeated measurements of relevant risk factors and health outcomes (e.g. Framingham, Tecumseh, Alameda County, and others). Such data allow analyses of different histories of, for example, health risk behavior or income/poverty on health outcomes at various points, and comparison of the predictive power of recent assessments vs. prior assessments on longer-term social and behavioral patterns. Those data sets may not, however,

include many newer social and behavioral risk factors. Retrospective data may be collected in some cases, but are often of limited validity. Thus, some new, long-term longitudinal studies will be needed for studying such issues. Efforts

should be made where feasible to exploit existing longitudinal studies (e.g. the National Longitudinal Studies) by adding health and risk factor modules.

Synthesis

Ronald Glaser, Ph.D.

Introduction

As students taking courses in anatomy and physiology we were taught the body's systems: the endocrine system, the immune system, the nervous system, the skeletal system, etc. At the end of these courses we were left with the notion that these body systems were independent systems which did not interact with each other.

The field of psychoneuroimmunology (PNI), which was resurrected in the late 1970's, is sending a message to the scientific and medical community that we were somewhat naive in the take home messages provided by our instructors. That is to say that we did not understand that these systems are not separate in the body. We now know that many of these systems interact with each other in a very complex way often involving two-way communications.

PNI is a good example of an area of research which concerns interactions between the central nervous system (CNS), endocrine and nervous systems, how the interactions have implications for health and the impact of behavior as an important modulator of risk for disease and patient management. Accordingly, any external stressor which stimulates the CNS will likely have an impact on the endocrine and immune systems. Factors such as psychological stress, environmental stress, exercise stress, i.e., behavior at several levels has impact on the physiology of the body and may impact disease processes and outcomes.

In a sense, the field of medicine today has evolved in many ways from a "Pasteurian philosophy" which one might call "mathematical medicine". If one can identify an infectious agent associated with a particular disease, then one can develop an antibiotic specific to that infectious agent (in the case of viruses, an antiviral drug) and theoretically, cure patients. Many medical researchers today think that approach may be somewhat simplistic and that there may be other factors that play an important role in the pathophysiology of human disease and that psychological and behavioral factors need to be studied as part of complete patient management.

To many medical scientists, the concept of behavior as a significant player in the pathophysiology of disease is still a new concept and one which still invokes skepticism. Healthy skepticism is important in pursuing research in any area, including medical research, but being open minded about these and other issues is also an important part of being a scientist. One must look at the data of well controlled, well designed peer reviewed studies that can be confirmed by more than one laboratory before one makes judgements, in favor or against, any scientific theory or medical practice. The change which appears to be taking place between "mathematical medicine" and approaching the patient taking behavioral issues into account may prove to be the best way of providing medical care for the future.

In sum, the evidence from human and animal studies clearly shows that behavioral and envi-

ronmental stressors can modulate the immune system (physiological responses) in a negative fashion. There are a few clinical studies which have been published that demonstrate that this modulation can have health implications. The importance of stress in cardiovascular research has been long established. We know that disease processes are affected by the genetics of the individual, the exposure to pathogens, and the physiological health of the individual at the time of exposure to an insult such as a pathogen or a toxin. To this list we now can add issues such as behavior and social support as potential co-factors which play a role in the ability to deal with an insult. The broad implication of the impact of behavior across multiple diseases are summarized in this document.

Disease Processes in Prenatal Infants and Children

The focus of disease processes in this group included the interaction of genetic propensities and expression of these propensities in different types of environments. The emphasis in the initiatives is not on genotypes and phenotypes but on larger issues of development, health and disease. For instance, one initiative examines the earliest of environments affecting health and disease, that is, the quality of the prenatal environment. Although a fetus begins to develop with a certain genetic endowment, the prenatal environment influences how genes are expressed. Healthy fetal development provides the foundation for all of subsequent development but there are few models for understanding the intricate interactions between development of the fetus and the health, life style, and behavior of the mother. Animal and human models for understanding and improving fetal development are greatly needed.

Advances in molecular biology have led to the ability to identify genes that are risks for specific diseases and to diagnose disease in the fetus. This new knowledge inevitably will lead to new stressors in families and the children so identified. Even in the presence of a known genetic defect, disease expression may vary with environmental circumstances that are subject to modification. The health care system has new responsibilities to help families and children deal with these stressors. Guidance is needed to design interventions to prevent disease expression and on how and when to tell children about their risk for developing a disease. There also is the need to determine how the disease risk affects cognitive and emotional development of the affected child.

Given that some children will develop chronic disease, what is needed is an examination of the interface between a normal developmental trajectory and the onset and course of chronic diseases. Recent research indicates that both genetic and experiential/environmental factors interact to influence the onset and trajectory of childhood disease but there is minimal data on the etiology of many chronic diseases. Specifically lacking are data on the interaction of the individual developmental, familial, and environmental factors that precipitate the expression and influence the trajectory of chronic disorders in genetically predisposed children.

The impact of cognitive, behavioral, social, emotional and familial processes on disease and disability in childhood is in need of much further elaboration. Specifically, childhood diseases and disabilities have implications not only for the involved child, but for the family as well. At diagnosis, parents are often confronted with difficult decisions regarding medical interventions and even decisions regarding

the balance between longevity and quality of life. The health of parents of children with chronic diseases is adversely affected as well. Finally, medical interventions may have long-term side effects for the cognitive, emotional, and social development of the affected child. Understanding the impact of childhood disease and disabilities on the child and family may improve the family's decision-making process, improve the child's and the family's ability to cope, and reduce the child's and the family's co-morbidity with other physical and psychological disorders.

Implications for research strategies.

The initiatives described by the Basic Processes Task Group mandates an interdisciplinary research approach. No one discipline possesses the innate wisdom to confront the challenges of combining genetic, behavioral, and environmental perspectives to develop testable theories and hypotheses regarding the onset and progression of both states of health and disease. Cross-institute collaboration is essential for solving these complex health problems.

The Task Group initiatives strongly endorse a developmental perspective to disease processes. Developmental changes within children, their families, and their environment affect both the onset and progression of acute and chronic disorders. To explain the developmental processes involved, a longitudinal research perspective is essential.

Disease Processes and the Adolescent/Young Adult Population

The Adolescent/Young Adult group identified the development of health-damaging behaviors during this critical life period as a key focus for research aimed at increasing our understanding of and ability to intervene on disease processes.

Initiatives take as a starting point the well-documented effects on health and disease of low socioeconomic status (SES). They propose longitudinal studies to evaluate the influence of factors in several domains—physical environment, sociocultural environment, individual neurobiology, and individual psychology—upon the adoption and maintenance of health damaging behaviors (e.g., smoking, alcohol and drug use, psychophysiological hyperactivity) across the adolescent years.

A key developmental milestone during this period—puberty—should be a focus of proposed studies of the interaction of biological, psychological, and social responses to puberty as they influence short- and long-term changes in health-relevant behaviors. We need to understand the underlying neurobiological processes at work during adolescence and early adulthood whereby the experience of stress/distress can lead to adverse health outcomes. It is important to focus on the major cause of death and disability in adolescence and young adulthood—violent events and accidents. Research should be performed to attempt to increase understanding of the basic underlying

processes—including biopsychosocial characteristics and health behaviors—that lead to behaviors that predispose to injury events. By seeking to determine the factors involved in the development of biological and behavioral characteristics that potentiate disease processes, the initiatives proposed can lead to identification of targets for interventions to prevent or ameliorate the development of these health-damaging characteristics.

Recommended research approaches.

Research designs should emphasize intermediate prospective studies which can capture developmental patterns that encompass the transitions from late childhood through the pubertal period, to young adulthood. Multiple studies should be funded to span the SES and ethnic spectra. Different applicant institutions should focus on key samples to characterize specific sub-populations. These initiatives have trans-NIH interests.

Disease Processes in the Midlife and Senior Adult Populations

A variety of behavioral and psychosocial factors have been identified as relevant to health. There is an emerging body of evidence that indicates an important role for behavioral and sociocultural factors in the incidence, progression, and consequences of disease. While more work needs to be done in this broad area, there is also a need for investigation of potential common mechanisms which may underlie the impact of behavioral and sociocultural factors, and ethnicity. The initiatives are targeted at examining potential common pathways, understanding the extent to which disease processes may reflect more distant versus more recent or

proximal effects, and the importance of minimizing 'disease'-related disabilities and maximizing function.

Common disease mechanisms that were discussed related to cumulative oxidative damage, down-regulated immune function, and sympathetic hyperactivity to stress. As one example, recent evidence highlights the importance of longitudinal studies of personal relationships: Convergent evidence from several laboratories suggests that social support may interact with chronic stressors to produce differences in sympathetic nervous system (SNS) reactivity, neuropeptide release, and immune function.

Consistent with these data, chronic stress has also been implicated as a factor in enhanced cardiovascular reactivity as well as higher levels of urinary catecholamines in two studies from Baum's laboratory (Fleming *et al.*, 1987; McKinnon *et al.*, 1989); they also reported that cardiovascular measures took longer to return to baseline levels in chronically stressed, compared to unstressed, subjects (see, also, Pardine and Napoli, 1983).

Recent studies of the immunological consequences of brief experimental stressors have provided preliminary evidence that individuals who exhibit the largest "sympathetically mediated" increases in cardiovascular reactivity also show the largest catecholaminergic actions and immune changes (reviewed in Kiecolt-Glaser *et al.*, 1992). If sympathetic activation is a marker or determinant of immune function, then the cardiovascular, endocrine, and immune changes evoked by brief experimental stressors may help to illuminate the nature of the interactions among these physiological systems. The age-related loss of beta adrenergic receptor sensitivity in the face of maintenance of alpha-1 adrenergic receptor sensitivity also highlights the importance of age-related changes in cardiovas-

cular reactivity and their relationship to endocrine and immune function (Lakatta, 1987), particularly in view of evidence that SNS activity can inhibit antigen processing and presentation (Heilig *et al.*, 1993).

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It has also been suggested that narrowing of physiological capacity and ability to maintain homeostasis may be involved in disease processes in the elderly. However, little is known about these changes, including whether they help to explain behavioral and sociocultural influences on disease. "Frailty" may reflect more generalized failure across multiple systems.

For example, immunological changes may also reflect changes in other systems. Evaluation of the blastogenic response in 403 older adults with a mean age of 86 showed that the lymphocytes of 18% of the sample did not proliferate in response to three mitogens (Murasko *et al.*, 1988). While the overall mortality of the population for a two-year period was 15%, negative responders had twice the mortality of positive responders. The major cause of death in both groups was sudden death or a diagnosable cardiovascular-related disease. The authors suggest that decrements in cellular immunity may reflect changes in other systems as well, and may provide one marker of physiological aging.

Similarly, a 16-year longitudinal study of 105 healthy elderly men showed that declines in the

absolute number of peripheral blood leukocytes (PBLs) were associated with subsequent mortality within three years of death when compared with 5 or 10 years before death (Bender *et al.*, 1986). There was no association between the decrease in lymphocyte numbers and age at death, smoking status, or prior cardiac illness. Moreover, a 20-year longitudinal study of 273 health adults over 60 showed that poorer skin-test responses were associated with subsequent morbidity and mortality (Wayne *et al.*, 1990).

While these are provocative studies, research that takes such a broad view of morbidity and mortality has been the rare exception, not the rule, and psychosocial factors have been only been considered infrequently, despite evidence of their growing importance.

Convergent evidence from psychosocial and immunological domains suggests that the links among depression, personal relationships, and immunity could be stronger and could have more potent health consequences for older adults than younger adults. The number of relationships diminishes as people age, and the quality of close relationships becomes more salient (Carstensen, 1992). Thus, troubled relationships could have a greater impact on older adults because of their smaller social networks (Levenson *et al.*, 1993). In addition, immune function declines with age, particularly functional aspects of the cellular immune response (Murasko *et al.*, 1988; Wayne *et al.*, 1990).

Finally, age and distress may interact to promote immune down-regulation: older adults show greater immunological impairments related to depression than young adults (Schleifer *et al.*, 1989). Thus, the increased distress associated with poorer or fewer close relationships could have a greater physiological impact in

older adults compared to younger adults, a process that clearly deserves further study.

Moreover, alterations in social support that result in increased depressive symptoms have important implications for functioning and well-being. Wells *et al.* (1989), reporting on 11,242 outpatients from the Medical Outcomes Study, showed that patients with either a current depressive disorder or depressive symptoms in the absence of disorder had worse physical, social, and role function, worse perceived current health, and greater bodily pain than patients with no chronic conditions. In particular, they noted that the poorer functioning that was uniquely associated with depressive symptoms was comparable or even worse than that uniquely associated with the eight chronic medical conditions they studied.

Depression interacted with these medical conditions in an additive fashion; for instance, among patients who had current advanced coronary artery disease and depressive symptoms, they found twice the reduction in social functioning associated with either of the conditions alone. Among the chronic conditions they studied (hypertension, diabetes, current coronary artery disease, current angina, current arthritis, current GI problem, current lung problems, or current back problems), the only chronic condition associated with greater functional problems than depression was current heart conditions. The authors emphasized that depressive symptoms even in the absence of depressive disorder were associated with considerably poorer functioning and had clear clinical significance. Since the chronic conditions studied by Wells *et al.* (1989) are all associated with increasing age, assessment and treatment of depression would seem important in minimizing the loss of function and disease-related disability.

Understanding possible common pathways is complicated by the unknown extent to which various disease processes in older adults reflect more distant versus more recent or proximal effects; for example, the extent to which the current health status of individuals who stopped smoking some years earlier continues to reflect residual risks or damage. Data from animal models suggest greater plasticity and recovery following chronic stressors in younger animals compared to older animals (Ackerman *et al.*, 1991). Thus, age may also interact with recency of disease processes to influence risk.

As outlined above, older adults represent an important population for whom the maintenance of function and minimization of disability are paramount. The enhanced understanding of common psychosocial and physiological links and pathways could lead to the development of more cost-effective interventions.

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BIOBEHAVIORAL RISK FACTORS

Reflections on Present and Future Research on Bio-Behavioral Risk Factors

George A. Kaplan, Ph.D.

There is a wealth of data linking behavioral and social factors to health outcomes, and these data have led to real advances in our understanding of the bio-behavioral basis of many health conditions, both physical and mental. That's the good news. The bad news is that we have a plethora of risk factors. Lack of integration among these factors has left the public confused as to the relevance and importance of the information available.

Further progress will depend on some fundamental changes in the way in which we conceptualize and investigate this area. This may be particularly true as we try to integrate knowledge of behavioral, social, psychological and socio-environmental factors in our understanding of the natural history of physical and mental health.

Table 1 presents a partial list of behavioral and psychosocial risk factors, very broadly construed, which have been shown to be related to a variety of health outcomes. This list could be three times as long. For example, when Jenkins

(1976) reviewed the evidence, a number of years ago, for the role of psychosocial factors in cardiovascular disease he referenced several hundred articles. If the same review were to be carried out today, the number would be, I imagine, an order of magnitude larger.

One can ask what the advances have been—there have been many—I will illustrate a few from the cardiovascular area. Some of the highlights will come from work in my laboratory and some from the work of others.

Some of the most interesting work in this area comes from the team of investigators at the University of Pittsburgh and the Bowman Gray School of Medicine (Manuck *et al.*, 1988). Their research with a non-human primate model has led to a series of exciting findings showing that sympathetic activation in response to a social stress leads to increased atherosclerosis (Figure 1). In this figure, you can see the extent of coronary atherosclerosis for monkeys raised in both stable and socially unstable conditions for both dominant and non-dominant

Table 1

Partial List of Behavioral and Psychosocial Risk Factors

Smoking	Anger expression/Control
Physical Activity	Cynical Distrust
Relative Weight	Control
Diet	Stress
Alcohol	Sense of Coherence
Coffee	Neuroticism
Antioxidants	Hardiness
Fat	Perceived Health
Social Class	Optimism
Social	John Henryism
Support/Networks	Job Strain
Life Satisfaction	Status Incongruity
Depression	Self-referent Speech
Type A Behavior	Personal Uncertainty
Pattern	Daily Hassles
Hostility	

monkeys. There is a substantial impact of the socially unstable condition on coronary atherosclerosis for the dominant monkeys. Dietary factors were held constant, in this case a mildly atherogenic diet for both experimental and control animals.

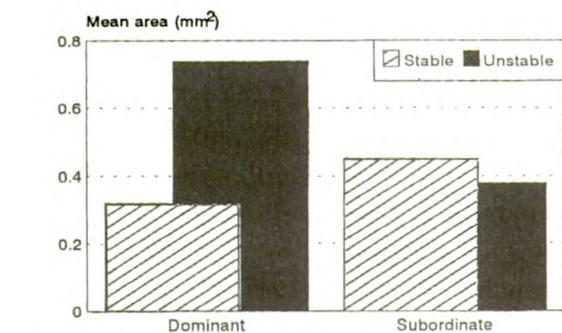
One of the most exciting results to come from this work is that treating the dominant monkeys with propranolol removes the effect of the unstable environment on the dominant animals (Kaplan *et al.*, 1987). This is a very elegant way to provide data which supports a role for sympathetically driven vascular reactivity in the face of social disruption as being important in the pathogenesis of coronary heart disease.

The development of non-invasive imaging techniques is beginning to revolutionize our ability to understand some of the pathways which link behavioral and social events to health outcomes. Figure 2 shows an example

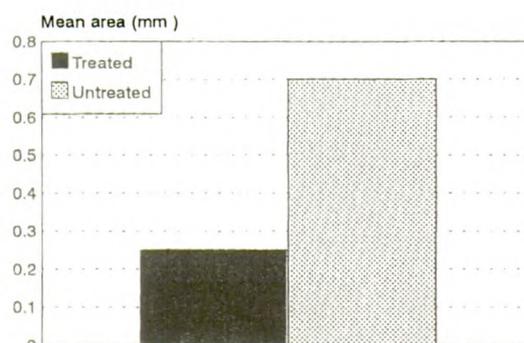
Figure 1

Extent of coronary atherosclerosis by environmental and individual characteristics, and Alteration of effect of social disruption in dominant cynomolgus monkeys by propranolol

(adapted ref. 2 & 3)



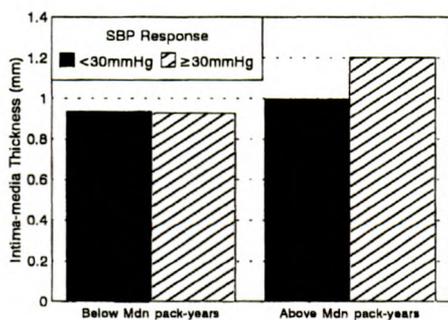
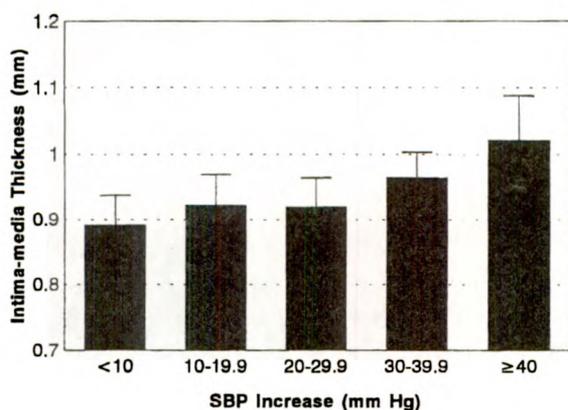
Kaplan, Manuck, Clarkson et al. (1982)



Kaplan, Manuck, Adams et al. (1987)

Figure 2

Extent of carotid atherosclerosis by anticipatory systolic blood pressure response, and Carotid atherosclerosis by anticipatory blood pressure response and smoking



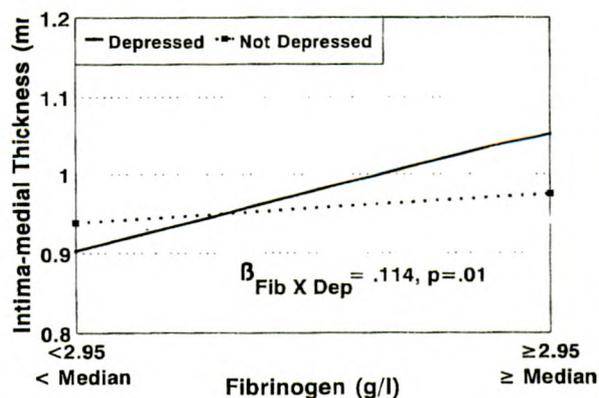
of the use of one such technique from my laboratory. The figure shows the association between systolic blood pressure response to an anticipatory stress—the difference between a resting systolic blood pressure taken during a standard blood pressure protocol and the same sitting, resting pressure taken just before the beginning of a maximal exercise—and the extent of carotid atherosclerosis determined by B-mode ultrasound. As you can see there is a regular and linear relationship between the anticipatory response and the extent of carotid atherosclerosis. This research, taken from a

study which we are conducting in eastern Finland again suggests a role for sympathetically driven vascular reactivity in the development of atherosclerotic vascular disease. The figure also shows the results when we took this systolic blood pressure response and looked at its association with carotid findings as a function of smoking. The association was found only in heavier smokers—so we see a bio-behavioral interaction, with the anticipatory stress response seeming to only be associated with carotid findings in heavy smokers.

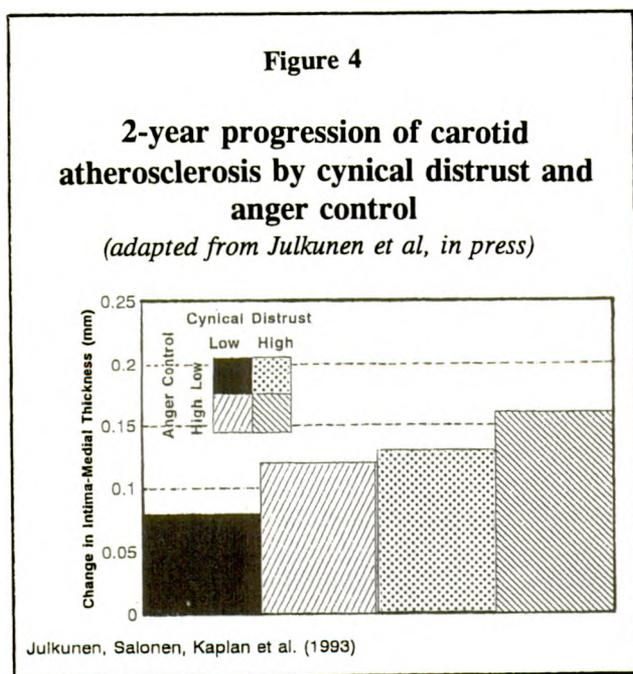
Similar kinds of bio-behavioral interactions were shown in another study from this cohort in which we examined the association of fibrinogen levels with carotid atherosclerosis (Figure 3). In the analyses shown here, we found that the association between fibrinogen and atherosclerosis varied as a function of depression measured by the MMPI. Depression seemed to potentiate the impact of fibrinogen on atherosclerosis. These studies indicate that psychosocial factors may play a very important role in the development of atherosclerotic heart disease.

Figure 3

Carotid atherosclerosis by fibrinogen and depressive status



Another factor which has received considerable attention is that of hostility. Figure 4, from the same study in eastern Finland, illustrates the importance of a factor related to hostility, cynical distrust, in the two year progression of carotid atherosclerosis. The figure shows the amount of change in carotid atherosclerosis as a function of cynical distrust and anger control, adjusted for baseline level of atherosclerosis and lipids, smoking, blood pressure and a variety of other factors. As you can see, those who were highest on cynical distrust and anger control had the greatest progression of atherosclerosis.



These are only illustrations of a vital and growing area of bio-behavioral research. We are getting more and more knowledge about some of the biological pathways which mediate psychosocial and bio-behavioral effects, in this case on cardiovascular disease. There are many important and substantial exciting contributions coming from this area.

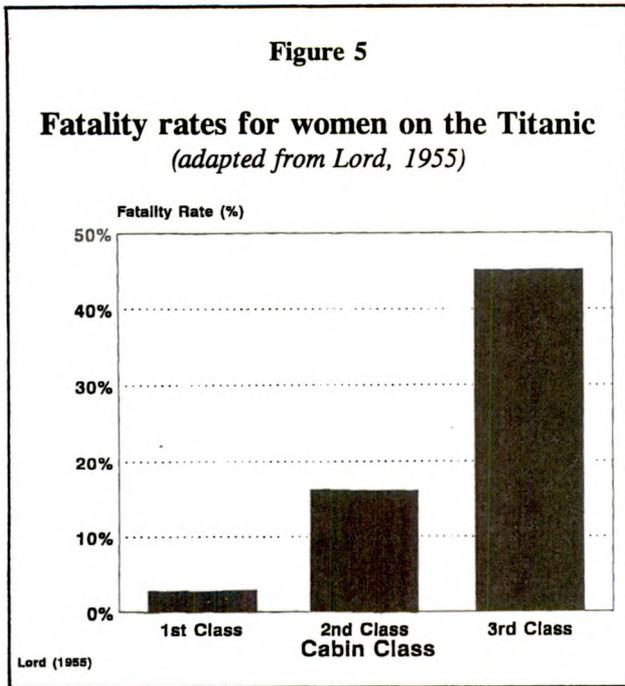
Having discussed some of the more successful findings, let us consider six areas in terms of future directions. The first is to take social class seriously. The second is the study of the natural history of risk factors. The third is to abandon the notion of independence. The fourth is to consider the ecologic niches in which people live. To probe diversity is the fifth. And the last, to examine the public health implications of bio-behavioral research. Now that these are stated very telegraphically let me go through them one at a time.

I. Take social class seriously

The association between various measures of social class and a wide variety of health outcomes has been known for hundreds of years. Anyone who has looked at this field cannot help being impressed by the stability of these associations across time, across measures of social class and across geographic place (Haan et al., 1989).

In fact it is so widespread that the way we deal with it is to control for it, adjust for it, pretend it's not there, or take out its impact in some other way. I would like to propose that we need to do just the opposite, to probe social class differentials in health much more extensively and to really see this as an important source of heterogeneity in the health experience of populations and one which is desperately in need of explanation.

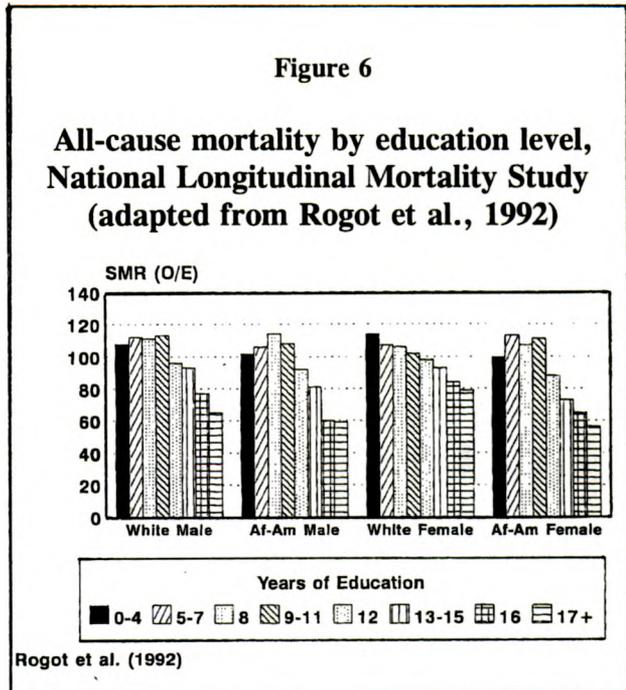
For example, Figure 5 shows the fatality rates for women on the Titanic as a function of a proxy for social class—ticket class. Although it was women and children first, not all women were first—the lowest mortality rates were among the first class women and the highest among those in third class. Figure 6, from a



study of over a million people in the United States, shows the association between all cause mortality and educational level. Generally speaking, people at the higher educational levels do the best and people at the lower levels of education do the worst. For those who remain alive the prevalence of fair or poor health by education from the National Health Interview Survey shows a linear relationship (Figure 6). From the same survey, there is a large list of health conditions which are more prevalent in those with less than a high school education (Table 2).

Survival also appears worse among lower social class patients. In this case (Figure 8), patients with documented coronary artery disease showed a monotonic increase in survival rates as a function of income even after extensive adjustment for prognostic indicators.

Quality of life is also related to socioeconomic factors. A recent study by Guralnik *et al.* (1993) examined active life expectancy as a



function of education level. The growing interest in active life expectancy is based on the observation that we want to "add life to years, not just years to life." These investigators found that those who had greater levels of education had greater active life expectancy (Figure 9). So if you survive to 65 years or beyond, your future quality of life will be heavily dependent on your current socioeconomic level. We are currently examining how this applies to domains beyond physical functioning in a 29-year followup of the Alameda County Study, a population-based study of approximately 7,000 people in Alameda County, CA.

Turning to mental health measures, there are also strong gradients associated with social class. Figure 10 shows nine year incidence of high levels of depressive symptoms as a function of education and income from the Alameda County Study. There is increasing incidence of high levels of depressive symptoms associated with low education and with low income.

Table 2

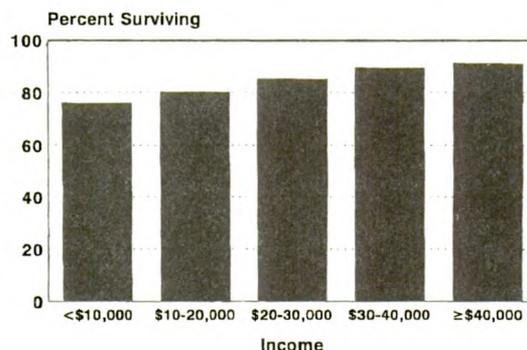
Chronic Conditions More Prevalent Among Those With <12 Years of Education

National Health Interview Survey, 1989: 65+ years

Arthritis	Goiter
Gout	Diabetes
Intervertebral disc dis.	Anemias
Bunions	Migraine
Psoriasis	Neuralgia/Neuritis
Visual impairment	Ischemic Heart Disease
Cataracts	Other Heart Disease
Hearing Impairment	Hypertension
Speech Impairment	Cerebrovascular Disease
Paralysis	Ulcer
Ulcer	Abdominal hernia
Abdominal hernia	Gastritis
Gastritis	Kidney disease
Kidney disease	Indigestion
Indigestion	Diverticulitis
Diverticulitis	Constipation
Constipation	Hardening of the Arteries
	Varicose Veins
	Hay Fever
	Chronic Sinusitis
	Emphysema

Figure 8

5-year survival of patients with coronary artery disease by income
(adapted from Williams et al., 1992)

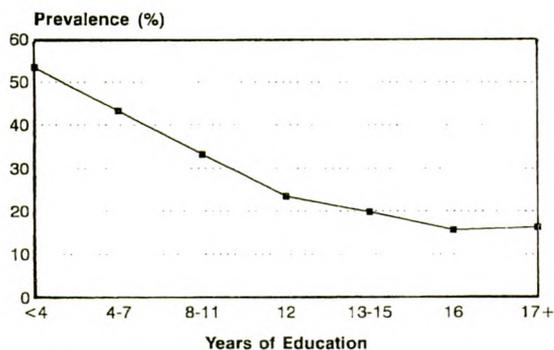


Williams, et al. (1992)

Figure 7

Prevalence with fair or poor health by education, National Health Interview Survey

(adapted from Series 10, No. 179)

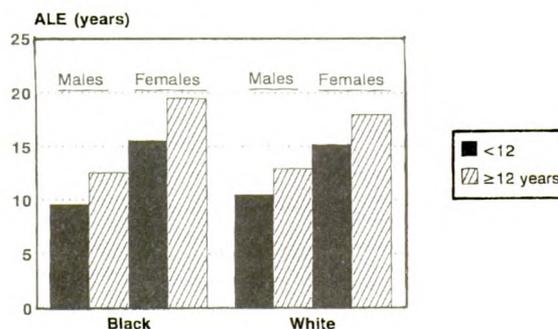


Series 10, No. 179

Figure 9

Active life expectancy at age 65 by education and race

(adapted from Guralnik et al., 1993)



Guralnik et al. (1993)

Similar relationships apply to many behavioral risk factors. Again from the Alameda County studies, Figure 11 shows that quitting smoking was related to income with those at the highest income showing the highest rates of quitting and those at the lowest income showing the lowest rates of quitting. In general, the adoption, maintenance and elimination of most high risk behaviors are related in the same way to socioeconomic factors.

In fact, most behavioral, psychosocial, and socioenvironmental risk factors are related to socioeconomic level. In another study in Alameda County, this done in 1989-1991, not only were behavioral risk factors, health conditions and preventive behaviors related to income level, but also living in an unsafe neighborhood, being a crime victim having less than two close friends, having no sources of tangible support, no sources of emotional support, no health coverage, no money to see a physician, no job control and feeling unappreciated.

For those interested in hostility and anger issues, the next figure (Figure 12) shows levels of cynical distrust, from a study we are conducting in eastern Finland, as a function of education, income or childhood socioeconomic conditions before age 10. The most cynically distrustful people are those who have the lowest education, the lowest income or the lowest childhood economic circumstances. This certainly suggests a strong environmental component for cynical distrust.

In attempting to understand these complex relationships the usual procedure is to statistically adjust, using some type of regression procedure, for a variety of behavioral and social risk factors to see if we can explain away the association. Figure 13 illustrates this approach with a measure of ischemia resulting from exercise obtained from a population sample in Eastern Finland. Those who are in the lowest income quintile had roughly twice the risk of showing an ischemic response to exercise. We then adjusted for a long list of behavioral risk

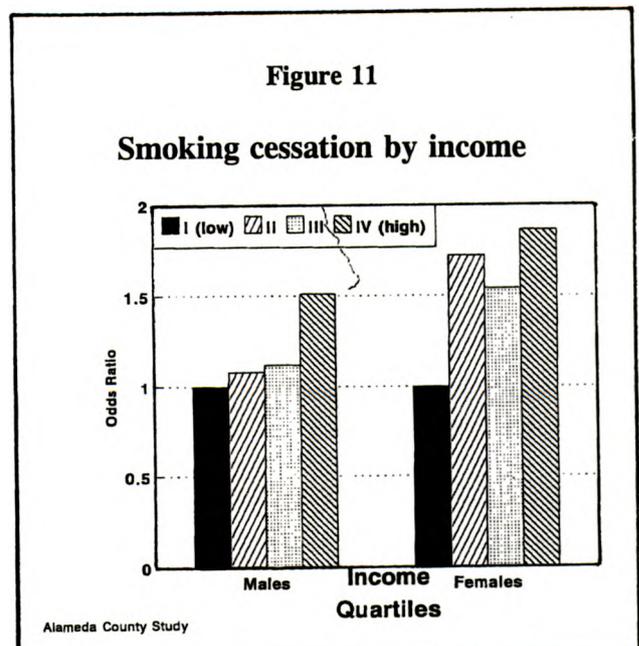
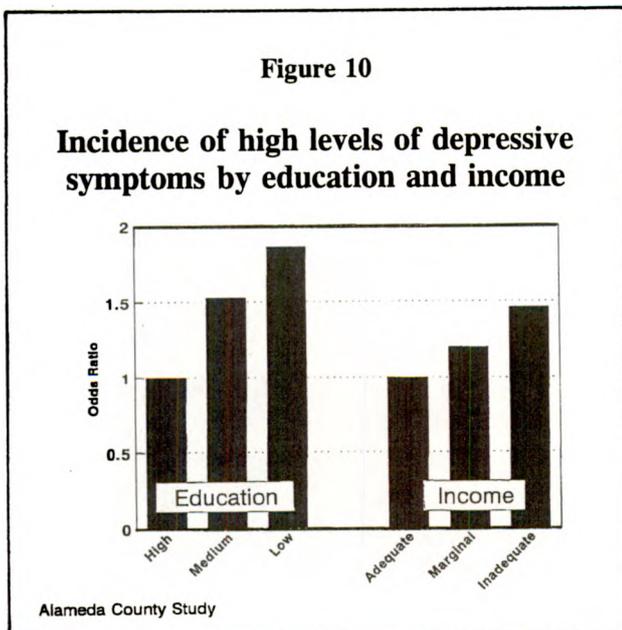


Figure 12

Cynical distrust by education, income, and childhood socioeconomic status

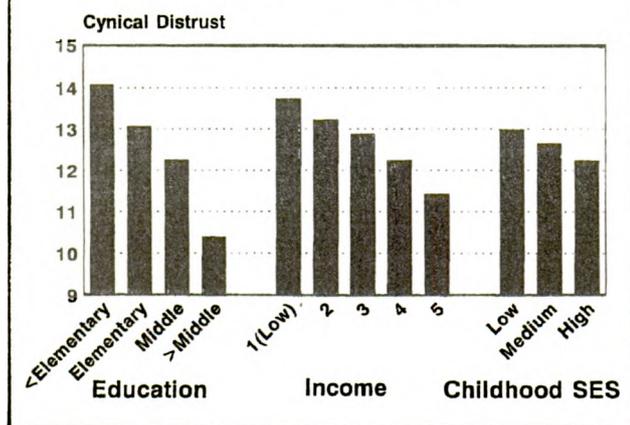
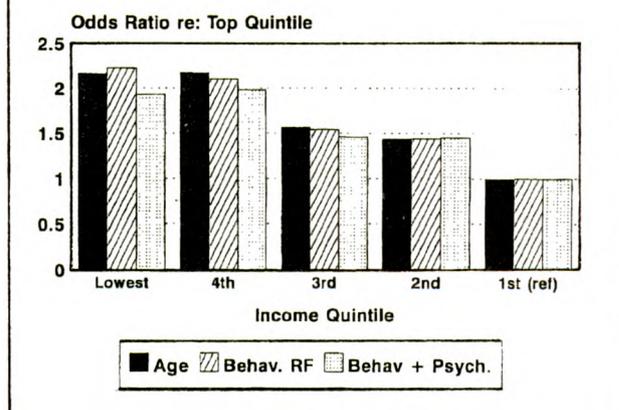


Figure 13

Ischemia on exercise by income with adjustment for age, behavioral, and psychosocial factors



factors: smoking, lipids, alcohol, relative weight, physical activity, and fibrinogen. Adjustment for these factors really made little difference in the income/ischemia on exercise association.

A number of psychosocial variables were then added to the analysis: cynical distrust, Jenkins Activity Survey Type A score, Framingham Type A score, MMPI depression, Sense of Coherence, John Henryism, and measures of job strain. The results indicated that these variables also did not influence this association. This is a recurrent pattern—when we see associations between socioeconomic factors and health outcomes, it is the rule rather than the exception that adjustment for other possible explanatory variables does not influence the results.

In addition to the social policy implication of socioeconomic gradients, and the changes in those gradients over time, we need to see socioeconomic gradients in health as an opportunity to understand much more about the

natural history of health status, and to use this knowledge to inform our understanding of the bio-behavioral links with health over the life span.

II. Study Natural History

It is common in bio-behavioral research, whether it be done in the context of behavioral medicine, epidemiology, psychosomatic medicine, health psychology, or other disciplines, to give scant attention to the natural history of risk factors, their introduction, progression, and disappearance over time. However, there is much to be learned, both substantively and methodologically, from the natural history of bio-behavioral risk factors.

For example, Figure 14 from the Alameda County Study shows changes in levels of leisure-time physical activity as a function of smoking, level of depressive symptoms, and social isolation (Kaplan *et al.*, 1991). As you can see, all of these factors were associated

with 9-year declines in physical activity. The next Figure (Figure 15) illustrates the role of depression and physical activity in the incidence of social isolation. As you can see, low levels of leisure-time physical activity and high levels of depressive symptoms are both strongly associated with increased incidence of social isolation. Similarly, social isolation and physical activity are related to the incidence of depression so that those who were socially isolated or who were sedentary tend over time to report much higher rates of high levels of depressive symptoms (Kaplan *et al.*, 1987) (Figure 16). Figure 17 verifies these observations in that those who were physically active at two points in time separated by nine years subsequently have the lowest levels of depressive symptoms, and those who were inactive at both times had the highest level (Camacho *et al.*, 1991). In addition, the Figure shows that changes in physical activity were also associated with the subsequent natural history of depressive symptoms.

Temporal factors are important in understanding the natural history of risk factors. For example, Figure 18 displays the association between childhood socioeconomic conditions (Kaplan & Salonen, 1990) and adult risk factors. Those who were poor as children had higher total cholesterol, lower physical activity, higher LDL, lower HDL, and were more likely to be smokers. Thus, longitudinal studies beginning in childhood are necessary to truly understand the natural history of risk factors.

Changes in smoking consumption in the United States are a good illustration that many of the important changes in risk factors levels in the population are not driven by individual decision making, but reflect large-scale social events (DHHS, 1989) (Figure 19). Many behavioral factors related to health outcomes are strongly driven by societal forces not under the control of individuals; behavioral medicine must consider larger units of analysis than the individual, i.e., changes in social norms and socioenvironmental events.

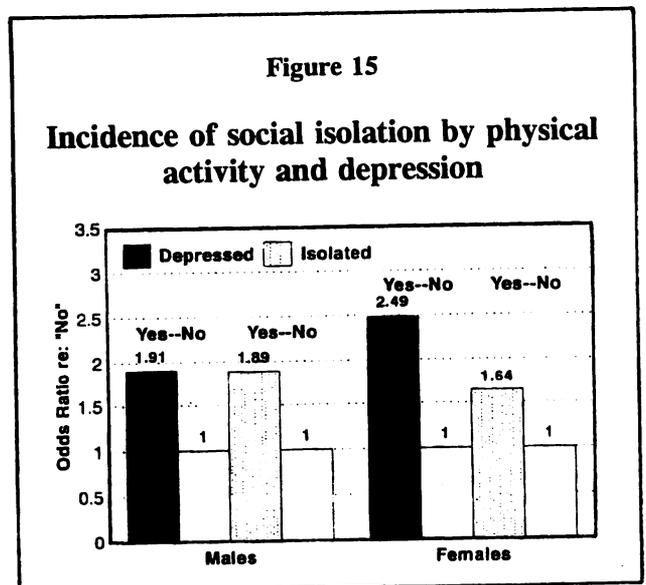
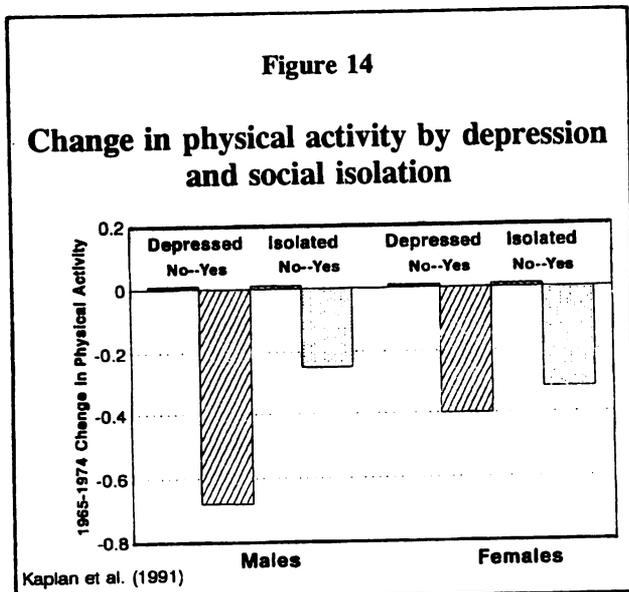


Figure 16

Incidence of depression by social isolation and physical activity

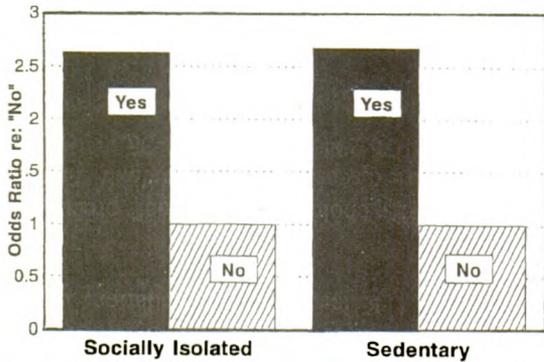


Figure 18

Childhood socioeconomic conditions and adult risk factors

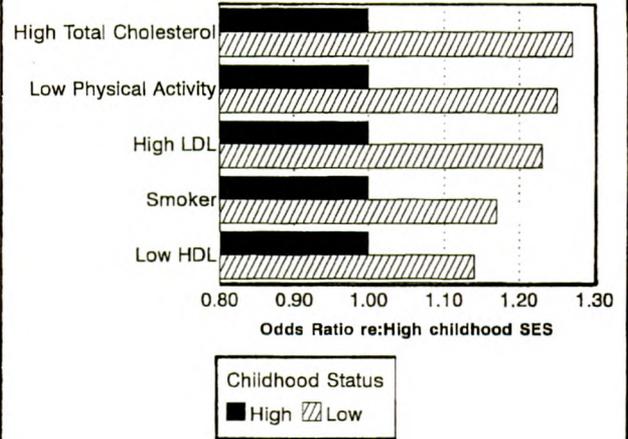


Figure 17

Incidence of depression by 9-year change in physical activity

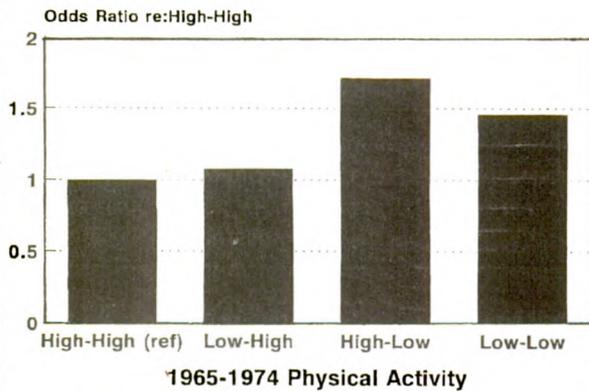
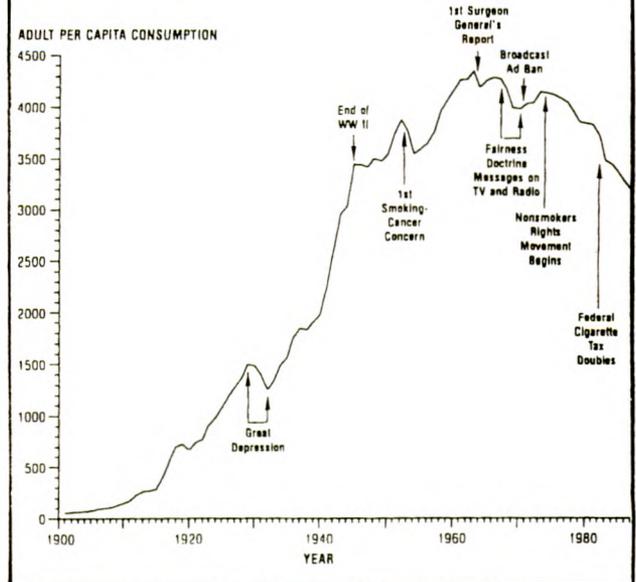


Figure 19

Cigarette consumption trends



III. Abandon the Notion of Independence

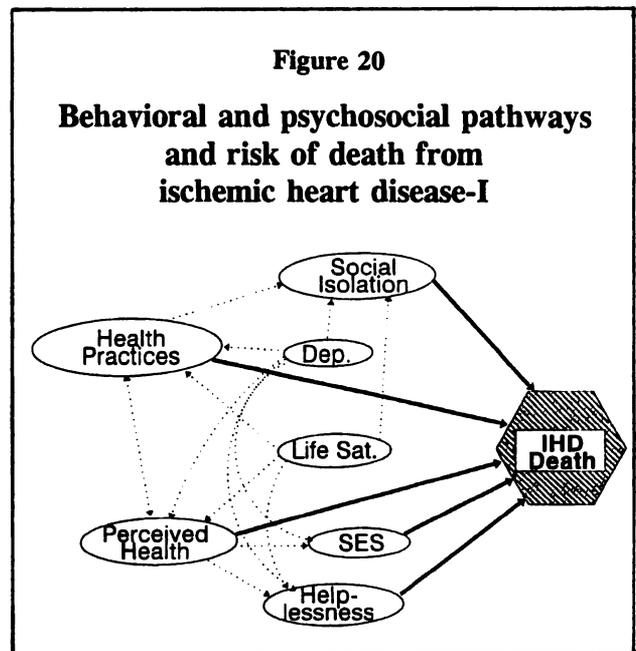
As mentioned earlier, there are methodologic issues to be addressed in understanding the relationship of biobehavioral factors to health outcomes. In the previous section on the natural history of risk factors, you may recall that everything was associated with everything—that is, level of depressive symptoms predicted changes in physical activity and incidence of social isolation; social isolation predicted changes in physical activity and incidence of high levels of depressive symptoms; and, level of physical activity predicted incidence of social isolation and high levels of depressive symptoms.

We need to start thinking seriously about our standard approach to analysis involving multivariate analyses which evaluate the "independent" effects of one factor on another. The standard approach is to put a series of potentially important factors into a multivariate model, let them compete in terms of effect sizes and variability, and finally come up the "independent" factor.

This focus on single independent risk factors leads to research which competes as to which bio-behavioral risk factor is the most important. Unfortunately, this distorts the complexity of the systems we are studying, and does a disservice to the complexity of the bio-behavioral determination of health status. Rather than trying to reduce everything to a single factor or pathway, we should be looking at patterns of associations, clustering of factors over space and time, and complexity in biological pathways.

Another example from the Alameda County Study (Figure 20) summarizes the results of

analyses of how well behavioral and social risk factors predicted the risk of death from ischemic heart disease. The solid lines show "independent" effects and the dotted lines show indirect pathways (Kaplan, 1985). If all of these factors were entered into a multivariate model, the results would focus only on the "independent" effects; the pattern of interconnections between all these variables and the system of relationships are, in fact, of greatest interest. This tendency to place multiple variables into a regression model does tremendous disservice to the dense recursive and reciprocal relationships between the factors we are studying.



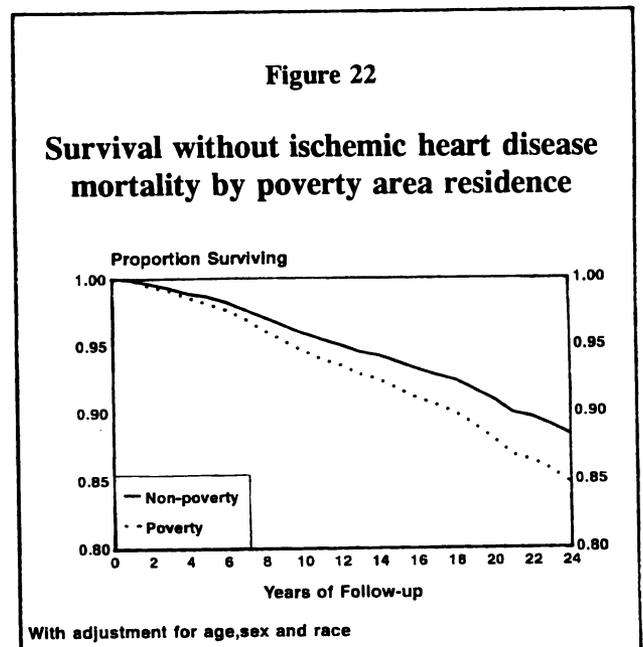
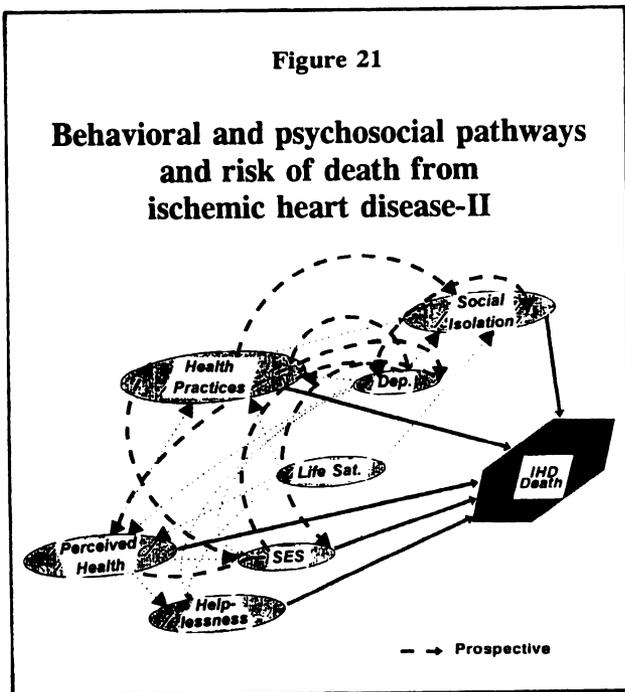
The cross sectional measurement of risk factors, even in a longitudinal study, is uninformative with respect to the casual ordering between variables. That is, when we do this kind of analysis in which all factors are measured at the same time we potentially lose the fact that one risk factor may be importantly involved in the development of the another risk factor.

When some of these temporal processes (Figure 21) are considered, the analyses become admittedly more complex, but it may be a much more realistic representation of the complexity of what we are studying. Also, cross-sectional measurements of variables and the typical "multivariate stew," may give us what are statistically independent estimates of risk factor effects, but this concept of statistical independence may bear little relationship to the real world. Risk factors cluster together cross-sectionally and over time, and the recursive and dynamic relationships between them, which may be of critical biologic importance, are not captured by the usual analyses. The simple cause-effect model of relationships characteristic of traditional physics simply does not hold for human behavior, nor for the complex bio-behavioral pathways which are the determinants of health status in individuals and in populations.

IV. Consider the Ecologic Niche

To address the problems noted above will require more than new models, however interesting and useful that may be. We must change our focus to consider the spatial and temporal clustering of risk factors and to view patterns of risk factors over time and in space, i.e., geographically, as the object of our analysis.

For example, a number of years ago we examined the association between residence in a poverty area and risk of death (Haan *et al.*, 1987). Figure 22 shows the probability of surviving without a death from ischemic heart disease for those residents of the Alameda County study who lived in a poverty area versus those who did not live in such a poverty area. We found, not surprisingly, substantially better survival among those who lived in the non-poverty area. What was surprising was

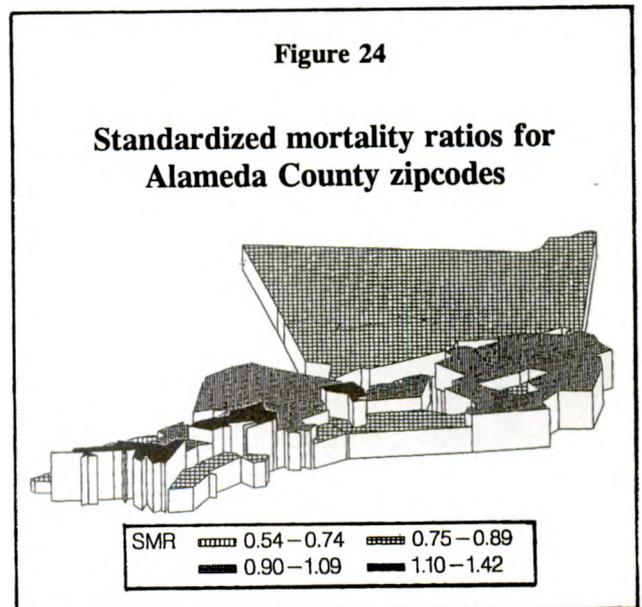
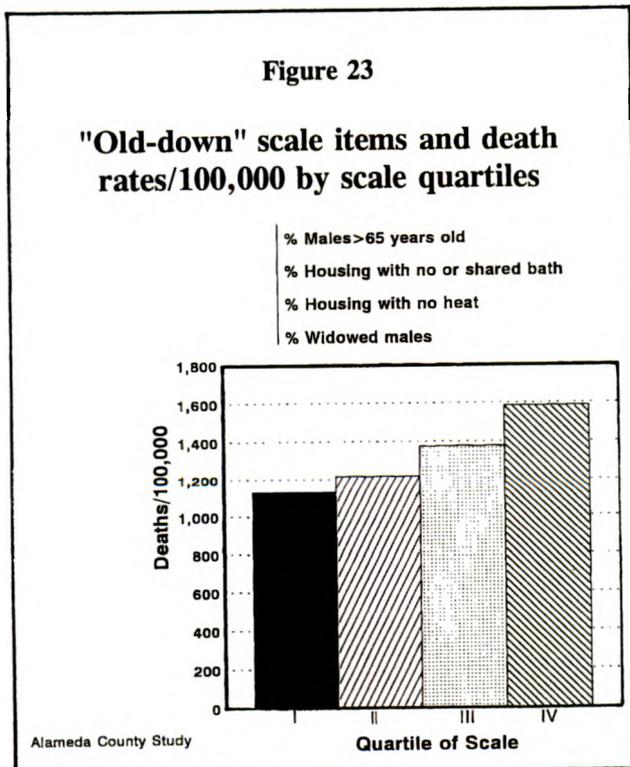


that when we statistically adjusted for age, sex, race, smoking, physical activity, income, education, access to health care, obesity, depression, social isolation, and other variables, those who lived in the poverty area were still at increased risk. The results were little different when we simply adjusted for age, race, and sex.

These results, among others, led us to speculate that there might be properties of the areas in which people live which convey risk, independent of individual characteristics. In some similar analyses, we constructed some scales based on analyses of census tract characteristics and examined whether these characteristics also predicted risk of death (Haan *et al.*, 1989). Figure 23 shows the results from one of these analyses. In this case this scale represents the percent of males who are old, percent housing with no or shared bath, percent housing with no heat, and the percent of widowed males. If you

live in a census track which is high on this scale you have a mortality rate about 30-40% higher than if you live in a census track which is low on this scale. Again, this finding persisted after statistical adjustment for dozens of covariates, in various combinations. These studies provide additional evidence that the properties of the area in which we live may be very important in terms of understanding the heterogeneity of mortality risk within the population.

In order to pursue this further, we turned to an examination of the small area variations in health status. Figure 24 shows standardized mortality ratios (SMR) for deaths from all causes for zipcodes in Alameda County California (Kaplan *et al.*, 1991). The SMR is essentially the ratio of observed to expected deaths for each zipcode. In this figure, the SMRs are plotted as altitudes, so a "mountain" corres-



ponds to an area of high excess mortality. Not surprisingly, we found that mortality is not randomly distributed in the county, and there was a mountain range of excess mortality. The same zones of excess mortality were found whether we looked at mortality among the young or the old, whether we looked at all cause mortality, cardiovascular, or lung cancer mortality, or whether we looked at hospital discharges.

There seem to be health characteristics of areas—while these health characteristics must be composed of the health status of individuals, a focus on the properties of areas leads to a different kind of analysis. For example, when we looked at the factors which were more prevalent in the high versus the low SMR areas, we found many differences. High SMR areas had higher prevalence of low education, being unable to fill a prescription in the last month because of inadequate money, having few friends, living in an unsafe neighborhood, low emotional support, low tangible support, being sedentary, low income, being a crime victim during the last year, having inadequate food at least once a month and being a current smoker.

These findings suggest that we need consider what you might think of as the "ecologic niche" in which individuals live. Our evidence suggests that a wide variety of hazards, at the personal and socioenvironmental level, cluster together in high SMR areas, and we suggest that the totality of these properties, and their interactions, define a unique ecologic niche which may carry with it health consequences. When we combined these characteristics into demands and resources (Table 3), we found that people who live in high SMR areas are ten times more likely to report high levels of demands and low levels of resources.

Table 3

Demands and Resources

Demands

- Daily activity is hard, repetitive, and fast
- Live in unsafe neighborhood
- Crime victim
- Poor health
- Inadequate money for food, medicine, or medical care

Resources

- Daily activity involves decision making and control
 - Top 60% income
 - ≥ High School Education
 - Some health insurance
 - ≥2 Close friends or relatives
 - ≥ Source of emotional support
 - ≥ Source of tangible support
-

These findings support the development of an approach to the socio-environmental conditions in which people live which is not simply focused on individual behaviors but which focuses on the entire complex of behavioral, social, psychological, and socio-environmental properties, and their relevance to the health experience of these individuals. While these are only preliminary findings, it suggests an expansion of the bio-behavioral agenda, perhaps to a consideration of specific patterns of physiologic response to particular types of ecologic settings.

V. Probe Diversity

It goes without saying that we need to do a much better job of looking at diversity in terms

of age, ethnicity, culture, and gender. But, our task extends beyond the now commonplace exhortation to be inclusive of age, race, ethnicity, and gender in our studies. We need to remember that there is considerable overlap between the distributions of risk factors and health measures in all these groups. To the extent that we address this situation by talking simply about men and women, young and old, blacks, Hispanics, whites, or other groups, we really lose substantial explanatory power. Our focus needs to include all groups in order to fully sample the heterogeneity of both the risk factor and health experience in the population. But, in addition, we need to be cognizant of the substantial heterogeneity within groups, the substantial overlap between groups, and the analytic imperative to examine contributors to both within and between group differences.

VI. What are the Public Health Implications of Bio-Behavioral Research?

We need to continually examine the public health implications of bio-behavioral research and its presentation to the public. The public is bombarded by information. They do not know the significance of it, they do not know who to believe, and they do not know if what they read about hostility or type A or depression or smoking or alcohol consumption or aspirin is true.

I believe it is the responsibility of bio-behavioral researchers to provide a context or metric by which to interpret findings. There are some very simple metrics that one can use: how much is the public's health can be explained by factor X; can the factor be modified; how important is the factor relative to other factors? To maintain our credibility with the public we

need to develop metrics which allow us to determine the extent to which we are talking about phenomenon which have a broad public health significance.

Now these are not simple tasks, they are quite complex; but behavioral, social, psychologic, and socio-environmental factors are at the heart of the public's health, influencing virtually every aspect of physical and mental health. This is a fact which will not be modified by molecular biology. To ignore this complexity is to trivialize the true contributions that studies of the behavioral and social foundations of health can make and to impair our ability to deliver on our obligation to develop bio-behavioral knowledge in service of improvements in the public's health.

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Prenatal/Infant/Child

Overview

Lewis P. Lipsitt, Ph.D.

More children die and become debilitated today from behavioral misadventures than from all diseases combined. Accidents, homicide, suicide, and the consequences of drug and excessive alcohol use, dangerous sexual practices, and violence of all sorts, are the principal causes in recent years of the increased mortality and morbidity of American children and youth.

The Task Group finds that stemming the rising tide of death and debility from essentially preventable environmental and experiential causes will require substantial investment in the acquisition of knowledge about our young people. In order for our culture to understand the precursors of life-span adversity, we must carry out extensive longitudinal studies of children from birth through adolescence.

Numerous studies have shown the great influence of socio-economic level on the course of development of children. Specifically, poverty has laid claim to a large part of the variance in young people's destinies, with most meta-analyses showing low-socioeconomic status carrying more of the variability than any other variable, or cluster of variables, in relation to the developmental and intellectual destinies of American youth. Additional research is needed to more adequately investigate the mechanisms

of development and processes of learning related to why children reared in such circumstances do so poorly, in terms of school achievement, anti-social behavior, delinquency and criminality, and other unfortunate outcomes.

At the same time, we are acutely aware that many children born into and enduring circumstances of poverty and other adverse conditions of early development grow up to become well-adjusted and productive citizens—even exceptionally well-performing individuals. Developmental psychologists have become increasingly curious about the protective factors in the lives of such individuals which make them "targets for developmental safety." How is it that of two children reared in adjacent homes under similar conditions of apparent adversity, one becomes a school failure involved in anti-social/criminal behavior while the other emerges free of these unfortunate outcomes?

The scientific investigations exploring these important aspects of human behavior and development will be costly; ignoring these issues, however, will be far more so in terms of the cost to the overall health and welfare of our citizenry. Our Task Group believes that appropriate studies will guide the way toward well-

considered, rational, and effective public health policy interventions. Without this information, it is doubtful that the piecemeal and palliative

approaches to these problems will be any more effective twenty years from now than they have been for the past twenty years.

Task Group Initiatives

✓ *Biobehavioral Protective Factors: A Prospective Study of Resilient Children (B-1-1)*

Need and Justification

The majority of lower SES children are exposed daily to many biobehavioral risk factors such as single head of household parents, working or absent parents, violence, exposure to environmental toxicants, poor access to health care, etc. A vast literature involving many longitudinal studies indicate that these children have high rates of morbidity and mortality as a consequence of being exposed to such risk factors.

There are a minority of these children, however, who despite deleterious environmental and behavioral circumstances, succeed by usual standards of assessment of unimpaired life-span development. If we could understand why and how these children are able to avoid adverse later development, this would contribute to successful interventions, theories and techniques that may benefit all children.

L.B. Murphy, a pioneer in conceptualizing resilience and protective factors, provided some

of the earliest examples of vulnerability in early development, and of protective factors in the environments of children that could obviate adverse outcomes. Garmezy, Rutter and Werner further contributed to the knowledge base with their studies of developmental factors in vulnerability. Much more remains to be learned about these important matters.

Research Approach/Methodology

A longitudinal prospective study in the context of a "Behavioral Framingham" should be undertaken with a cohort of at-risk children to determine which factors convey protective resilience and allow for normal development, and how they do so.

Cross sectional retrospective studies based on extant data bases should also be done to identify likely variables to focus upon in proposed longitudinal prospective studies.

✓ **Mechanisms/Processes Underlying Unintentional Injury in High Risk Children (B-1-2)**

Need and Justification

Unintentional injury is the leading cause of mortality in childhood, accounting for more than half of all childhood deaths. Demographic predictors include age, race/ethnicity, gender, and socio-economic status. For example, children under age 5 are most at risk for drowning. Children under 5 who live in substandard housing are most at risk for lead poisoning and fatality from fire. Death from motor vehicle accidents is the most common cause of death in childhood. While all 50 states now require safety restraints for young children, many do not mandate safety restraints after 5 years of age. More than half of adolescents report that they do not use seat belts despite the fact that motor vehicle accidents are the number one killer of children in this age group. Although the risk of head injury for unhelmeted bicyclists is more than 6.5 times greater than for helmeted bicyclists, only 8% of U.S. bicyclists wear helmets. (Source: Healthy People 2000)

While epidemiological data suggest important associations between demographic factors and unintentional injury, the mechanisms underlying these associations are poorly understood. Possible mechanisms include cognitive (e.g., attitudes, beliefs), behavioral (e.g., impulsivity), and environmental (e.g., readily accessible environmental hazards) factors. These mechanisms need to be studied both in the child and in the child's social environment (e.g., parents, peers, school and community). For example,

children's activity level, and beliefs/expectations may influence risk-taking behavior. Similarly, parents' beliefs/expectations may influence parenting behaviors such as the extent of supervision or effort to modify the environment or the child's behavior. Environmental hazards that are left within easy access to children, may "set the stage" for injuries to occur.

Not all at-risk children have unintentional injuries. Of interest are child as well as parental/peer environmental variables that seem to differentiate those children who remain safe from those who are injured.

Research Approach/Methodology

Known high-risk groups should be targeted. Retrospective studies of seriously injured children compared to noninjured children may serve a role in developing hypotheses. A prior injury group may also serve informatively for prospective study since prior injury is predictive of subsequent injury. Prospective studies which include minor injury or "near-injury" (e.g., mother catches child falling off a table) may assist in identifying underlying mechanisms since serious injury may be too infrequent to study easily using prospective designs. Although most research designs may focus on individual behavior (of the parent, peers, or child), studies of community norms or standards could be helpful.

✓ **Determinants of Health-Promoting Lifestyles/Behaviors (B-1-3)**

Need and Justification

Substantial data from epidemiologic and clinical studies of adult populations link patterns of dietary intake and physical activity with premature morbidity and mortality. For example, sedentary lifestyles have been associated with increased mortality from all causes. Data generated from pediatric population-based studies, including Bogalusa, Muscatine and the LRC Prevalence Study, indicate that dietary intake and physical activity are associated with physiologic risk factors for cardiovascular disease (CVD) including lipid profile, blood pressure and adiposity. Data indicate that these physiologic risk factors demonstrate considerable intraindividual clustering and tracking, albeit generally increasing with age throughout childhood and adolescence. Minimal data exist, however, on the emergence of risk for CVD during infancy, a time of rapid growth and developmental change, and early childhood, a formative time in the development of health-promoting lifestyles.

Health-promoting behaviors including patterns of dietary intake and physical activity are established early in childhood and are influenced by both individual and familial factors.

Lacking are data on the specific determinants of these lifestyle/behaviors. Specifically, minimal data exist regarding the interaction of genetic and environmental influences on the individual and familial determinants of patterns of dietary intake and physical activity in early life. While evidence suggests that familial factors can facilitate or impede the adoption of health-promoting behaviors, lacking are data on family composition, ethnicity, gender and socioeconomic status. Further, minimal (scattered) data exist regarding the influence of dietary intake on physiologic risk factors for CVD (and other chronic diseases) including lipid profile, blood pressure and adiposity during infancy. Collectively, these data suggest that prospective, longitudinal studies of the determinants of these lifestyle behaviors and their association with selected health-related outcome parameters (i.e., risk factors for CVD) beginning in early life are warranted.

Research Approach/Methodology

Multidisciplinary, longitudinal studies incorporating both developmental and epidemiologic methods are recommended.

✓ **Effect of Early Family and Environmental Stressors on Development of Physical Illness in Infants and Children (B-1-4)**

Need and Justification

Despite a general belief that certain family and environmental stressors have negative impacts on infants and children, there is a lack of clarity with respect to which physical illnesses are mediated by stressors, and how individual differences in behavior and neuroendocrine responses to stress may impact on disease development. We do not know whether or not there are individual differences in the propensity for specific diseases triggered by stressors. There are few relevant studies which have bridged the gap between the basic physiology studies in animals and the biobehavioral aspects of disease in children. We do not have a good understanding of how specific stressors can lead to illnesses which occur months or years following the stressful events or, on the other hand, how such events may be positive with respect to health. There is speculation about the early "inoculation" effect of early life experiences on subsequent health and coping, but this has not been documented in prospective, long term studies in childhood.

Research Approach/Methodology

These research questions require

- ▶ a multi-disciplinary approach involving experts from a diverse array of biomedical and behavioral sciences.

- ▶ attention to the interaction of life stressors with other psychological and biological processes in the etiology of diseases.
- ▶ definitions of stressors including physical environment, family structure, parenting styles and functioning, exposure to natural disasters, social turmoil, loss of significant caretakers and peers, and medical interventions.
- ▶ dependent outcome variables to include physical illness such as growth disorders, autoimmune diseases, asthma, and diabetes.
- ▶ independent variables to include intrinsic differences in personality, autonomic responses, neuroendocrine responses that may mediate responses to specific stressors.
- ▶ a firm theoretical perspective related to how events may lead to distal disease events with respect to both processes and mechanisms.
- ▶ the refinement of mathematical models that permit the analysis of complex arrays of longitudinal, sequential data.
- ▶ the development of appropriate animal models to investigate the processes linking early life stressors as a risk factor and later illness.

Adolescent/Young Adult

Overview

Leonard Epstein, Ph.D.

Adolescence is an important period for the onset of many health behaviors such as drug use and abuse, sexual activity, and eating disorders occurs during adolescence and young adulthood. During these developmental periods there are a unique set of biological and behavioral conditions that may be important in the development of healthy and unhealthy behavior. Biological changes, such as maturation of brain structures and sex-specific hormone changes, in combination with changes in family and peer influences and new freedoms and responsibilities make this period especially important for understanding variables that influence biobehavioral risk factors. Adolescence may contribute to adult health by initiation of health behaviors that track or persist into adulthood, or by more distal influences in which changes that occur during adolescence can influence morbidity or mortality in later life.

One of the main themes in studying the biobehavioral risk factors that are initiated in adolescence is that many behavioral and biological risk factors cluster together. Among the most important biobehavioral risk factors that appear to cluster are substance abuse, sexual activity, eating disorders, and ingestive behaviors and activity patterns. Likewise, biological risk factors that may cluster together include elevated body weight, blood pressure, serum

lipids, and insulin. Analyses of biobehavioral risk factors should seek to understand the interrelationships among these risk factors in terms of the development of these risk factors patterns as well as implications for intervention.

The developmental changes that occur during adolescence may be of particular importance in understanding children who are at particular liability for initiation of unhealthy behaviors and disease processes. Adolescence includes important neurobehavioral changes and maturational processes that are responsible for self-regulation, impulse control, and responsivity to environmental stresses. Deviations from normative development could signal an important set of risk factors that contribute to a wide variety of biobehavioral risks that persist through the life course. In addition, analyses of adolescence should consider the profound biological and behavioral changes that normally occur during this period to represent a proximal risk factor for problems such as eating disorders, substance abuse, and unsafe sexual activity.

A developmental analysis of health behaviors should include the contribution of genetic and environmental influences to health behaviors. Genetics can influence the predisposition to a wide variety of biobehavioral risk factors; there

may be periods of particular vulnerability that may correspond to the unique biological and behavioral changes that accompany adolescence and young adulthood. Behavioral genetic models provide insight not only into the role of genetics, but also to the potential influence of the environment and interactions between genetics and the environment. The environment can influence the expression of predispositions, as well as genetic predispositions influencing how people structure their environments.

Finally, any analysis of adolescence should consider the unique psychosocial factors in this developmental period that contribute to biobehavioral risk factors. One of the most salient sets of psychosocial variables are peer and

cultural norms. There is a shift in influence from the family to peers that begins in preadolescence and continues through young adulthood. Understanding how these norms influence adolescent behavior, and how these norms are formed and modified are critical to improving adolescent health and reducing biobehavioral risk factors.

The four initiatives that follow will provide important directions for further studying the structure of the relationships among adolescent health behaviors, and developmental, biobehavioral and psychosocial factors that may influence biobehavioral risk factors in adolescents and young adults.

Task Group Initiatives

✓ *Determinants and Consequences of the Clustering of Biobehavioral Risk Factors (B-2-1)*

Need and Justification

Cross-sectional studies have suggested that biobehavioral risk factors associated with a number of adverse health outcomes (e.g., hypertension, HIV infection, unintended pregnancy, problem drinking behavior, drug abuse, and obesity) tend to cluster within adolescents and young adults. Such biobehavioral risk factors include: smoking, alcohol and drug use, early onset and high risk sexual intercourse, eating disorders and problems in weight regulation, and depression. Combinations of these factors may synergistically interact, increasing the likelihood for adverse health outcomes both during adolescence and young adulthood.

Data from longitudinal studies are limited and have produced inconsistent findings with respect to the "cluster phenomenon." While some studies have found a high correlation among risk factors over time, others have not. Furthermore, most longitudinal studies of adolescents have tended to focus on single risk factors and their health consequences rather than examining the effects of different **clusters** of risk factors on a variety of adverse health outcomes and disease processes. To develop more effective behavioral interventions designed to prevent disease and promote health, more precise data are needed about this "cluster phenomenon" and its association with adverse health outcomes among adolescents and young adults.

A number of critical questions need to be addressed. First, do clusters of biobehavioral risk factors occur differentially in different socio-demographic or ethnic groups? Further, there is little information available describing the temporal sequencing for the initiation of biobehavioral risk factor clusters. For example, what is the time period between initiation of one risk factor and the onset of another risk factor? What risk factors can be identified as predisposing to the onset of other risk factors? Moreover, to what extent are these risk factor clusters stable across the adolescents' developmental life span? Do risk behavior clusters change over time as adolescents mature into young adulthood? To what extent is the risk of adverse health outcomes related to different clusters of specific risk factors? To what extent does change in a single risk factor result in changes in the prevalence or magnitude of other biobehavioral risk factors within a cluster and in the likelihood of developing adverse health outcomes?

Data for identifying and characterizing the underlying mechanisms associated with the "cluster phenomenon" also are limited. Such data have important implications for understanding the development of risk-taking behavior among adolescents and young adults and for designing effective prevention and behavior intervention strategies. In particular, we need to understand the relative contributions of

biological, psychological and socioenvironmental influences in the development of risk factor clusters. Are there different underlying mechanisms associated with specific risk factor clusters or is there a similar constellation of determinants which serves as a common pathway to the development of all such clusters? Are these mechanisms similar across sociodemographic groups?

Research Approach/Methodology

Many of the risk factors associated with adolescent morbidity and mortality have their onset

early in life. To study clustering of biobehavioral risk factors across the adolescents' developmental lifespan will require a prospective cohort study design initiated prior to adolescence. Moreover the research design will require repeated biobehavioral assessments to characterize the natural history of the cluster phenomenon and capture the temporal sequencing of the onset of various risk factors. Both biological and psychosocial measures are appropriate to characterize risk factors, their adverse health consequences, and the underlying mechanisms. Diverse populations should be included in the study with particular emphasis on women and understudied ethnic minorities.

✓ **Models for Studying Behavioral and Genetic Interactions (B-2-2)**

Need and Justification

Psychological, behavioral, and environmental factors influence disease processes and the health of adolescents in the context of a multifactorial model. Genetic susceptibility, both to various disease processes and to various behavioral and psychological patterns, also contributes to various pathologies. Consequently, there is a high degree of individual variability both in vulnerability to addictive disorders and diseases and in response to various treatments for them. This variability affects the choices of optimal prevention and treatment strategies. Research on the extent and nature of these genetic and environmental interactions is crucial to clarifying models and improving the effectiveness of interventions in behavioral medicine.

There are several health-related problems that may particularly lend themselves to exploring the interaction between genetic predispositions and behavior during adolescence using this conceptual framework. The problems of obesity, alcohol dependence, skin cancer, and asthma have a set of shared issues relating to their causal pathways, maintenance and cessation. We illustrate with discussion of the first two disorders.

1. **Obesity:** Obesity is a highly complex, multifactorial condition with genetic, behavioral, and environmental components. Certain rare endocrine disorders that lead to obesity (e.g., Prader-Willi syndrome) clearly result from major genetic defects. It also is likely that so-called "susceptibility" genes account for

about a third of the variance in weight in the general population. For example, overfeeding studies with identical twin pairs show that variations in weight gain were greater between twin pairs than between twins within a pair, indicating the importance of genes in obesity. In addition, there are dramatic differences in obesity prevalence in different populations, with higher levels in minority populations.

It also is clear that behavioral influences critically affect obesity. Obesity has been increasing for three decades in the U.S. American children weigh more and are less active than in the past, suggesting cultural and behavioral influences on obesity that have not been well researched. Little is known, for example, about factors that precipitate binge eating, mediate physical activity levels, or regulate appetite.

Studies suggest that obesity in adolescence is associated with increased morbidity and mortality in later life, in many instances, independent of adult weight. One longitudinal study found that the relative risk of death was doubled for men who had been overweight adolescents, with increased risk particularly for atherosclerosis, diabetes, gout, colorectal cancer, hip fracture, and arthritis.

2. **Alcohol dependence:** The familial nature of alcoholism, particularly in males,

has stimulated research on the causes and mechanisms of transmission of alcoholism in families. These studies, focused on genetic or psychosocial factors or their interaction patterns, have found both genetics and environment are involved in alcoholism. A causal role for genetics is supported by twin, adoption, and genetic marker studies and by studies of genetic variations in alcohol metabolism that seem to provide some degree of protection against alcoholism in some populations. Psychological and social factors also influence drinking behaviors and the development of alcohol dependence. These factors include the pharmacologic effects of alcohol; the drinker's psychological state, particularly expectations of alcohol's effects; and the characteristics of the drinking setting. Positive expectations about alcohol's effects appear to be significantly involved in the initiation, continuation, and frequency of drinking.

Evidence of the importance of cultural factors also comes from a study that found a steady increase in frequency of alcoholism and decrease in the age of onset in comparing different age cohorts. These secular trends, found in both the general population as well as in the relatives of alcoholics, suggest that broad social factors also influence the

risk of alcoholism. Thus there appears to be an underlying quantifiable liability for alcoholism which manifests phenotypically when some threshold value is reached, and this liability is subject to both genetic and environmental influences.

Research Approach/Methodology

The methods of behavioral genetics provide a range of paradigms which can inform about the origins of individual behavioral differences, their distribution in the general population, and the interaction between behavioral variation and environmental factors to determine outcomes. Family, twin, and sibling comparisons and analyses afford the opportunity to delineate the mechanisms underlying behavioral variations, the contribution of specific phenotypes on the risk for adverse outcomes, and the contextual variables (familial, personal, SES, culture, demography, etc.) which augment or attenuate the risk. Methodologies such as factor and path analysis may also be useful in these studies.

A detailed series of approaches and questions could also be generated for health problems related to skin cancer, asthma, alcohol dependence and obesity. Alternatively, a general approach could be adopted to address some basic underlying mechanisms relevant to a variety of disease processes.

✓ **Development as a Risk Factor (B-2-3)**

Need and Justification

Adolescence is a period associated with the onset of numerous patterns of behavior related to poor health, such as disordered eating, high-risk sexual activity, and substance abuse. Changes specific to this period of life in physiology, psychology, and the social environment create a background against which these and other problems occur. Hence, development itself may be a risk factor, and in combination with other risk factors (e.g., genetics, social factors), is important in understanding the genesis of disease. An important research priority is to identify interactions between development and other disease mechanisms to explain diseases with their origins in this stage of the lifespan. We will focus on three such interactions.

1. Premature medicalization or development of psychosocial symptoms. Current estimates find that 30%-50% of visits to primary care physicians represent non-medically diagnosed complaints. Often these non-specific physical symptoms are regarded as expressions of common forms of mental disorders—depressive and anxiety states.

In other instances this pattern of presenting physical symptoms representing the expression of emotional problem onset is associated with such terms as hypochondriasis, hypertensial conversion, neurasthenia, chronic fatigue syndrome, fibromyalgia, chemical sensitivity, and, most important, diffuse chronic pain, a condition that represent a major

health cost and burden to the nation. These aberrant patterns of health-related behavior are commonly reported as arising in adolescence.

A related developmental issue is determining which psychological, social, and environmental factors influence the processes by which developmentally-appropriate physiological changes undergo misperception and misattribution and become associated with excessive preoccupation with physical illness, the premature medicalization or physical or psychosocial dysfunction that appears in early and middle adulthood.

2. Sequential acquisition of multiple risk behaviors. Population-based research suggests that certain individuals are involved in the performance of two or more behaviors that put their health at risk. These studies suggest that these "risky" behaviors are acquired during their adolescence and, it is hypothesized, that these behaviors are acquired sequentially over the adolescent years. For example, it has been demonstrated in several longitudinal studies that adolescents who begin smoking tobacco and/or imbibe alcohol at early ages are more likely to use marijuana and other drugs, such as heroin. Factors associated with the initiation of these behaviors are being examined: however the temporal sequencing of other risky behaviors known to be associated with alcohol and drug abuse such as unprotected sexual activities or having multiple

sexual partners, and eating disorders have not been examined. Furthermore, it is evident from longitudinal studies that not all individuals initiating these 'risky' behaviors continue them into adulthood. Determinants for the desistance from these behaviors have not been identified in these studies nor has the sequence for discontinuation of these behaviors been established.

3. Neurocognitive development and adolescence. Neurocognitive development, beginning at birth, continues into late adolescence. Variation in cognitive and neurological maturation insofar as it impacts on outcome is poorly understood. Specifically, the development of the prefrontal lateral cortex, where the highest cognitive capacities and behavioral regulation are subserved, if delayed, may result in age-inappropriate behaviors. The behavioral features which are incongruent with chronological age include impulsivity, imperistence, disinhibition, and high behavioral activity level. Cognitive correlates include reduced formal operational reasoning, poor self-monitoring of behaviors, and poor planning ability. How these deviations or slowing in the development of these neuromaturational processes predispose to, as well as impact on, adverse outcomes and influences the acquisition of maladaptive health-related behaviors remains unknown.

Research Approaches/Methodologies

Two general design strategies are applicable for addressing these issues. First, the high risk paradigm can be used to contrast youth at putative high and low risk on salient developmental parameters to elucidate how they interact with environmental conditions to promote adverse outcomes. Second, prospective developmental research can inform about the onset and maintenance of health risk behaviors. In this regard, the methods of behavior genetics may be especially useful insofar as they can delineate the factors underlying biobehavioral variation and the relative contributions of shared and unshared environmental influences.

A number of specific research techniques are applicable for understanding the contextual basis of development. A key factor is the dramatic change in reproductive physiology which also impacts on cognitive and affective states. Another set of methods pertain to the use of neuroimaging procedures, for documenting functional brain changes. Neurophysiological methods, especially event-related potentials enable clarifying changes during adolescence in cognitive information processing as well as in understanding changes in sleep physiology in relation to waking behavior and the links between morphologic development and self esteem. Additional research questions related to acquisition and maintenance of attributions about health related behavior may be addressed through survey methodologies.

✓ **Development and Impact of Sociocultural Norms on Health-Related Behaviors (B-2-4)**

Need and Justification

Sociocultural norms, including social values, beliefs, attitudes, social expectations, legal sanctions, customs, and mores affect a variety of positive and adverse health-related behaviors as well as the utilization of health care services. For example, adverse health behaviors such as the use of alcohol, tobacco, and other drugs appear to be governed, in part, by perception of the social acceptability of these behaviors as communicated by significant role models such as family members and peers.

Society also influences the adoption and maintenance of health behaviors when standards for acceptable or desired behaviors are conveyed through media messages/advertising, community-sanctioned practices, and the enactment and enforcement of relevant health policies and regulations. The influence of social norms on health behaviors is particularly important during the formative years of adolescence and young adulthood when important health practices are established.

A wide variety of health behaviors appear to be influenced by health-related social norms. For example, how fast we drive, whether we use seatbelts, how and what types of food we eat, personal hygiene practices, the use of alcohol, tobacco, and other drugs, sexual practices, and levels/types of exercise are significantly influenced by our perceptions of the social norms salient to each of these behaviors.

Although it is widely accepted that social norms are an important influence on health behaviors,

etiologic, epidemiologic, and ethnographic studies are needed to better understand how social norms are formed, change over time, and help govern specific health behaviors.

Questions for study might include the following: What factors affect the transmission of norms across generations and subcultural groups within a society? What is the relationship between the perception of social norms (either real or imagined) and changes in personal health behaviors? Why and how do health-related norms change over time as illustrated by shifts related to smoking, underage drinking, sexual behavior, and standards of physical attractiveness? What role do parents, schools, peer groups, health care providers, religion, law enforcement, and the mass media play in the establishment, maintenance, and modification of personal health behaviors? How do health-related norms vary across SES, ethnic, and gender groups?

Research Approach/Methodology

Prospective and cross-sectional etiologic studies are needed to determine the relationship between sociocultural norms, health-related norms, and the adoption and maintenance of both positive and adverse health behaviors. Further, epidemiologic research using a single protocol might assess both the incidence and prevalence of salient health behaviors and related social norms that may influence behavior change.

Midlife Adult

Overview

William Redd, Ph.D.

The initiatives developed by the Task Group focused on: prospective analysis of the effects of psychological and social factors on specific diseases, examination of the mutability of behavioral risk factors, behavioral sequelae of disease and its treatment and insulin resistance syndrome in hypertension, dyslipidemia, and NIDDM.

The Task Group felt there is a strong need for prospective, longitudinal analysis of psychological and social variables as risk factors for the development of specific diseases. Although many studies have identified certain associations between various psychological and social factors in morbidity and mortality from a number of diseases, specific mechanisms underlying such relationships have not been studied in depth. Little information is available regarding the determinants of these characteristics, their familial origins, stability over time and the relative importance of gender and ethnicity in these relationships. Although the Task Group felt ill-equipped to develop a specific research agenda in social epidemiology, the members felt that it was critical that psychosocial and behavioral factors be studied longitudinally. There was strong agreement that such work would require close collaboration across a number of research centers.

A second theme concerned the need for research to identify factors that affect individuals' ability to change their behaviors relevant to health and to adopt more healthy life styles as a means of primary prevention. The group recognized the general lack of success in intervening to alter behaviors that affect health status. In addition to feeling that there was a need to refine our understanding of principles of behavioral change, the group felt that it would be important to examine basic personality constructs to identify possible relationships between factors such as self efficacy, control, optimism, among others, and positive behavior change. Future proposals might address risk factors relevant to health maintenance or disease prevention, behavioral and psychological processes which facilitate behavioral change and the role of traits, states and group characteristics in the modification of life style.

The third research topic was the examination of behavioral sequelae of specific diseases and their treatment. The consensus was that greater effort must be directed towards the examination of the effects of common physical diseases on normative adult behavioral function. Similarly, attention must be directed towards the examination of neuropsychological and quality of life sequelae of interventions designed to ameliorate

or prevent disease. It was proposed that research be conducted to address five major issues: 1) What common behavioral effects are associated with specific disease and treatment modes; 2) how do such effects vary between individuals and what are their determinants; 3) how do the behavioral sequelae of disease and treatment affect activities of daily life; 4) what are the psychological and physiological mechanisms underlying change in health behavior; and 5) what prognostic implications do such life style changes have for the course of disease.

The fourth topic concerned the role of behavioral factors in the expression of insulin resistance syndrome (IR), a disorder which has been associated with central obesity, hyperglycemia, mild hypertension and atherosclerosis. While there is clear evidence that the tendency to develop the syndrome is inherited, behavioral factors appear to play a modulating role. Research is needed with high risk populations to study changes in central obesity, hyperglycemia, mild hypertension and/or dyslipidemia in relation to insulin metabolism as a function of diet, exercise, and/or stress reduction. Both animal and human studies would be appropriate.

Task Group Initiatives

✓ Factors Associated with Mutability of Behavioral Risk Factors (B-3-1)

Need and Justification

A major accomplishment of the behavioral medicine approach has been the application of knowledge about risk factors to programs for behavior change leading to a nationwide reduction in morbidity and mortality related to cardiovascular disease. Success in inducing widespread changes in smoking, diet, and exercise has resulted in marked reductions in coronary disease. This striking success in primary and secondary prevention holds promise for application to other risk behaviors. The need is more pressing given the spread of infectious diseases such as HIV, and the rising mortality from cancer due to increases in smoking among women, making lung cancer the leading cancer killer of women.

One of the difficulties in the application of knowledge about risk factors to health promotion and disease prevention is the difficulty of inducing behavior change. Some behaviors are easier to change than others; some individuals, groups, or communities are more open to change. Successful implementation of behavioral medicine techniques in health care requires knowledge about 1) the salient risk factors; 2) the accessibility of such risk factors to change; 3) those populations most likely to benefit from intervention or to change spontaneously. Large scale intervention trials, such as the Multiple Risk Factor Intervention Trial (MRFIT) have

suffered from poorly considered control comparisons and failure to select among interventions and susceptible populations. Furthermore, many risk behaviors, such as smoking, have been labelled "addictions," offering little hope for change and possibly providing smokers with a rationalization for maintaining health-damaging behavior.

Research has shown that variables such as self-efficacy (Bandura), control (Rodin), the absence of 'learned helplessness (Seligman), and optimism (Taylor) facilitate positive behavior change. Behavioral treatments have added a cognitive component, recognizing that restructuring of cognition and affect is a powerful tool in facilitating change (Spiegel, Beck). In addition, individual variables such as repression/sensitization (Weinberger), absorption (Tellegen), and hypnotic responsiveness (Hilgard, Spiegel) have been found to be moderator variables in treatment response. There is a need to identify approaches in interaction with individual and group dispositions which will help to identify modifiable risk behaviors.

Research Approach/Methodology

Proposals should involve systematic study of the relationships among three domains:

1. risk behaviors relevant to health maintenance or disease prevention;

2. processes which facilitate behavior change;
3. individual traits, states, or group characteristics which facilitate behavioral change.

Protocols may involve naturalistic analyses of successful versus unsuccessful attempts at behavior change, utilization of standardized measures of constructs for their power to predict behavior change, or surveys of the application of change techniques in different populations. Studies may involve comparisons of

various change techniques for variables common to their effectiveness. The research should add to fundamental knowledge about the characteristics of successful change strategies and populations most likely to benefit.

Designs with well-defined clinical populations; systematic assessment of all variables, controlled interventions; comparison among relevant populations, including study of gender, social class, ethnicity, and other variables are encouraged. Proposals may be broad and generic or be targeted to specific diseases.

✓ ***Behavioral, Social, Economic and Cultural Antecedents of Disease (B-3-2)***

Need and Justification

Disease is not randomly distributed throughout populations; it concentrates in poor urban areas, in populations inadequately provided with services, such as African-American, Native American and Hispanic populations. Recent work by Pappas and others at the National Center for Health Statistics has demonstrated the tremendous differences in mortality between the American population as a whole and inner city poor African-Americans. Additionally, the interplay of individual, behavioral and cultural factors plays a role in the susceptibility of individuals to disease. The mechanisms for this phenomena include lifestyle, inadequate access to services or health education, inadequate social support, high levels of stress, diet, inadequate coping skills, marginalized or stigmatized social status.

These factors are significant not only for chronic diseases, but for emergent infectious diseases such as AIDS and TB. Additionally, a number of adverse social conditions such as violence and drug abuse appear to be conditioned by these factors.

Despite the growing body of evidence linking these factors, researchers have often focused only on more proximate or precipitating causes, instead of examining more general issues. Often, the mechanism for the action of these factors may involve multiple pathways and interactions, which have been inadequately examined. Few studies have identified the multiple underlying psychological, individual and structural factors that constitute the risk

factors and antecedents of disease. The vast body of evidence on TB demonstrates the social, economic, nutritional and exposure factors that contribute to infection, as well as adherence to treatment. The ultimate goal of this study is to identify and understand the role that these social, economic and behavioral factors play in infection, so that better treatment and prevention programs can be designed. In addition, in light of national health care reform principles, such research would contribute to better access, utilization and targeting of effective prevention and treatment approaches.

Research Approach/Methodology

Because the body of literature in this area is diffuse and often not intervention oriented, a multiple step approach is proposed. First, an expert scientific panel bringing together intra- and extramural experts in the fields of epidemiology, medicine, behavioral medicine, public health, economics and other health social scientists would be held. The goal of this panel would be to identify testable behavioral models of disease transmission that link social, cultural and economic factors to the incidence of disease across the life-span. These models would constitute the basis for cooperative agreements in this research area to be announced by the relevant Institutes working in collaboration.

Distinct entities such as AIDS, substance abuse, tuberculosis, and hypertension may be explored by the team of intra- and extramural researchers across the various Institutes. One emphasis of these studies would be the exploration of dis-

ease state co-morbidity that we know to influence incidence of new diseases or morbid conditions. A limited number of study sites, perhaps three, would be identified to examine the social, economic, and behavioral vulnerability factors specific to particular diseases and across disease states.

For example, in exploring antecedents of disease, one study could focus on the influence early in life of abuse and violence, poor schooling or educational opportunities, lack of preventive and health care services and the impact of deteriorating family and support structures on substance abuse, high-risk sexual behavior, low

self-esteem. In turn, the impact of these factors on incidence and prevalence of HIV and other STDs, TB, violence, and stress related disorders could be assessed.

Multimethod designs, from multicenter prospective designs through case-control studies, risk factor studies to small-scale observational and pilot intervention studies would be encouraged. A special focus in analysis would be the interpretation of complex confounders and covariation, and triangulation of data from different sources. The example presented above might involve retrospective techniques and multifactorial analyses.

✓ **Prospective Study of Psychological and Social influences on Disease (B-3-3)**

Need and Justification

Evidence from numerous studies has established the importance of psychological and sociological variables as risk factors for the development of several somatic illnesses, including cancer, diabetes, cardiovascular diseases, and others. Individual characteristics which have been so identified include affective traits (depression, hostility, cynicism) as well as personality characteristics (time-urgency, ego-centrism). Although many of these studies have established an association with morbidity and mortality, conclusions often have been based on retrospective and cross-sectional data. Little information is available regarding determinants of these characteristics, their familial origins, stability over time, and their relative importance as a function of gender and ethnicity. The relationship of these psychosocial attributes to physiological states (cardiovascular reactivity, autonomic function) as well as to other risk factors (diet, smoking, serum cholesterol) is also poorly understood.

Research Approach/Methodology

Multi-center, longitudinal studies of several thousand healthy, young adults (18-22 years of age at entry), from centers geographically distributed so as to assure inclusion of all major minority groups in sufficient number to provide statistically meaningful data should be consid-

ered. Particular issues in relation to women include premenopausal ovarian function and behavioral factors potentially associated with chronic ovarian endocrine dysfunction (i.e., as analogous to social subordination in experimental studies of nonhuman primates).

Recruitment would take place over a period of 2-3 years, with each year's sample constituting a single cohort for purposes of initial and follow-up examinations to be conducted at three year intervals. Although the initial duration of the study would be seven years, it is expected that it would be renewed for additional intervals, so that a life-course perspective could be developed.

Although the Task Group felt ill-equipped to develop a more complete proposal for a research agenda in social epidemiology, it nonetheless felt that a decided need exists in the risk factor area for initiation of a large, multi-center study of psychological and social influences on disease. Properties of any such study should involve: (a) adequate size (power); (b) inclusion of all psychological and social parameters figuring prominently in existing literature; (c) repeated measurement of putative risk variables thought to mediate psychosocial influences on disease (e.g., psychophysiological reactivity); (e) and identification and evaluation of intermediate clinical endpoints wherever possible (e.g., non-invasive assessment of carotid atherosclerosis, left ventricular mass by echocardiography).

✓ **insulin as a Risk Factor For Hypertension, Dyslipidemia and NiDDM (B-3-4)**

Need and Justification

The Insulin Resistance (IR) Syndrome refers to a constellation of disorders associated with increased insulin concentration (DeFronzo & Ferrannini, 1991). These include tendencies toward hyperglycemia, hypertension, central obesity, and atherosclerosis; hyperuricemia and renal dysfunction are also sometimes included.

There is now abundant evidence that the tendency to develop IR is inherited (Laws *et al.*, 1989). Behavioral factors, however, play a major role in the expression of IR. Obesity, for instance, is strongly associated with IR and weight loss results in improved insulin sensitivity (Olefsky *et al.*, 1974). Sedentary behavior also appears to contribute to IR (Laws & Raven, 1991), whereas physical exercise increases insulin sensitivity (DeFronzo *et al.*, 1987). Activation of the sympathetic nervous system (SNS) is stimulated by overfeeding (DeHaven *et al.*, 1980) and suppressed by caloric restriction (Young & Landsberg, 1977) with the effects apparently mediated by insulin (Landsberg & Young, 1985). Although the extent to which insulin resistance may interact with emotional stressors is not known, the metabolic pathways, by which hyperinsulinemia induced by IR can facilitate SNS activity have been described (Howard *et al.*, in press).

Research Approach/Methodology

Studies are needed in high risk human populations to study changes in central obesity, hyperglycemia, mild hypertension and/or dyslipidemia in relation to insulin metabolism as a function of diet, exercise, and/or stress reduction. The extent to which changes in caloric intake include factors which concomitantly influence IR and the SNS is also appropriate for study. Animal models relating diet, exercise and/or stress to change in IR are also appropriate for study. Techniques for assessing the effects of insulin-stimulated glucose uptake would be useful for studying the impact of experimental variables upon IR.

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Senior Adult

Overview

Barbara Rimer, Ph.D.

The proportion of the population that is over age 65 will increase dramatically in the next decade. An understanding of how risk factors are caused, maintained and changed and how they affect disease progression is important for this stage in the lifecycle. There is a new appreciation of the fact that changing risk factors, such as smoking, even at older ages, can produce substantial health benefits. There is also a growing recognition that ill-health and disability are not the inevitable burdens of aging. The proposals from the conference in this area are based on the premise that research is needed to understand how culture affects disease as people age, to identify how the social and physical environment affect health and health behaviors and how sociocultural, behavioral and psychological factors affect the course of disease among older adults.

There was a recognition that the study of risk factors is complex, because risk factors rarely occur in isolation. A trans-NIH approach is needed. This is preferable to the "boutique" approach in which risk factors are studied in isolation because they fall within the purview of a particular NIH institute.

The discussion was guided by several goals:

- ▶ to understand successful aging as well as disease progression;
- ▶ to understand the context of risk factors, including physical environment, race, gender, beliefs and spirituality;
- ▶ to understand the clustering of risk factors and how they vary over the aging process;
- ▶ to study the role of risk factors on disease incidence, disability, progression and recovery (since people do recover).

A number of methodologic issues were discussed and emphasized; several recommendations were made:

- ▶ to study biobehavioral risk factors in a meaningful way, there is a need to conceptualize and carefully measure key concepts such as social class;
- ▶ there is a need for longitudinal studies that describe how risk factors cluster and

change over time and how they interact with disease;

- ▶ there is a need for theory based explanations of how risk factors interact;
- ▶ more attention should be paid to analyses that examine the role of culture and race. As Betancourt and Lopez (1993) recently noted, in the rush to control for these variables, researchers may lose their meaning;
- ▶ risk factors should be viewed in clusters since a focus on single risk factors may reduce meaningful complexity.

Three separate proposals were developed to address the concerns and priorities articulated during this session. They are summarized briefly.

1. *Sociocultural, Behavioral and Psychological Mechanisms: Modifying the Course of Disease and Its Consequences in Older Adults:* Research is needed to identify the strategic points in the disease-disability process and to identify the sociocultural, behavioral and psychological factors that affect disease and disability. Longitudinal, cross-sectional and intervention research are needed.
2. *Aging and Sociocultural Influences on Risk Factors for Disease, Functioning and Health-Care Utilization:* This proposal is based on the premise that more

research is needed to elucidate the pathways by which sociocultural factors affect risk factors. Both longitudinal and cross-sectional studies are recommended.

3. *Impact of the Social and Physical Environment on Health and Health Behaviors:* There is ample evidence that social and physical environments affect health. But, little is known about how these interactions affect older adults. A major initiative is recommended to assess the environments in which people live and work and their relation to health and health behaviors.

The Task Group recommends research to better characterize the social and physical environment and to assess the impact of the environment on older adults' health and health behavior, controlling for individual risk factors.

Together, the research proposed here would provide much needed information about the many rich influences on biobehavioral risk factors among older adults.

Reference

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Task Group Initiatives

✓ ***Sociocultural, Behavioral, and Psychological Mechanisms: Modifying the Course of Disease and its Consequences in the Elderly (B-4-1)***

Need and Justification

The changing age structure of the population of the U.S. and other countries has resulted in increasing numbers of elderly citizens, with the potential for increased prevalence of chronic diseases and disability, and greater dependence and higher utilization of health care resources. There is a growing body of evidence which suggests that dependence and disability are not the inevitable consequence of growing older. Because dependency and disability often are the result of chronic and acute diseases, research is needed to identify the strategic points and sociocultural, behavioral, and psychological factors that affect the progression of these conditions and the resulting disability.

An increasing body of evidence indicates that personal, family, household, community, and environmental factors influence the course of disease and resultant disability, and the ability of individuals to maintain independent living. For example, social support, smoking cessation or weight reduction, treatment of depression, and modifications of the physical environment may all decrease progression of disease and risk of disability associated with a variety of chronic conditions. However, considerable questions remain concerning the content, timing, and efficacy of potential interventions. Research is

needed to identify the particular factors which are associated with slowing down the progression of disease and risk of disability, and the generalizability of these factors across gender, race/ethnicity, and specific chronic disease processes. Advances in this area could contribute considerably to adding life to years and reducing health care costs.

Research Approach/Methodology

A broad range of approaches are needed to address these issues. For example, longitudinal research is needed to identify patterns of disease progression and disability in individuals and groups with specific chronic diseases as well as comorbid conditions. Longitudinal research is needed to appropriately observe changing patterns of disease progression and disability. Theoretically and empirically based interventions need to be tested to assess effective strategies. A broad range of sociocultural, behavioral, and environmental factors should be taken into account. For example, personal characteristics, familial and social support, environmental modifications, and community/organizational factors could all be considered. Approaches to examining the cost effectiveness of alternative strategies should be encouraged.

✓ **Aging and Cultural influences on Risk Factors for Disease, Functioning, and Health-Care Utilization (B-4-2)**

Need and Justification

Too often, the role of cultural factors is ignored in understanding the onset, progression of, or recovery from disease in older adults. Researchers often treat race, social class, ethnicity, and gender as control variables instead of explanatory/causal variables. These variables are especially understudied in older adults, where "age" is simultaneously a marker of different cohort experiences (e.g., immigration) as well as reflective of biological susceptibility. Ignoring cultural factors can result in failure to include older adults in disease prevention and health promotion programs. Such neglect can be a factor in misdiagnosis, inappropriate treatments, and unneeded health care.

Examining these factors may help explicate disparities between disease severity and level of functioning and reveal strategies for moderating the impact of functional declines associated with aging. The identification of cultural factors regarding reactions to disease and the functional consequences of disease can guide interventions. An understanding of the influence of culture is important for designing health interventions to promote beliefs that contribute to "successful" aging.

Research Approach/Methodology

We recommend attention to the following research questions/issues:

- ▶ cultural factors that give "meaning" to demographic categories (e.g., SES, ethnicity, race/, gender, age) and that impact on disease, functioning and health-care utilization. In particular, we need to specify the means through which culturally determined values (e.g., self-reliance) and belief systems (e.g., nature of illness) influence disease, functioning, and use of health care services.
- ▶ do cultural factors affect diseases processes directly through their impact on underlying biological functioning (e.g., immune functioning, cellular changes) or indirectly through their impact on health practices?
- ▶ better understanding of the multiple pathways through which cultural factors may influence health outcomes (e.g., does religiosity/religious beliefs affect sense of personal efficacy, social integration or health practices?)
- ▶ the impact of cultural factors in different age cohorts or changes in the potency of cultural factors as people age.

Both qualitative and quantitative research approaches are needed to explicate the influence of cultural factors. Longitudinal studies are recommended as are methodological studies to improve the conceptualization and measurement of key constructs (e.g., social class, ethnic ideologies, religious beliefs). Studies should further attend to within and cross-group

analyses. A research agenda-setting conference would be useful in reviewing what is known

about aging and cultural influences and developing trans-NIH program initiatives.

✓ **Impact of the Social and Physical Environment on Health and Health Behaviors (B-4-3)**

Need and Justification

Health and health behaviors are determined not only by choices and attributes of individuals, but also by the social and physical environments in which they live and work. For example, The Alameda County study has shown that mortality risk is increased by living in poor areas or neighborhoods, over and above the effects of personal income and other psychosocial risk factors. Thus, it appears that the residential environment itself, as well as individual SES, is a significant risk factor for health.

Similarly, persons of lower SES are more likely to exhibit unhealthy patterns of smoking, drinking and eating. These health behaviors may also be a function of the environments and life situations of lower SES people. For example, we now recognize that advertising and sale of cigarettes, alcohol, and many less healthy foods are concentrated in lower SES communities, which are often heavily populated by minority

groups. Thus, it is plausible that these environmental forces are a major determinant of health behaviors.

A major initiative is needed to assess the environments in which people live and work and their relation to health and health behaviors. The impact of social or physical environmental hazards are likely to be particularly important for older persons (and perhaps also the very young) whose mobility and capacity to adapt to environmental forces may be more limited.

Research Approach/Methodology

Assessment of the impact of environmental measures on health and health behavior is needed, controlling for individual level risk factors. This includes determining the extent to which the environment operates through social, psychological, and physiological risk factors and mechanisms at the individual and small group level.

Synthesis

James House, M.D.

The general initiative to expand the role of behavioral medicine in NIH and in efforts to improve the health of our nation is an enterprise with great promise, but not without problems. From the initial presentations of this conference onward, we have noted and built upon the remarkable progress made in the last several decades in understanding the role of social and behavioral factors in health and illness.

The last three decades, and especially the last 10-15 years, have seen many advances, among others:

- (1) the first and second Surgeon General's Reports on Smoking and Health, and a steady decline in smoking in many portions of our population;
- (2) recognition of the great importance for health of other behavioral or lifestyle factors such as diet, drinking, exercise, and sexual behavior;
- (3) the identification and certification of the Type A or coronary-prone behavior patterns as a risk factor for CHD (now largely supplanted by more refined psychosocial variables);
- (4) the rediscovery of the importance of social relationships, integration and support for health;
- (5) the delineation of a number of personal dispositions such as self-efficacy and

hostility as significant risk factors for health; and

- (6) the development of the report and goals of *Healthy People 2000*.

We have also made great progress in understanding the relation between psychosocial and biological variables and mechanisms and in increasing the sophistication of biomedical scientists about psychosocial matters and of social and behavioral scientists about biomedical matters. The development of new initiatives for the study of what have been termed biobehavioral risk factors that has taken place in this conference, and has been reviewed in the reports of the working groups, builds upon and extends the accomplishments of recent decades. Indeed, the kind of conference and enterprise we have engaged in would have been inconceivable prior to the developments of the last two decades.

We are now attempting to plan another great leap forward. The initiatives developed by the working groups on biobehavioral risk factors suggest some of the new directions which will be essential in this next stage. Socioenvironmental and behavioral factors are of increasing importance as determinants of the etiology and course of health and disease at all stages of the life course. A recurrent theme across all of the working groups is the need for longitudinal studies of the impact of psychosocial risk factors on health, and of the psychosocial and biological processes which may mediate and

moderate their effects. This involves looking across the full life course, and at relations between the stages of the life course which have been separated somewhat arbitrarily in our discussions.

The particular psychosocial risk factors and health outcomes of greatest interest vary somewhat across the life course. Unintentional injuries are the leading causes of death in adolescence and early adulthood. In middle and later life, chronic diseases are the leading causes of morbidity and mortality, and in older age the problem of maintaining function in the face of disease becomes equally or more important than preventing disease onset or achieving full recovery or remission.

Intentional and unintentional injuries are purely behavioral phenomena, though with biological as well as behavioral precursors and sequelae. Functioning in the face of disease is arguably as much a psychosocial as a biomedical problem. And even the onset of chronic disease increasingly involves psychosocial factors.

As the initiatives of the working groups suggest, we now know a good deal about the role of separate psychosocial risk factors in predicting all of these health outcomes, at least in the short- or medium-term. Much needed, however, are studies which focus on the interrelations among or clustering of these various risk factors at all stages in the life course. Also essential are more and better prospective and longitudinal data on how these risk factors may cumulate or interact over time. For example, what are the long-term as well as more immediate effects of experience in utero on health and functioning in infancy or childhood, or of risk-taking and poor health behavior in childhood and adolescence on health and functioning in adulthood, and even later life. Similarly, how do psychosocial risk factors and resources affect health during

midlife, and how do both psychosocial and biomedical functioning in this midlife period shape processes of health and aging in later life.

Such longitudinal studies are needed not only to understand how psychosocial factors affect health but also how the experience of disease and disability shapes psychosocial functioning—again across all stages of the life cycle. All such research must recognize and investigate the heterogeneity of responses to both psychosocial risk factors and disease. Why and how are some resilient in the face of stress or deprivation or disease, while others are more adversely affected?

Somewhat less well embodied in the research initiatives, but usually implicit in them and occasionally more explicit in our discussions and presentations, is a need to move beyond the past and present paradigms of behavioral medicine to think in more social and environmental as well as psychological, behavioral, and biological terms. There is naturally ambivalence about moving in such directions within NIH, which has historically been a largely biomedical organization, more recently an increasingly psychological and behavioral one as well. And similar ambivalence is natural among biomedical and psychological scientists, who constitute the majority of the participants in this meeting and in the field of behavioral medicine and whose focal concern is the functioning of individuals and organisms.

This is not an issue of pitting one approach against another; rather it is an issue of adopting an even broader perspective on health than has generally characterized NIH and the field of behavioral medicine to this point.

Trends in health within our society and comparisons of the health of our society with that of other societies suggest the need for such a

broader focus—one which might better be described as social and behavioral medicine or psychosocial medicine. Despite our national preeminence in both biomedical research and in health care technology and expenditures, the health of the U.S. population has not advanced as rapidly in recent decades, either relatively or absolutely, as has the health status of other developed countries ranging from Japan to the countries of northwest Europe. And even some less developed countries have arguably made greater relative progress. I do not believe we can look to biology or psychology alone to explain or counteract these trends.

In her introduction to the 1991 NIH report on Health and Behavior Research, Bernadine Healy rightly identified disparities in health within our society as a central focus for new initiatives in health and behavior research. Disparities in health by gender, race/ethnicity, and especially socioeconomic status, sometimes compounded by place of residence, have remained very large over the past several decades, and in some cases have become larger.

Indeed, portions of our population defined by these variables exhibit patterns of health more similar to populations in third world countries than to the more advantaged portions of our own population or the populations of other highly developed countries. As a number of speakers have noted, we can no longer just control for such differences, we must focus on understanding and reducing them. And this requires recognizing that individuals' biology and behavior are heavily shaped by their social and physical environment. An essential element of what it means to be male or female, white or black, more or less educated, or richer or poorer is to live and work in very different social circumstances and environments.

These environments shape people's health behaviors and life styles, their experiences of chronic and acute stress, their social relationships and supports, and their dispositions toward self-efficacy and hostility. Through these mechanisms, and via other more direct effects, these environments affect psychological and biological functioning, so that, for example, regardless of their individual characteristics or risk factors, individuals living in poor, disorganized, and high stress areas have been found to manifest higher levels of adverse health outcomes from hypertension to mortality. Because of their prior social, psychological, and biological history, women, minorities, and persons of lower SES may also be more likely to respond to adverse environments in ways deleterious to their health. And the health risks associated with gender, race, and SES may cumulate, not just additively, but also synergistically.

To understand and reduce these disparities in health may require transcending some of the tried and true ways of biomedical research. The classic paradigm has been to work backward from a disease to identify the antecedents and mechanisms producing it. This necessarily involves a focus on biological and psychological mechanisms and processes. When a risk factor for health is relatively more distal, as are the social environments and roles of women, minorities and lower SES persons, however, the risk factor is less likely to be closely linked with any single disease or psychological and biological process and more likely to be productive of poor health and functioning from a wide range of diseases and through a wide variety of mechanisms.

Thus, we may come to understand more efficiently and effectively how these social environments affect health by studying them direct-

ly and trying to understand how they shape people's social, psychological, and biological functioning and hence both general and specific health and disease outcomes. To do so may require that NIH invest more in supporting broader social science research, involving disciplines such as sociology, anthropology, and economics, as well as current behavioral medicine research.

Susan Blumenthal reminded us that Franklin Delano Roosevelt recognized that health research and policy were essential components of broader socioeconomic research and policy.

Equally, we need to recognize that socioeconomic research and policy are important elements of health research and policy. Over the course of this conference, we have seen an increasing concern with social and environmental variables and processes in our discussions of disease processes, risk factors, treatment, and health promotion and disease prevention. I hope that one of the outcomes of this conference will be to encourage and accelerate these trends, not as an alternative to existing research paradigms and processes, but as an increasingly necessary and useful complement to them.

TREATMENT INTERVENTIONS

Intervention Research in Behavioral Medicine

W. Stewart Agras, M.D.

The last twenty-five years, and particularly the last decade, have witnessed a remarkable surge in both the scope and volume of intervention research in the field of behavioral medicine. The conditions for which such interventions have been developed span a wide range of disorders including: obesity and the eating disorders, asthma, pain control, hypertension, hypercholesterolemia, Type II diabetes, cancer, fear of medical procedures, and compliance with the medical regimen, to mention only a few of the areas in which a substantial body of intervention research has been developed (Blanchard, 1992). This development recognizes the importance of behavior in the maintenance of health and disease, and rests on basic research concerning behavior change stemming largely from social psychology.

By changing behavior, propitious alterations in important physiological, neurochemical, and immune systems, may occur (Ader *et al.*, 1991). While there is no competition between pharmacological and behavior change interventions (indeed many studies of the combination of these treatments have appeared in the last few years), in some instances it has been shown that

behavior change procedures may have significant advantages over pharmacological agents used in the same disorder, as is the case in bulimia nervosa (Mitchell *et al.*, 1990; Agras *et al.*, 1992).

In a study of mild hypertensives, the antihypertensive agent, propranolol, was compared with a multicomponent behavioral intervention comprising weight loss treatment, dietary intervention to lower salt intake, and relaxation training (Rosen *et al.*, 1989). All three of these components have been shown effective in lowering blood pressure in controlled trials. Blood pressure was reduced equally by the medication and behavioral treatments, both being superior to placebo. However, the behavioral treatment demonstrated broader advantages, including lowering weight and cholesterol levels to a significantly greater extent than the medication condition. Whether or not such advantages will continue over time remains to be determined. However, such a treatment may be a useful first step in the treatment of the mild hypertensive who will comply with such behavior change methods, and may significantly delay the time at which medication needs to be used, hence

avoiding both the side effects and often lowered quality of life associated with taking antihypertensive medication.

Despite the existence of well controlled studies demonstrating effective applications of behavior change methods, ranging from cost-effective educational strategies, e.g. in asthma, to the more expensive cognitive-behavioral treatment e.g. in bulimia nervosa, there are a number of methodological problems which deserve discussion. In turn, these methodologic problems highlight new directions for intervention research. For the sake of coherence, most of the examples used will be drawn from the eating and weight disorders. However, such examples are widely generalizable to other disease entities.

The Need for Educational Programs Concerning the Nature and Effects of Treatment

There is often a lack of congruence between the goals of patients and those of therapists concerning the desirable outcomes of treatment. One of the best examples of this lack of congruence is in the management of obesity. Patients not only want a "quick fix" but also want to lose a good deal of weight, often unrealistically wishing to regain their former sylvan selves (Brownell & Wadden, 1992). On the other hand, there is evidence that modest weight losses between 10 and 20lbs are associated with positive health gains (Blackburn & Kanders, 1987). In a typical weight loss program, while less than 5% of individuals might reach their ideal weight, some 70% of individuals may lose enough weight to confer significant health benefits. This suggests that educa-

tional programs should be developed for those conditions in which behavior change treatments work, delineating what the potential benefits are, and what they are not. The effects of such educational programs on patient entrance to treatment, on patient knowledge of, and acceptance of reasonable treatment goals, and on the outcome and maintenance of treatment, should be evaluated in controlled studies.

Effectiveness Is in the Eye of the Beholder

Reported success rates of treatment may vary with the denominator used to denote success. Take the example of a treatment study that reports a 60% success rate. Yet, 120 patients meeting entry criteria may seek treatment, with 100 deciding to follow through with treatment. Twenty patients, not an unusual number, may drop out of treatment along the way, and 48 of the patients completing treatment may meet criterion for recovery, usually reported as a 60% rate of success. More conservatively, the rate of success might be reported as 48%, with the denominator being those who actually entered the study, and counting the dropouts as failures. Even more conservatively, the rate of success might be reported as 40%, with the denominator as the 120 patients wanting treatment in the first place. The message from this is that we need to study the reasons why 20 patients did not follow through with treatment initially, so that treatment can be modified to meet their needs. We also need to study the dropouts from treatment. Unfortunately, most studies have too small a sample size to generate enough dropouts to study, hence we know very little about such individuals or how to minimize the dropout problem.

Long-Term Effects are Desirable, But May be Unattainable Without Continuing Treatment

All too often, applications of behavior change procedures to health problems have been of too short a span to throw light on long-term effectiveness. In the case of chronic disorders such as obesity, the majority of studies have spanned weeks or months at the most, giving little opportunity to make definitive statements regarding long-term outcomes. Follow-up studies of treated obese populations demonstrate considerable relapse after treatment has been terminated. For example, in a study comparing behavior therapy, with or without an appetite suppressant (d-fenfluramine) over a six-month treatment duration, those treated with fenfluramine with or without behavior therapy lost the most weight (Craighead *et al.*, 1981). But after treatment was withdrawn, there was a considerable relapse in all the treated groups, especially marked in those receiving fenfluramine.

This study can be interpreted in several ways. First, that behavior therapy is the preferred treatment because patients in this condition had regained less weight at follow-up. In this interpretation, medication was not helpful. A second interpretation, might be that medication was very helpful as long as it was continued.

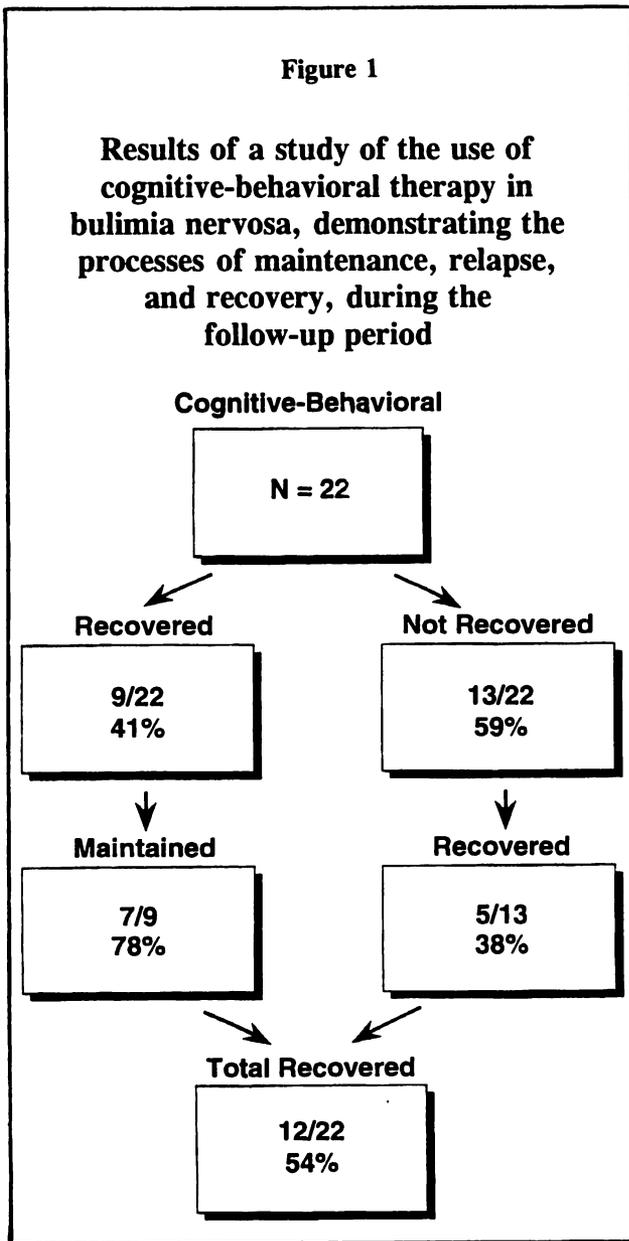
More recently, long-term studies of a combination of appetite suppressants and behavior therapy have appeared. In one such study, at any point that active medication was replaced by placebo, patients receiving placebo gained weight faster than patients continuing to receive active medication (Weintraub *et al.*, 1992). This suggests that continued treatment is the way to approach chronic health problems such as obesity. After all, no one would suggest that

patients with essential hypertension should be treated short-term. Hence, research designs that allow both continued treatment and long-term assessment of outcomes are needed for such conditions.

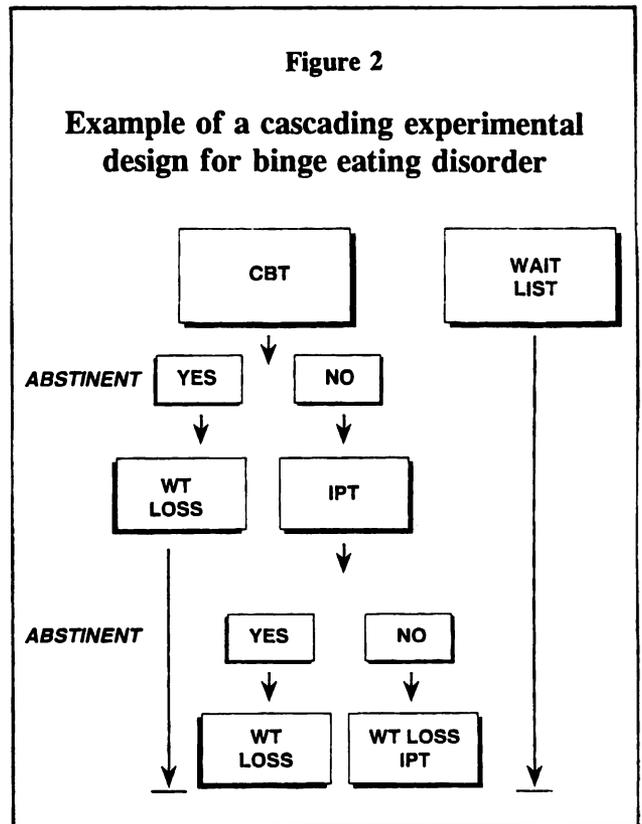
In some disorders, for example, bulimia nervosa, the outlook is more encouraging. Patients who do not relapse during the first six months following treatment continue to do well, at least over the two or three year follow-up studies that are presently available (Fairburn *et al.*, 1993). Yet even here, the results of such maintenance studies are often reported in such a way that important therapeutic processes may be overlooked. Usually, investigators report the percentage of patients recovered immediately following treatment, e.g., 41% in Figure 1, and the percentage recovered after follow-up, 54%. But as shown in Figure 1, what actually happens is that some patients relapse after having recovered, while others recover during the follow-up period. These appear to be two distinct phenomena, the second of which has not received any formal investigation, yet would seem to constitute an important group. If we could understand this effect, perhaps we could enhance recovery in other patients.

Intervention Design Options

The classical outcome research design is one involving parallel groups. While such studies form the backbone of intervention research, they do not model the decision-making process of the clinician who may need to use a second (or third) treatment if the first fails to produce clinically significant results. An alternative approach is the "cascading" therapeutic design, a simple example of which is shown in Figure 2. This study examined the treatment of obese patients with binge eating disorder, a condition



closely related to bulimia nervosa, but one in which, since purging is usually absent, the patients struggle with overweight.



CBT = cognitive-behavioral therapy; IPT = interpersonal therapy. A clinical outcome of abstinence from binge eating is used at the end of the first treatment phase. Yes = patients who meet criterion for recovery. No = patients who do not.

The basis for this design is the observation that cessation of binge eating is essential for weight loss to occur, hence it seems reasonable to precede weight loss treatment with cognitive-behavioral therapy which has been shown in controlled trials to be as effective in binge eating disorder as it is in bulimia nervosa. About half the patients treated with cognitive-

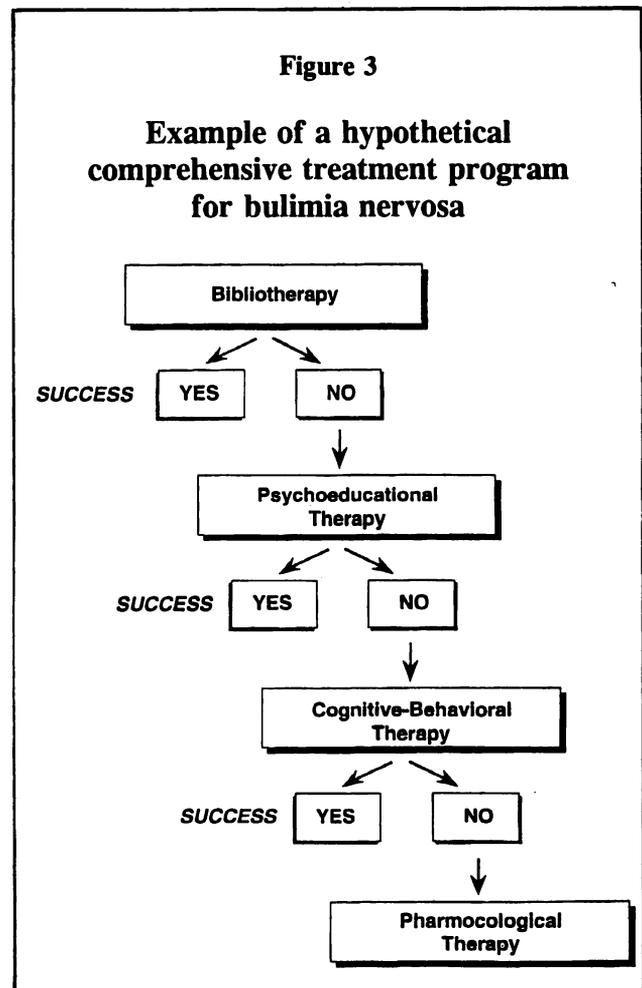
behavioral therapy would be expected to achieve abstinence from binge eating and hence would proceed to a second phase comprising weight loss treatment. Since interpersonal therapy has been shown to be as effective as cognitive-behavioral therapy as a first line treatment, and is procedurally different from cognitive-behavioral therapy, it might be expected that a proportion of patients not responding to cognitive-behavioral therapy would respond to interpersonal therapy and would then be able to proceed to weight loss treatment. Such sequential treatment processes better reflect the thinking of most clinicians, i.e. using a stepped care model similar to that used in the treatment of essential hypertension, and may better identify the optimal approach to patients not responding to initial treatment.

Moreover, such cascading designs may also be useful in identifying effective maintenance treatments. In this way complex treatments including initial treatment, a secondary treatment for failures, and a maintenance strategy, might be compared with one another. Alternatively, different sequences of the initial and secondary treatments might be examined. It should be noted, however, that the comparison of two or more complex cascading treatments will undoubtedly require the use of multicenter designs.

Multicenter designs are already much used in other medical fields and may be a useful corrective for the relatively small, and often inadequate, sample sizes commonly used in intervention studies in behavioral medicine. Relatively small scale, single center studies form an important background for the design of multicenter studies, they often lead to uncertain conclusions because of lack of statistical power, with some studies showing positive results and others not, hence providing inadequate guidance to the clinician.

Designing Therapeutic Systems

Beyond the relatively simple cascading design, it will be necessary, from the viewpoint of providing comprehensive care at the least possible cost, to consider the design of therapeutic systems for particular disease entities. Such a therapeutic system that might be used for many disorders, but certainly, with our present knowledge base, for bulimia nervosa, is outlined in Figure 3.



Studies have shown in many disease entities that information, denoted here as bibliotherapy, leads to recovery in a proportion of patients with a particular disorder. Such therapy may

rely on written material, or on videotapes, or in the future on interactive forms of media presentation.

For those who do not respond, this therapy forms a background for the next level of treatment, denoted here as psychoeducational therapy. Such therapies, carried out in group format, have been shown effective in a number of conditions, and combine more individually targeted education with simple behavior change procedures. Those not responding to this treatment would advance to the more expensive cognitive-behavioral therapy provided either in group or individual format. For the hopefully small number of non-responders, a medication treatment may now be tried, at least in the case of bulimia nervosa, where medication has been found less effective than cognitive-behavioral treatment, although more effective than placebo (Mitchell *et al.*, 1990; Agras *et al.*, 1992). Such therapeutic systems, based upon the research literature might be tested against more expensive treatments such as cognitive-behavioral therapy, to determine their cost-effectiveness. Again, a multicenter trial will be needed in such cases.

While intervention research proceeds mainly through individual investigator initiatives, it may be important to begin to design more effective planning mechanisms to advance particular fields in a more rational manner. After all, aircraft are not designed by numerous small companies, each independently developing some aspect of the airplane. Rather, there is a careful planning mechanism for the overall design of the aircraft taking into account the prevailing state of the art. Similarly, it may be important to bring together groups of key investigators to work together over an extended time to plan a more rational approach to the formulation of the needed research in a particular area. This would allow for the development of the most efficient research strategy, particu-

larly the development of background methodology and of the necessary multicenter initiatives. Such an approach would not replace the traditional individual research initiative, but would rather supplement and integrate the results of such initiatives into a more rational developmental pattern.

Behavioral Assessment

The paper and pencil approach to assessment abounds in the field of intervention research as a "stand-in" for behavior. It has been shown in a number of contexts, not at all surprisingly, that there is much inaccuracy in such methods. For example, although everyone tends to underestimate caloric consumption collected by self-monitoring, the obese may underestimate by a greater fraction of their caloric intake (Lichtman *et al.*, 1992). Even more problematic, there is considerable variation in accuracy between individuals. Unfortunately, inaccurate data about behavior may mislead researchers as to the directions to follow in intervention research, wasting a good deal of money in the process. While the measurement of behavior in the real world may be difficult and expensive, it is eminently worthwhile to develop such methods using the latest technology, so that our assessment is as accurate as possible and does not mislead.

Behavioral Processes

It is not obesity, *per se*, that is altered by behavior change procedures, but the various behaviors that impact upon obesity, such as food consumption (both amount and composition), food buying, food storage in the home, the circumstances surrounding eating, eating behavior, and activity patterns, to mention only a few obvious behaviors. The very first behavioral approaches to overweight assumed that

slowing eating would be helpful in reducing caloric consumption. But it took 25 years before an investigator actually demonstrated that slowing eating reduced caloric consumption (Spiegel *et al.*, 1991). We cannot afford such delay in examining the process of behavior that we are attempting to change, and the importance of detailed studies of such behavior, often suitably carried out in the laboratory, cannot be underestimated.

Conclusions

The suggestions incorporated in this paper that are needed to enhance intervention research in behavioral medicine are summarized below.

- ▶ Behavior change interventions may have broader health effects than medication, often making them a suitable first line of treatment.
- ▶ Broad scale education programs are needed to inform the public about the most advantageous approach to the treatment of common problems, so that the discrepancy between patient and therapist expectations regarding treatment can be minimized. Such education programs should be subjected to rigorous controlled testing.
- ▶ Intervention research should examine the reasons why patients seeking treatment do not follow through with such treatment, and to investigate more thoroughly the exact reasons for the substantial number of patients that drop out of treatment.
- ▶ Maintenance/relapse data should be reported more accurately, such that the reasons that patients that recover during the follow-up period can be investigated, and that such patients can be differentiated from those that relapse during the same period.
- ▶ Novel experimental designs that better model therapist decision-making should be encouraged.
- ▶ The design of therapeutic systems that offer more cost-effectiveness should be strongly encouraged.
- ▶ Multicenter designs in behavioral medicine will be needed.
- ▶ The investigation of behavioral processes and the development of behavioral measures should be strongly encouraged.

Finally, as we move toward the consideration of a health service with access to care for all, it will be important to develop a mechanism capable of reviewing the evidence for the effectiveness of the various therapies in use today. Only those therapies with evidence for effectiveness should be reimbursed under the auspices of a health service.

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Prenatal/Infant/Child

Overview

David Mrazek, M.D.

The first initiative was an amalgamation of a number of specific issues linking pediatric medical regimens with health outcomes in a systematic way to improve quality of care. We reviewed the need for addressing problems in compliance, feeling that there has been little empirical testing of the precise health behaviors required to correctly deal with appropriate medical monitoring of chronic illnesses. A very specific example is the management of diabetes, where there are variable numbers of daily blood glucose recommended and very little empirical evidence suggesting which frequency leads to better overall control.

Two major methodological issues need specific attention. The first is the need to study individual differences, i.e., tailoring specific treatment protocols and regimens to specific sets of risk factors or sets of physiological characteristics. These analyses would result in a better understanding of treatment efficacies.

The second major methodological issue is the need for developmental 'quality of life' measures. As quality of life is a key factor in many medical decisions related to chronic illness, developmentally focused measures of quality of life are required. Once reliable and valid instruments were established, they should become a standard component of all random-

ized clinical trials designed to measure the impact of treatment.

The second initiative, entitled Strategies to Improve Practice Behaviors of Health Care Providers and Health/Medical Care Systems for Optimal Child Health Services, emanated from an extensive discussion of the problems within the health care delivery system that have been particularly resistant to change. One strategy sought to better understand patients' learning styles in order to help health care providers to improve dissemination of information, i.e., transferring what we know about learning disabilities to improve communication skills and teaching strategies. Another issue is how to change the health care delivery system to facilitate communication. This must be done within the appropriate cultural context.

The third initiative is the development of multi-center clinical trials. Progress has been made on specific methods for improving pediatric health care, yet many of these methodologies have been developed at single sites and, despite having received exposure through publication, have not really made an impact on overall pediatric practice. One way to increase the credibility of these newly developed methodologies would be to give high priority towards the development of multicenter trials using essen-

tially the methodologies developed for pharmacological treatments but targeting them to nonpharmacologic treatments. Specific areas ready for such extensive testing would be the treatment of migraine, management of post surgical pain and consideration of paranatal and neonatal issues in the neonatal care unit. For example, these might include skin to skin postnatal contact and other parameters that significantly affect the environmental experience of the neonate. A successful multicenter trial which led to consensus on practice guidelines would be an effective way to speed dissemination.

Our final initiative targets one of the greatest pediatric health problems in our society: childhood violence and abuse. Early childhood abusive experience and early exposure to violence appear to be linked to the high prevalence of accidents, suicide and homicide that is the largest single pediatric problem we face today. One of the key problems in dealing with these

issues is access to patients. This has led to a consideration of methodologies to identify appropriate cohorts at different stages in the process of development of these problems. Clearly one of the most relevant sites is the pediatric trauma center or the pediatric emergency service. Through the development of appropriate services, children could be provided intervention and be identified as being at risk. Ongoing support for that particular incident could facilitate their inclusion within the health care system.

One of the opportunities provided by the utilization of emergency rooms to identify children is the high volume of patients. Given the unfortunate reality that in most major urban areas there is high patient flow through these systems, a randomized trial could be developed. Standard treatment versus an intensive behaviorally designed program could be studied longitudinally, focussing on differential outcome between those two cohorts.

Task Group Initiatives

✓ Improvement of Health Outcomes through Better Caregiver Management Behaviors (C-1-1)

Need and Justification

The management of all chronic disease depends on multiple self-care behaviors throughout the child's life. Many of these medical regimens are complex, exacting, painful, or distasteful. Furthermore, they may require significant lifestyle changes.

Compliance with these regimens is known to be highly variable. For some diseases, self-care behaviors may have a profound impact on health status. For other illnesses, patient behavior is less related to health outcome. Even within a disease, few studies have addressed the question of which of several self-care behaviors is the most efficacious. Most studies of self-care behaviors have failed to address the question of the minimal changes in behavior that are required to induce a desired health outcome.

Similarly, most studies have failed to address the range of improvement in health status that can be expected under conditions of rigorous adherence to recommended treatment. Such studies should include quality of life as an important component of the risk/benefit equation. Many self-care behaviors have multiple "costs" in terms of lifestyle changes and discomfort. A quality of life assessment will permit a more complete understanding of overall costs in relationship to health care benefits. Such an analysis should assist patients and

families in the decision-making process, identifying which behaviors are most strongly related to good health and the relative "costs" of those behaviors in relationship to the expected benefit.

Research Approach/Methodology

Most patients are given a standard treatment protocol that could be utilized to define the relative contribution of specific health care behaviors to health outcome. Investigators are also encouraged to examine individual differences in terms of which self-care behaviors most influence health outcome for an individual patient. The standard care approach assumes that recommended treatments will have similar effects on all individuals with the same disease. The individual differences approach assumes that individuals vary in terms of the relative contribution of certain self-care behaviors to health outcome. For example, in childhood diabetes, insulin action may differ across patients. If so, timing of insulin injections appears to have different effects for different patients. Variables that could affect individual treatment efficacy might include physiological and hormonal differences as well as socio-cultural acceptance, family structure, gender and the child's developmental level. The creative application of within-subject research designs would be particularly helpful.

A central need for this field is to establish developmentally sensitive measures of quality of life in children. These measures need to be reliable, valid and standardized. Wherever possible, quality of life measures that can be

applied across many diseases and which can be adapted to different racial/ethnic/socioeconomic groups are preferred. Once established, these measures should become standard tools in behavioral and biomedical treatment.

✓ **Strategies to improve the Practice Behaviors of Health Care Providers and Health/Medical Care Systems for Optimum Child Health Services (C-1-2)**

Need and Justification

The practice behaviors of physicians and other health care providers as well as the operation of health/medical care systems are critical to the quality of care that is provided to infants and children. Numerous factors are involved, including (but not limited to): 1) the time lag between the establishment of health promotion or disease management guidelines and the placing of these guidelines into practice; 2) specialization in medical care requiring patients to seek care from several providers at different sites; 3) the lack of continuity of care for chronic conditions; 4) communication problems between providers and patients/families, especially with increasing diversities of cultures in the United States; 5) differing goals between patients/families and providers; 6) inadequacy of counseling and educational skills by providers.

It is essential to develop, implement and evaluate interventions that will result in improving not only the knowledge and attitudes of physicians and other health care providers, but also their practice behaviors, so that patients receive the best possible care. Modifications are also needed in the health/medical care systems that will promote appropriate behavior change among patients and their families. The interventions directed toward providers and the system should ultimately contribute to the improvement of the health of infants and children. The goal of this initiative is to develop

and test programs for use by practitioners in a variety of health care settings.

Research questions include:

1. How can state of the art diagnosis and treatment guidelines for children and adolescents be incorporated rapidly into the routine practice of primary care providers?
2. What are the most effective ways to organize health care systems to serve the diverse needs of different cultural and socioeconomic learning styles of children and parents?
3. What modifications in health care systems result in improved continuity of care, early detection of health problems/disease, and improved adherence to treatment regimens?
4. How can communications be improved between members of the health care team and between providers and patients/families?
5. How can the differing learning styles of providers, patients, and parents be used to reduce barriers in communication?
6. Where learning disabilities exist, what practical teaching strategies can be applied to a child in health care settings?

7. What roles can lay advocates/teachers play in changing child/family health behavior?

Research Approach/Methodology

NIH-initiated intervention research programs.

✓ **Fostering Multi-Center Trials for Behavioral interventions (C-1-3)**

Need and Justification

Pharmacological treatments routinely undergo multi-center trials before practice guidelines are determined. Behavioral interventions, however, have not followed the same rigorous testing procedure, which has resulted in a questioning of the credibility and robustness of studies, a lack of dissemination, and a failure to establish standard treatment regimens. Multi-center trials of select behavioral interventions could provide a systematic assessment of efficacy, as well as serve as a catalyst for dissemination. For many of the behavioral interventions proposed in pediatric care, there is still a compelling need to establish a more substantial data base and to achieve consensus.

Several nonpharmacological pediatric treatments for a variety of conditions including migraine headaches, enuresis, preoperative anxiety and postsurgical pain have been developed, tested

and replicated in individual studies and now may be ready for multi-center trials. In addition, there have been a number of sensory treatments evaluated in premature infants and neonates. These treatments include touch, skin-to-skin contact, decreased light and sound, and parental contact.

Multi-center trials are also needed for nonpharmacological treatment for oppositional behavior, conduct disorders, attention deficit disorders, and hyperactivity in young children.

Research Approach/Methodology

- ▶ Longitudinal studies involving multi-disciplinary teams.
- ▶ Efficacy and cost-benefit evaluation of pharmacological and nonpharmacological treatments.

✓ **Early intervention with Children at Risk for Exposure to Violence and Child Abuse (C-1-4)**

Need and Justification

A constellation of violence-related phenomena exists which constitutes the largest pediatric health problem in the United States. A great deal of research shows that a history of violence or sexual abuse places children at risk for significant morbidity and mortality. Further, studies suggest that children prone to behavioral misadventures of various sorts, such as accidents, suicide, homicide, and other serious developmental and behavioral problems are products of a social and familial environment which may be characterized by specifiable risk factors.

The sequelae of exposure to violence are only now beginning to be understood. Early findings suggest that there is a higher incidence of a broad range of emotional disorders and physical illnesses. The escalating exposure to violence has placed children and youth at great risk, not only for death by violence but for significant emotional disorders, and other sequelae. Research indicates that many children growing up in violence-ridden environments become desensitized to the violent aspects of their environment, while others are so perturbed by their life circumstances that they become socially isolated.

How do we approach the problem from a research standpoint with a view toward intervening successfully with such children and youth? It is important to discover the affected persons early; for example, one site where one might find such at-risk children would be the emergency rooms of major pediatric hospitals.

These facilities presently are focused exclusively on life support with little consideration of how behavioral interventions could reduce the risk of morbidity in these children.

Emergency rooms, community health agencies, the school system, community counseling centers, and other local facilities may be the contact points best suited for health and behavior interventions. Of paramount importance is the opportunity for the children to make contact with professionals prepared to discuss their injuries, their anxieties, and their future. The advantage of emergency room attention to behavioral and emotional concerns of afflicted youngsters is the immediacy of the situation—i.e., the present urgency of their clinical needs.

Research Approach/Methodology

Documentation is needed of the effectiveness of emergency interventions with afflicted children and families coming to the attention of the emergency room for abuse, assault, or injury stemming from interpersonal conflict. We believe it is feasible to mount an informative and valuable study that would provide intensive psychological care to a substantial number of patients of the above description appearing in the emergency room, or coming to the attention of the police department, school facilities dealing with crises, and protective service agencies.

Outcome variables: Attention would focus on behavior problems, school performance, and other manifestations of attentional deficits. In

addition, a primary effort would be made to document the differential susceptibility of afflicted youngsters to accidents, injuries, and excessive risk-taking.

The design of proposed studies should include random assignment to treatment and control groups. In some ERs of major hospitals in this country, as many as 10 cases per day arrive who could be candidates for this study because

of physical abuse (assault), sexual abuse, or neglect. Thus a large cohort could be introduced into a longitudinal study beginning on the day of the subject's arrival at the ER. The objectives of the study would be, first, to document the characteristics of children who come to the attention of the ER, and secondly, to implement intervention strategies which have demonstrated effectiveness in reducing risk of subsequent adversity for affected children.

Adolescent/Young Adult

Overview

Kelly Brownell, Ph.D.

Introduction

Behavioral medicine research pertaining to the health of adolescents and young adults is important for several reasons. First, a number of developmental changes occur during this period of life which are manifested in alterations of physiology, psychology, and social interactions. These create an environment placing some individuals at risk for problems such as eating disorders, drug and alcohol abuse, automobile accidents, teenage pregnancy, sexually transmitted diseases, AIDS, homicide and suicide. These problems can be best understood with conceptual models (and ultimately prevention programs) rooted in integrating biological, psychological, and social factors.

The second factor underscoring the importance of this age group is that critical attitudes, intentions, and behaviors are formed during this period. These can affect the individuals' health and well-being for decades to come. Examples are attitudes such as concern with health, respect for others' safety and perceived risk/benefit of health-related behaviors, such as cigarette smoking, diet, physical activity, use of seat belts, and sexual practices.

Using cigarette smoking as an example, research has shown that nearly all of adult smokers began smoking in the teenage years. A number of factors, including genetics, peer group, gender, socioeconomic status, and family smoking patterns converge to make a person susceptible to beginning smoking. An addictive process ensues, fueled both by physiology and psychology, which makes the habit extremely resistant to change, even if the reasons for initiation have vanished. While the health consequences occur later in life, the primary solution lies in prevention during the first two decades. Similar arguments can be made for diet, physical activity, drug use, alcohol use and other factors.

A number of factors were considered by the Task Force in developing specific research initiatives. These included prevalence of specific health problems in adolescents and young adults, developmental issues relevant to this age group, the likelihood that attitudes and behaviors in this age group will persist into later life, and cost-effectiveness (i.e., whether initiatives will have a significant impact on major health problems). In this process, several overriding issues were put forward. These are considered central to conceptualizing behavioral medicine research:

- ▶ **Use a Broad Definition of "Treatment."** "Changes in health can occur via many routes other than the traditional health provider/patient relationship. Peers, self-help groups, the media, and self-change programs are examples of channels through which interventions can be devised and delivered. These should be considered because of the potential decrease in cost and increase in effectiveness.
- ▶ **The Essential Role of Evaluation and Dissemination of Interventions.** Considerable knowledge is available on health issues in adolescents and young adults, but often the work is fragmented, occurs in different disciplines, is not integrated, and is not disseminated to health professionals. The NIH, perhaps in conjunction with other agencies, could take the lead in an evaluation and dissemination effort. One such possibility might exist in interactions between NIH and the Agency for Health Care Policy Research, which undertakes comprehensive evaluations of treatments for some health problems.
- ▶ **Basic Research on Behavioral Processes is Crucial.** Compared to the biological, medical, and physical sciences, relatively little support has been earmarked for basic research on health-related behavior. Basic neuroscience, work in cognition, and learning research are examples of where more work is necessary to provide a foundation and a theoretical framework for intervention and prevention.
- ▶ **Research Should Be Based in Theory.** This point may seem obvious, but even in today's competitive funding climate, much health research is taking place outside the context of theory. This leads

to haphazard research with little applicability beyond the target population. The entire field could advance more rapidly if increased emphasis was placed on theory-based research.

Specific Research Initiatives

Four specific initiatives have been proposed and are covered in detail in accompanying material. The initiatives are:

1. **Development of Community-Based Models of Intervention to Minimize/Mitigate Social/Environmental/Individual Barriers to Delivering Treatment and Disseminating Effective Approaches.** A great deal is known about the treatment and prevention of some health problems in adolescents and young adults. Barriers intrinsic to the individual and the environment hinder the effective delivery of these programs. This initiative focuses on the identification and modification of these barriers.
2. **Social Relationships-Based Interventions.** Social variables are clearly important in health. Peer groups, families, and other social influences are key factors in understanding the development of health problems and must be considered in designing interventions. This initiative focuses on the development and refinement of interventions based in social networks. Examples would be family-based interventions, peer counseling, and group treatment.
3. **Maintenance and Relapse in Behavior Change.** Relapse and problems with maintenance of behavior change are

major issues in a number of areas relevant to adolescents and young adults. Relapse rates are high in individuals attempting to change drug and alcohol use, smoking, diet, exercise, and sexual practices. Some programs are effective in helping individuals change these behaviors, but much more research is needed on the basic processes of behavior change, risk factors for relapse, and relapse prevention strategies.

4. **Matching Individuals to Treatments.** Multiple approaches are available for the treatment and prevention of many problems. The field has progressed by comparing one approach to another in randomized trials. This work is important, but overlooks the fact that different individuals will respond to different approaches. This initiative calls for a generation of studies which would first identify possible matching factors and then test these factors in treatment and prevention studies.

Task Group Initiatives

✓ **Development of Community-based Models of Intervention to Minimize/Mitigate Social/Environmental/Individual Barriers to Delivering Treatment and Disseminating Effective Strategies for Treatment (C-2-1)**

Need and Justification

Research suggests that social/environmental and individual barriers can affect the ability to deliver treatment services to adolescents and young adults. Factors at the individual level include patient motivation, preparedness for treatment, lack of health insurance, and minority status of adolescents.

At the care-provider level, barriers may include cultural insensitivity, stigma associated with the presenting problem or presenting client, and failure to recognize other related problems. In addition, at this level, providers may be overwhelmed by the magnitude and complexity of these problems and the lack of resources needed to address them adequately.

At the social level, the barriers can include community-held values that stigmatize the problem, inadequate resources to address the problem, discrimination against those with the problem, and, geographic inaccessibility of services. The development of strategies to address these barriers would facilitate early diagnosis and treatment, lower health care costs and improve health status.

Research Approach/Methodology

Depending upon the state of development of these strategies for particular health problems, a range of research approaches and mechanisms could be pursued, including RO1 grants, small grants, demonstration projects in multiple sites, and multicenter studies.

In developing this initiative, emphasis should be placed on requiring appropriate dissemination of effective models.

Examples of specific areas of research include:

1. Improving the ability of agencies to serve the homeless;
2. Improving outreach to treatment-resistant populations such as drug abusers;
3. Developing new models of treatment for people with comorbid conditions;
4. Improving treatment adherence for adolescents with STDs, hypertension, Type I diabetes, and other illnesses requiring prolonged treatments;
5. Developing strategies for disseminating models with demonstrated effectiveness.

✓ **Social Relationship-Based Interventions (C-2-2)**

Need and Justification

Research has highlighted the importance of family, community, and other social interactions to the development and maintenance of a variety of health behaviors. Social relationship-based interventions, including peer group programs, group therapy, self-help, and family-based interventions appear particularly well-suited to adolescent and young adult health problems, given the important role of social context and environment. For example, family-based intervention research has documented long-term effectiveness. Multiple component intervention research focused upon social networks, peer group formation, group therapy, care-giver programs and case management also have yielded promising program results in a number of disease categories.

Research Approach/Methodology

Where possible, these studies should employ controlled randomized designs. Where appropriate, other research designs such as matched community control studies, descriptive studies and quasi-experimental designs that control for possible threats to internal and external validity could be employed. Mediation analyses of predictor variables and mechanisms related to outcome are essential.

For example, family-based intervention research that involves the patient and other family members that share the disease or related behavior should be supported. Research that targets multiple family members has the potential for broad treatment effects across individuals with potential enduring results. This research offers an excellent return on research funding and is cost beneficial.

✓ **Maintenance and Relapse in Behavior Change Among Adolescents and Young Adults (C-2-3)**

Need and Justification

Many health-related behaviors are initiated in adolescence and young adulthood, including smoking, drinking and eating patterns, and sexual activities. A subset of this age group develops problems with these behaviors which are associated with a variety of adverse health outcomes (e.g., HIV infection, obesity, substance abuse and dependence, accidents), both in adolescence itself and later in the adult lifespan. Although a number of behavioral interventions have shown efficacy in reducing these behaviors, a major problem is that treatment effects are not maintained after treatment is terminated. Given the high social and economic costs of these behaviors, it is imperative that factors that may facilitate maintenance and reduce relapse rates be identified.

Research Approaches/Methodology

Research options include:

1. assessment of the role of treatment goals for behavior change; e.g., total abstinence vs. harm-reduction goals for alcohol use or sexual activities; or reduced caloric intake and modification of eating behavior patterns vs. fixed weight loss goals associated with traditional diets;
2. establishment of health-promoting norms for the maintenance of these behaviors across the adolescent lifespan;
3. assessment of the natural history and learning context in the development of individual factors (such as cognitive processes, affect regulation, and coping skills associated with self-regulation) so as to better tailor treatment interventions to the developmental stage of adolescence;
4. development of treatment strategies that are matched to the individual's unique position or progress in the stages of behavior change (e.g., readiness for change, severity of relapse pattern);
5. assessment of situational, personal, social and environmental risk factors for initial lapses, relapses, and treatment drop-outs; and
6. evaluation of processes that enhance successful long-term maintenance of behavior change in this age group (e.g., supportive peer environment, general coping capacity; change in living environment).

Attention should be paid to special populations and diverse ethnic and socioeconomic groups in the design of research studies.

✓ **Matching Individuals To Treatments (C-2-4)**

Need and Justification

Many attempts have been made to intervene to alter risk factors, treat disease, and facilitate rehabilitation. Traditionally these interventions proceed as if populations are homogeneous. The results have been equivocal, with the same interventions showing beneficial effects in some studies but not others. Research must address the great diversity of target populations to understand how physiological, psychological, and social variables interact with treatments. An important priority is to support research to identify methods for treating individuals with different approaches.

Research Approach/Methodology

Matching individuals to treatments must be done with consideration of physiological, psychological, and social variables. Research is needed to identify individual differences in these domains for specific risk behaviors, diseases, and injuries, and then to develop and evaluate both matching criteria and interventions to facilitate the matching process.

Examples of target areas are:

1. **Obesity.** Numerous treatments are available for obesity. They differ in fundamental ways in philosophy, structure, and emphasis on key issues such as cost, duration, and emphasis on nutrition, physical activity, and behavior change. Research is necessary to define the variables which would indicate one treatment over another for individuals.

Examples of such variables might be metabolic rate and appetite dysregulation in the physiological domain, readiness and body image in the psychological domain, and social support and peer influences in the social domain.

2. **Hypertension.** Behavioral interventions for hypertension show significant blood pressure reductions in some individuals and no reductions in others. Since hypertension can involve different pathophysiological systems (e.g., the renin angiotensin systems, salt sensitivity, sympathetic hyperactivity, insulin resistance) it is logical that behavioral intervention is more relevant for some persons than others.
3. **Hostility and Depression.** Persons with certain psychological characteristics are more likely to engage in health damaging behaviors (e.g., smoking, alcohol abuse, overeating). Examples are hostility and depression. Research is needed in which individuals being treated for smoking, obesity, as other disorders are assessed and treated for hostility and depression.
4. **Chronic Pain.** Individuals with chronic pain vary in levels of dysfunction in work, school, and interpersonal interactions. Persons with significant life disruption may require different treatment than those less disabled. Understanding the factors that indicate specific treatments for individuals is important to dealing with this chronic problem.

Midlife Adult

Overview

Fawzy I. Fawzy, M.D.

Much research has been done that helps us to understand the psychological distress that patients with major medical illness and their families experience (Weisman, 1979; Cohen *et al.*, 1982). A number of reports have also appeared in the literature about interventions that effectively help individuals to deal with the diagnosis and treatment of cancer (Spiegel *et al.*, 1981; Linn *et al.*, 1982; Cain *et al.*, 1986; Fawzy *et al.*, 1991). The most exciting aspect of these reports is that these interventions may contribute significantly to both psychological and physical health outcome (Spiegel *et al.*, 1989; Ornish *et al.*, 1992; Greer, 1991; Fawzy *et al.*, 1993).

These promising studies show that psychosocial interventions have medical as well as psychosocial effects. The latter effects alone warrant widespread application. In addition, such techniques are inexpensive and help reduce misuse of medical services. Yet they are not widely applied. There is pressing need to study the generalizability and replicability of these findings, and test the application of these methods to populations with a variety of illnesses, SES, gender, and ethnicity in community as well as university settings.

It is essential that we begin to document the effects of psychological interventions on the

course of an illness as well as on the coping abilities of patients. These interventions may work in conjunction with standard medical treatment to increase psychological and emotional well-being and to improve the course of a devastating illness such as cancer.

Advances have been made in the field of psychosocial therapy for oncology patients and others who are medically ill (Fawzy *et al.*, 1983; Cohen *et al.*, 1982; Fawzy & Fawzy, 1982). Different intervention models have been utilized as part of the psychosocial response to the needs of cancer patients and those with other catastrophic disease (Bloom *et al.*, 1978). The goals of these interventions, according to Holland (1982), are to decrease feelings of alienation by talking to others in a similar situation, reduce anxiety about the treatments, assist in clarifying misperception and misinformation, and lessen feelings of isolation, helplessness, and being neglected by others. Interventions are designed to help a person feel less helpless and hopeless, and perhaps take more responsibility for getting well or for complying with medical regimens. The public is well aware of many psychosocial therapeutic interventions for cancer patients, and with the popularity of some approaches (such as hypnosis, relaxation training, and guided imagery), patients may often specifically request such services.

NIH should encourage large sample size, multi-center trials of promising intervention techniques for the medically ill. Such large studies will allow for subgroup analysis to answer the following questions:

- ▶ which components of multimodal interventions work best;
- ▶ what are the mechanisms of treatment efficacy; social support, cognitive restructuring, behavior change, symptom control, etc.;
- ▶ what are the physiological mechanisms which mediate effects of treatment on disease progression;
- ▶ how can the intervention be tailored to the needs of specific subsets of patients;
- ▶ which individuals are best suited to respond to a given intervention;
- ▶ which patients are most at risk without benefit of intervention; and,
- ▶ what are the most effective means of teaching and disseminating this intervention?

Randomized, controlled studies of strategies to enhance adherence during initial and/or maintenance phases of clinical care are desired. Studies should include an evaluation of predictors of both adherence and response to the behavioral intervention.

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✓ **Multi-site Trials of Psychosocial Interventions for the Support of Individuals with Major Medical Illness (C-3-1)**

Need and Justification

Numerous studies have demonstrated the efficacy of supportive psychotherapeutic and behavioral interventions as part of comprehensive management of medical illness. Various supportive group and individual interventions have been shown to reduce mood disturbance, enhance coping skills, reduce social isolation, and improve adjustment to illness among patients with cancer, AIDS, and heart disease.

In addition, recent research has provided provocative evidence of biomedical effects of psychotherapeutic and behavioral interventions. Three studies have shown that cancer patients randomly assigned to psychosocial intervention (two group, one individual/psychoeducational) lived longer than control populations receiving routine care (Spiegel *et al.*, 1989; Richardson *et al.*, 1990; Fawzy *et al.*, 1993).

In HIV, intervention studies show a decrease in stress related to the diagnosis, with limited evidence of slowed progression of disease, and decreasing titers of EBV which can serve as a reservoir for HIV infection.

A study at Mt. Zion of approximately 1,000 men and women post-MI showed a decrease in recurrence as measured by mortality and morbidity among those randomly assigned to a group intervention designed to alter Type A behavior. This has been replicated in Europe. Frasure-Smith and colleagues in Montreal demonstrated that post-MI patients offered a

nurse-run psychosocial intervention involving psychoeducation and counseling showed better survival in the year following their infarct. Ornish showed that cardiac patients offered group support, training in meditation, and a vegetarian diet showed improvement in coronary artery disease.

These promising studies show that psychosocial intervention has medical as well as psychosocial effects. The latter effects alone warrant widespread application. In addition, such techniques are inexpensive and help reduce misuse of medical services. Yet they are not widely applied. There is pressing need to study the generalizability and replicability of these findings, and test the application of these methods to populations with a variety of illnesses, SES, gender, and ethnicity in community as well as university settings.

Research Approach/Methodology

Large sample size multicenter trials of promising intervention techniques for the medically ill are needed. These should have populations homogeneous for medical illness, with attention to prognostic variables in the randomization process, either through careful sample selection, blocking, or stratification. Interventions, group or individual, should be carefully defined, preferably with manualized protocols, and study of the effectiveness of implementation should be included. Outcome evaluations should include:

1. **Medical Outcome:** disease progression, such as cancer recurrence, subsequent MIs, or conversion from HIV infected status to AIDS, mortality, and other physiological variables; and,
2. **Psychosocial Outcome:** standard measures of mood disturbance, quality of life, and specific dimensions of relevance to the disease studied, including coping skills, personality, family functioning, and social support, as well as cost-effectiveness.

Such large scale studies will allow for subgroup analysis to answer the following questions:

- ▶ which components of multimodal interventions work best?
- ▶ what are the mechanisms of treatment efficacy: social support, cognitive restructuring, behavior change, symptom control, etc.?

- ▶ what are the physiological mechanisms which mediate effects of treatment on disease progression?
- ▶ how can the intervention be tailored to the needs of specific subsets of patients?
- ▶ which individuals are best suited to respond to intervention?
- ▶ which patients are most at risk without benefit of intervention?
- ▶ what are the most effective means of teaching and disseminating this intervention?

Designs with well-defined clinical populations; systematic assessment of all variables; controlled interventions; comparison among relevant population, including study of gender, social class, ethnicity, and other variables are encouraged.

✓ **Predicting Response to Behavioral Treatment of Disease (C-3-2)**

Need and Justification

Research on the application of behavioral techniques to the treatment of somatic disease has suggested that there is often considerable variability in the response of individual patients to these treatments. Self-control techniques such as relaxation, meditation and biofeedback have all been shown to be useful for individuals in the treatment of a variety of conditions including hypertension, Raynaud's disease, and diabetes mellitus. However, when applied to large numbers of subjects, mean effects are small. Similarly, the variability of individual response to weight loss programs, smoking cessation programs, and other behavioral intervention strategies often obscures the fact that some patients respond dramatically to treatment. Recent research has suggested that personality variables may be useful in predicting which patients are most likely to benefit the most from these sorts of interventions.

Understanding the variables that predict response to behavioral treatment of disease is important for several reasons. First, methods to identify those patients likely to benefit from

behavioral treatment will allow primary care providers to make appropriate referrals; second, by minimizing treatment failures, accurate selection of patients will increase the cost-effectiveness of behavioral treatment; third, understanding the variables that predict treatment success may lead to a greater understanding of how these treatments affect the disease process.

Research Approach/Methodology

Clinical studies should be undertaken of the following behavioral treatments, incorporating psychometric assessment of individual differences:

- ▶ of self-control strategies such as biofeedback, relaxation, meditation, etc.
- ▶ of behavioral weight management approaches
- ▶ of behavioral treatments of addictive disorders
- ▶ of compliance-enhancing strategies

✓ **Development of Experimental Designs and Methodologies Appropriate for Behavioral Interventions (C-3-3)**

Need and Justification

Clinical studies utilizing behavioral interventions encounter several methodological problems which have hindered their acceptability to the scientific community. Acknowledging the inherent differences between studies using such interventions compared to studies using surgical or pharmacologic interventions, new designs and methodologies must be developed and tested. Specifically, there is a need to examine the conceptualization and design of control groups, placebo interventions and assessment of outcome in behavioral research. There is also a need to determine the significance and implementation of "blinding" in behavioral medicine studies, and to examine the importance of developing standard protocols which facilitate generalization. The issues of distinguishing behavioral interventions which are adjunctive to "standard care" as opposed to behavioral intervention which are alternative to standard care must also be addressed.

In many conditions, assessment of symptoms is difficult, independent of self-report. This also limits the external validity of clinical studies, especially if double blind designs are cumbersome or impossible to carry out. Technological advances in micro-electronics and miniature transducers must be exploited to develop tools suitable for monitoring and assessing treatment outcome in ambulatory patients.

Research Approach/Methodology

Proposals which seek to test the influence of novel or unique approaches for control groups, randomization procedures, exploitation or control of expectancy effects and assessments are responsive to this solicitation. Utilization of quasi-experimental designs or pre-randomization procedures would be appropriate and are encouraged. Intervention studies which focus on the relationship of predictor variables, or mediating variables on intervention efficacy, would also allow some flexibility in interpretation of outcomes without necessarily including traditional control or placebo conditions. In addition, the development of designs which phase-in or cascade intervention sequentially would provide alternative strategies for assessment of intervention efficacy. Designs focused on determining the "average efficacy" of interventions for patients rather than testing the average response of experimental groups compared to control groups could also be considered. The most significant issue of methodology is the development of designs which would allow empirically sound assessment of behavioral intervention without compromising scientific rigor but at the same time acknowledging the special issues inherent to behavioral research.

✓ Behavioral Strategies to Promote Adherence in Health Care: Active Treatment and Maintenance (C-3-4)

Need and Justification

One of the major problems impinging upon the successful management of care is initial and continuing adherence. Adherence poses a problem in both medical and behavioral therapies. The problem crosses the age span, diseases and intervention methodologies and impedes the attainment of treatment objectives for a significant proportion of patients. For example, as many as 20% of organ failures in transplantation (Didlake *et al.*, 1988; Rovellie *et al.*, 1989), the development of antibiotic resistant tuberculosis (Bloom & Murray, 1992), and failures of chemotherapy and/or radiation therapy for cancer (Klopovich & Trueworthy, 1985) have been attributed to partial adherence. Pediatric problems ranging from repeated ear infections (Bergman & Werner, 1963), seizures (Hazzard *et al.*, 1990), and asthma attacks (Lemanek, 1990) to hospitalizations for ketoacidosis (White *et al.*, 1984) have been linked to problems with adherence. Similarly, the management of chronic illness, such as hypertension (Dunbar-Jacob *et al.*, 1991), diabetes (Ary *et al.*, 1986), asthma (Horn *et al.*, 1990), and arthritis (Bradley, 1989), has been compromised by partial adherence to prescribed treatment. Poor adherence is also reflected in the failure to attain weight loss, dropouts in exercise rehabilitation programs, and smoking relapse, among others. While there is a large literature on adherence, very few randomized controlled studies have been conducted to evaluate the efficacy of strategies to enhance adherence in clinical settings.

Research Approach/Methodology

Randomized, controlled studies of strategies to enhance adherence during initial and/or maintenance phases of clinical care are desired. Studies should include an evaluation of predictors of both adherence and response to the behavioral intervention. Studies may also include the evaluation of adherence-improving strategies for the patient on multiple therapies. The feasibility and cost effectiveness of implementing these strategies within a clinical care setting should be assessed. Studies should also include the impact of adherence on therapeutic outcome, quality of life, and a broader assessment of its impact on the patient. The studies selected will represent a balance of populations, including age, gender, and ethnic group status.

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Senior Adult

Overview

Jimmie Holland, M.D.

In considering treatment research initiatives for senior adults, two dimensions must be considered from a behavioral medicine perspective. The first is that the number of healthy elderly are increasing and we need to develop effective means to keep them healthy. The second dimension concerns the number of frail and vulnerable elderly which are also increasing in our society.

The first two program initiatives deal with the interventions for older people that cover social, physical, and behavioral approaches directed toward improving quality of life. The second two initiatives deal with medical care interventions, medical decision-making and health care systems issues as they impact upon quality of life, medical outcome and ethical dilemmas.

Task Group Initiatives

✓ Social and Physical Environmental Interventions for Senior Adults (C-4-1)

Need and Justification

Behavioral medicine has a scope that extends beyond individual, disease-specific interventions that are associated with a more "traditional" definition of treatment. For the rapidly growing older population, this breadth has particular salience as the "health" issues for an aging society encompass the interrelated areas of disease, well-being, independence, and quality of life.

In this framework, the social and physical environment must be acknowledged as a component of treatment for it may impact on the disabilities, functional status, and quality of life of older persons. The great majority of older persons, including those with some level of disability and/or chronic conditions or illness, remain within the community. Consequently, their living conditions, (the physical environment including housing, personal assistance devices and aids,) and the nature and scope of social relationships (family, neighbors, community) have significant impact on overall health in later life. However, little is known about the actual effects of the existing physical and social milieu and how best to target interventions on this environment for elder individuals with

- ▶ an identified condition or disability,
- ▶ needs related to cultural differences, such as among special populations of older

people (racial and ethnic minorities, rural elders), or

- ▶ special needs such as those living alone, or who have no nearby family members.

Advances and new developments in the physical environment include ways to intervene through "hard technology," such as smart houses, interactive and computer-related devices, and other complex approaches. Interventions may also include "soft technology" manipulations, like color coding in the home, providing flexible living arrangements, or even such simple changes as homes that allow an older person access to a window or garden. Thus, attention to the social environment as it may facilitate independence and wellbeing becomes an integral part of a coordinated plan of treatment.

Research is needed to determine what are the most effective social environmental interventions, where they are provided (e.g. in what setting), who provides the interventions (e.g. extended family members, primary care provider, churchmember) that would maximize older persons' functioning and quality of life. In particular, looking at the existing support networks of the older person, such as significant family members, and social organizations/institutions such as religious organizations, is considered especially important, because these relationships may be the most effective (and

cost-effective) intervention units. For example, previous intervention research, delivered through churches in African American communities has demonstrated significant improvements in health outcomes and behaviors (e.g. hypertension, smoking cessation); such settings are often a focus for activities of elders. Also, interventions which include personal care assistants (those who deliver services, such as grooming, shopping, yardwork, laundry) where the goal is to maximize functioning and maintain residence in their home, need to be studied.

Variations in the acceptability and effectiveness of both environmental and interpersonal interventions in groups which differ with respect to race, ethnicity, culture, geographical location, socioeconomic status, need to be examined.

Research Approach/Methodology

Social and environmental interventions may be assessed with a range of survey, qualitative, and controlled designs. In some cases, experimental methodologies are appropriate for the initial testing of technological innovations. However, further study must apply and evaluate these interventions in a "real world" setting and thus may call for demonstration and education approaches. Social interventions may be assessed with a range of survey, qualitative, and controlled designs. An interesting approach would be the adaptation of a "cascading" model that would be able to test the least complex interventions before the addition or substitution of more intensive or costly treatments.

✓ **Behavioral Interventions in Adults With Chronic Disease (C-4-2)**

Need and Justification

Depression, inactivity and social isolation have been identified as common problems in elderly individuals with chronic disease. There are few studies on the effects of behavioral/psychotherapeutic interventions in older people with chronic disease. For example, there are no controlled studies on the efficacy of behavioral interventions for depression in stroke patients, or counseling strategies in elderly cancer patients. Little is known about how factors such as comorbidity and absence of social support may affect treatment efficacy.

There is a need to train older people with chronic diseases to be educated consumers of health care. Knowing what the medical systems offer and how to communicate with health care professionals is an urgent need.

Research Approach/Methodology

Interventions should be developed to include individual and group approaches and might test different models of group leadership. Adaptations for studies across different types of diseases should be considered.

Types of interventions might include aerobic and strengthening exercises, cognitive behavior therapy, constructive use of leisure time, self help approaches, etc. Novel approaches should attempt to address issues of social isolation, particularly in older women. Interventions which could be delivered in the home or other naturalistic settings are to be encouraged.

✓ **Medical Decision-Making and Effects on Illness Outcomes (C-4-3)**

Need and Justification

As capacities for early detection and intervention increase across a wide range of conditions, the opportunities to aggressively address illness multiply. Large uncertainties exist as to the treatment value and cost-effectiveness of early identification and intervention in a wide variety of instances. Sophistication of new technologies results in the detection of abnormalities of unknown significance and may tend to increase the use of aggressive interventions that contribute to high costs and iatrogenic effects.

Research is needed to identify the benefits and costs of intervening relative to watchful waiting, and their relative effects on function and quality of life. The balance of aggressive uses of technology versus other forms of intervention may change as people age and disabilities progress. This research program would define contributions under which aggressive treatment is appropriate and cost effective.

Research Approach/Methodology

Research in this case should include multidisciplinary, randomized clinical trials to assess the relative outcomes associated with different treatment approaches. Epidemiological study of

the natural history and treatment patterns of various diseases will improve our understanding of changing patterns and provide the basis for randomized clinical trials.

Such trials require continuation of the functional outcomes and quality of life under alternative treatment protocols, with particular attention to disability. Areas which require evaluation include hysterectomy, treatment of prostate cancer, cataracts, hip replacement, hypertension, depression, coronary bypass and angioplasty, and estrogen replacement in older women. Evaluation should focus on both over-aggressive and under-aggressive care in elderly populations.

Research is also needed on broad social and ethical questions concerning the provision and withholding of care. For example, to what extent are recent health care policies and laws (e.g., the do-not-resuscitate laws and health proxy designations) impacting upon appropriate care of the elderly and what are the ethical implications? It is well recognized that inappropriate and overly aggressive care in the last weeks of life is sometimes undertaken without the clear consent of the person and without attention to their prior wishes. What are the implications of these decisions for the surviving family members, as well?

✓ **Aging Populations and Evolving Health Care Systems (C-4-4)**

Need and Justification

As the population ages, with increasing prevalence of chronic disease, the demand for health care is expected to continue to increase. There are a range of alternative approaches to financing, organizing and delivering health care, and the mix of medical and medically-related social services needed may vary with disease profiles, age, and social circumstances.

As the nation moves to more organized forms of health care delivery, and more forceful cost containment, research is needed to identify the most cost effective approaches for containing disease processes, maximizing functioning and independent living, and maintaining quality of life. There are concerns that the pressures of managed care may encourage undertreatment of older people with multiple chronic diseases or restrict the range of services available (for example, home and community-based care, case management, mental health services, etc.).

Examples of the kinds of questions that should be addressed include: does capitated payment lead to neglect of persons with multiple long-term chronic conditions? To what extent can enhanced service delivery systems, such as social health maintenance organizations, overcome existing tendencies to define needed care in a narrowly-focused acute care mode? How can current health care systems (e.g., hospitals) evolve their structures and functions to be more adaptive to growing long term care needs of an elderly population?

Research Approaches/Methodology

A variety of research approaches are needed to address these important issues, including descriptive research on the outcomes of persons with particular illness patterns in varying health care delivery settings, experimental trials of alternative delivery systems and service modalities, and qualitative assessments of peoples' experiences with the health care system and their impact on outcomes.

Synthesis

David Spiegel, M.D.

This is an era of unprecedented opportunity for behavioral medicine. The reunion of the NIMH with the NIH provides an opportunity for broad collaborative research in behavioral medicine. Second, the massive health reform movement now taking place in the United States provides an opportunity to reassess the role of psychosocial treatments and behavioral medicine techniques in the delivery of health care services.

Treatment intervention research has a pivotal role to play in developing and evaluating new treatments and documenting the extent of their utility and cost effectiveness. There was general agreement that these techniques are efficacious but underutilized, and are relatively undervalued in comparison with invasive biotechnological procedures. Furthermore, a variety of recent studies in heart disease and cancer have raised the possibility that psychosocial intervention may have biomedical effects ranging from reducing the rate of recurrence of myocardial infarction to prolonging survival time among cancer patients. This is thus an intellectually exciting time in which not only efficacy, but mechanisms of the effects of these treatments demands serious exploration.

The intervention initiatives were divided into six broad categories:

1. definition of methods;
2. development of interventions;
3. discrimination among subjects most and least likely to respond;

4. deliverers of health care services;
5. the domain of social and physical support in which people live; and
6. dissemination of results.

1. Definition:

Methods of research in psychosocial intervention need further refinement. This involves two agendas. One is to bring this field of research up to standards set in clinical trials in other parts of medicine, particularly the use of randomized prospective designs, which are not always the rule in behavioral research. A carefully conducted randomized trial has the potential of evaluating even rather complex interventions in a rigorous way.

Other design issues that demand further exploration are the notion of placebo control and blinding. The idea of constructing placebo interventions in behavioral medicine poses rather formidable problems. It is one thing in a drug trial to produce an inert pill; it is another thing to attempt to construct a psychotherapy of no value. However, such techniques have been deployed, for example, in the collaborative depression trial in which periodic non-specific attention from a physician was a control for various types of psychotherapy. However, this "placebo" contact proved rather more powerful an intervention than expected. Indeed, trial participation and non-specific expectancy and

supportive factors have proven important in many behavioral medicine trials, most notably in MRFIT, the Multiple Risk Factor Intervention Trial. Improvement in the intervention arm was hard to demonstrate because of nearly comparable improvement in the 'control' group.

Two specific initiatives were recommended: one involving the assessment of individual differences in children in regimens required for adequate disease treatment; for example, the number of daily blood sugar assessments necessary for a child who is diabetic. The refinement and standardization of quality of life measures is another component of this initiative. The second initiative involved the development of methodologies for comparing the appropriateness of control groups.

2. Development:

There was considerable enthusiasm for the development of new interventions and trials. It was believed that these trials should be based on broad definitions of intervention strategies, ranging from the individual to social and community. Also, attention should be given to special populations, such as the aging and minorities.

Four specific initiatives were proposed. The first involved an early intervention in child abuse and family violence. The goal involved early identification of abuse victims and comparison of the relative efficacy of standard treatment vs. intensive behavioral interventions targeted for use by emergency room health care personnel.

The second initiative involved systematic examination of barriers to medical treatment: individual, social, and environmental.

A third involved problems of maintenance and relapse. The majority of behavioral medicine interventions focus on initial treatment with comparatively short-term follow up. Such problems among adolescents as addiction should be followed with studies that examine risk factors for early relapse, while developing interventions to maintain abstinence and relapse. Alternative strategies include intensive followup of successful individuals in order to determine individual and social attributes associated with maintenance of abstinence.

The fourth proposed initiative recommended the study of behavioral interventions for older populations, a comparison of different types of interventions (cognitive behavioral vs. self-help, for example), as well as, systematic study of the efficacy of individual vs. group therapy. There is a general feeling among investigators that group therapies have some unique advantages, but there have been very few systematic comparisons of the two modalities.

3. Discrimination:

The investigators felt that it was especially important to utilize sophisticated research methodology in order to examine those factors which allow certain individuals to succeed in a given treatment while others failed. While some of the variance in response may primarily have to do with treatment-related factors, marginal efficacy due to poor conceptualization or implementation, another portion of the variance in outcome may be due to individual variables such as expectancy, self-efficacy, learned helplessness, repression/sensitization, depression, hypnotizability, and other dispositional variables. Successful identification of variables predictive of outcome would allow for more efficient and effective application of behavioral interventions.

The specific initiatives proposed involved matching individual characteristics to treatments for problems such as obesity, hypertension, hostility, and Type A behavior.

4. Deliverers of Service:

There was agreement among investigators that effective interventions can and should go far beyond one to one or group interventions with patients. An alternative site of intervention is with providers of health care. Initiatives suggested included study of means of improving communication with health care providers, changing the health care delivery system to make it more accessible and useful to patients, and teaching providers how to help patients change health-related behaviors.

A second important area involved an initiative regarding decision making. Two major themes were noted. One involved the conflicting imperatives in health care of highly technological and aggressive medicine which is sometimes applied in situations where the cost/benefit ratio is rather poor. There has been recent reconsideration of aggressive treatment for diseases like prostate cancer, which tend to have a fairly indolent course even without treatment.

The role of watchful waiting needs further evaluation, especially in terms of its impact on patients. At the same time, pressures to contain costs at times have led to the opposite problem of depriving people of needed treatment. The elderly are especially vulnerable to this danger. Half of all health care expenditures occur in the last year of life. Since they are high utilizers of health care services, prolonging life also increases costs. And this may conflict with our ethical imperative to provide the best possible medical care.

A third issue involved the important role of participating in choice regarding options in health care. As an example, recent research produced the surprising finding that women who received modified radical mastectomies fared no worse than women who received breast sparing lumpectomies and radiation. Indeed, in some studies, they were less anxious and depressed at followup. One reason for this seemed to be that lumpectomy patients receive less support from spouses since the illness is more easily denied. However, studies show that patients who participate actively in the choice about which treatment to receive are better adjusted, regardless of procedure. Thus, this literature demonstrates that patient participation in medical decision-making may be a more powerful determinant of adjustment to disease than the nature of the medical and surgical procedures. This area merits further systematic investigation.

A related proposed initiative involved assessment of the psychosocial impact of managed care.

5. Domain:

The fifth set of recommendations involved intervening in the social network. Research reviewed by House and colleagues in 1988 demonstrated that social integration reduces mortality risk. The magnitude of the effect, with relative risks in some studies more than twice that for socially-isolated individuals than for those who are socially integrated, is comparable to that found linking serum cholesterol or smoking behavior to mortality. These studies suggest that intervention in the social network should have powerful effects on psychosocial and perhaps medical well-being.

The initiatives proposed involved interventions with peers and other social groups for adolescents with infectious diseases such as AIDS, tuberculosis, diabetes, asthma, hypertension, intestinal disease, and addictive disorders. Families were another portion of the social network recommended for involvement in intervention trials.

The Senior Adult Task Group suggested the study of systematic interventions in the social and physical environment of older adults. They recommended using a "cascading" model allowing the testing of a series of interventions in sequence to individuals resistant to earlier interventions, with attention paid to the social environment as well as to the individual.

6. Dissemination:

The task groups were strongly enthusiastic about the implementation of multicenter trials. This methodology has been extremely successful in other fields of biomedicine, for example, collaborative trials being sponsored by the National Cancer Institute and the National Heart, Lung, and Blood Institute. These trials provide an opportunity to develop standardized interventions with manualized protocols. Since assessment of adequacy of implementation of techniques for training those providing the experimental intervention are necessary, they test the generalizability of the findings in a way that no single trial can. They involve diverse populations in different locations with a variety of service providers, often in non-university as well as university settings.

The increased sample size in multicenter trials provides for meaningful sub-group analyses, allowing questions about individual characteristics in relation to treatment responsiveness, variations in the effectiveness of implementa-

tion, and also a convincing demonstration of efficacy. Furthermore, multicenter trials are an important way of disseminating new treatment techniques by training a variety of providers in many settings.

Multicenter trials were recommended for the study of non-pharmacological interventions for the treatment of migraine headache, enuresis, pre-operative anxiety, and post-surgical pain among children. A second multicenter trial was recommended to study the efficacy of psychosocial interventions with the medically ill. Implementations of group therapy protocols for patients with cancer and cardiovascular disease were recommended, with systematic evaluation of both medical and psychosocial outcomes. Such techniques have been shown in single trials to be effective in reducing mood disturbance, as well as risk of recurrence of heart attacks and slowing progression of cancer. These rather striking results require replication on a large scale in order to provide definitive evidence about the relationship between psychosocial intervention and medical outcome.

There was also a recommendation that "FDA" like criteria be established for the evaluation of psychosocial interventions analogous to those for drug intervention. Such certification might facilitate the more widespread application of behavioral medicine techniques.

There was general agreement that psychosocial and behavioral interventions have already been shown to have substantial efficacy and that the reduction in mortality from cardiovascular diseases in this country is in good measure attributable to behavior change in diet, exercise, and tobacco use. This is a period of rapid development of our knowledge of the relationship between social and psychological variables on the one hand, and somatic variables such as endocrine and immune function, health status,

and disease incidence and progression on the other. A vigorous research program will provide further systematic guidance in the develop-

ment of effective and cost-effective intervention, prevention, and management of medical illness.

DISEASE PREVENTION/ HEALTH PROMOTION

The Role of Behavioral Research in National Health Policy

J. Michael McGinnis, M.D.

Three points are important at the outset:

1. Behavior is the central challenge for the health policy agenda today—indeed, it is the central challenge for the broader public policy agenda today.
2. Taking on that challenge is the most complex task yet confronted by science.
3. To competently address that challenge, the Public Health Service's research community—and dominantly that means the National Institutes of Health—must simply do more and do better in certain key research areas.

The first point—on the centrality of behavioral medicine to public policy—takes me substantially beyond the bounds of my putative charge: to address the relationship of behavioral medicine research to disease prevention and health promotion.

But there is no denying behavior's impact on the human condition that it both defines and

measures. We need merely look at the trends for what many biologists and psychologists would tell us is the most basic behavioral drive—reproductive behavior—to assess some of the consequences. The world's population, which had remained below 1 billion until well into this century, has exploded past 5 billion with a trajectory that shows scant signs of slowing. I know that many in this room can recall a world that noted passage of the 2 billion mark with questions about the sustainability of that growth rate. Since then, the rate of growth has been both blurred and numbing.

One of the most immediate consequences has been the development of a staggering gap in economic well-being between wealthy and poor countries. Those countries with the most rapid growths in population are those that are poorest. In 1988, the richest 750 million people had a per capita income of \$17,000, in contrast to the \$320 per capita income of the poorest 2.9 billion people.

We in the United States of course are not immune to our own set of problems derivative of reproductive behavior. Take a look at just one dimension—the changes in births to unmarried women over the last generation. In 1950, 4% of births were to unmarried women. In 1989, it was 5 times that rate—22%. In conjunction with a higher divorce rate, the corollary consequence has been an erosion in the family unit and an increase in the number of families headed by a single parent.

Some of today's most prominent social problems—crime, violence, poverty, the gap between rich and poor—can be tied in part to this trend. And the solutions to these problems are not to be found in space-stations, super-conducting super-colliders, high speed transport systems, or enhanced radiographic imaging. The solutions to these problems are rooted in behavior and the interventions necessary to change it.

Having suggested the dependency of the world's future on your deliberations, you'll not be surprised at the special emphasis I give to the role of behavior change for health policy in this Nation. It has already been noted that my responsibility in the department relates to our national policies in disease prevention and health promotion. If we accept the notion that health can be defined as "one's status with respect to the predisposition, presence, or absence of disease, impairment, or sense of well-being", the central role for behavior in affecting health status is readily apparent. Similarly, our prevention strategies—whether defined as health promotion or disease prevention—are heavily dependent upon behavioral interventions.

Health promotion is defined for our purposes as "personal, environmental and social interventions to facilitate behavioral adaptations to improve health, level of function and sense of

well-being." Behavior is its anchor. Disease prevention is defined as "personal, environmental and social interventions to impede the occurrence of disease, injury, disability, death, or the progression of detectable but asymptomatic disease". So, regardless of one's perspective, behavior is key to our health policy agenda.

Just how key it is may be surmised by looking at several motivating factors or targets for health policy. The top ten causes of death are shown in Table 1. Obviously, one of our central aims is reducing the occurrence of unnecessary deaths among Americans. Another way of looking at challenges to health policy is in terms of potential years of life lost, presented in Table 2. A third issue, and one of great prominence in the discussions around health care reform, relates to the cost burden of illness noted in Table 3, especially when many of these costs are preventable. Treatment costs for selected preventable conditions are shown in Table 4. Common, of course, to each of these perspectives—whether one considers numbers of deaths, potential years of life lost, costs of illness, or the morbidities and disabilities for which they are surrogates—is the central role of behavior.

Table 1
Leading Causes of Death, 1990

Heart Disease	720,058
Cancer	550,322
Cerebrovascular Disease	144,088
Unintentional Injuries	92,983
Chronic Lung Disease	86,679
Pneumonia and Influenza	79,513
Diabetes	47,664
Suicide	30,906
Chronic Liver Disease/Cirrhosis	25,815
HIV Infection	25,188

Table 2

Years of Potential Life Lost

	1989-1990	1990	1991*
Injuries	-41.0%	2.14	2.10
Cancers	+0.8%	1.85	1.87
Suicide/homicide	+6.5%	1.49	1.56
Heart disease	-2.5%	1.38	1.38
Congenital defects	+1.0%	.67	.61
HIV Infection	+12.7%	.66	.78
Prematurity	-9.2%	.44	.44
SIDS	-3.9%	.35	.33
Stroke	+1.3%	.24	.23
Liver disease	-3.9%	.22	.21
Pneumonia/influenza	<u>-4.2%</u>	<u>.17</u>	<u>.17</u>
Total	-0.8%	12.24	12.28

* Provisional

Table 3

Costs of the Leading Causes*

Injuries, Intentional & Unintentional	\$ 150 Billion
Heart Disease	\$ 75 Billion
Cancer	\$ 72 Billion
Cerebrovascular Disease	\$ 19 Billion
Chronic Lung Disease	\$ 15 Billion

* Estimates of annual direct + indirect costs

This is, after all, the very purpose for this conference: to help us better address the fact that heart disease, cancer, stroke, injuries, and so forth, all have major identifiable risk factors as primary determinants. In fact, when you think about it, our real leading causes of death among Americans, are not heart disease, cancer, stroke, and injuries, but their origin: behavior. Among the most prominent behavioral contributing factors are tobacco use, dietary and physi-

Table 4

Cost of Treatment for Selected Preventable Conditions

Condition	Avoidable Intervention	Cost Per Patient
Heart Disease	Coronary bypass surgery	\$30,000
Cancer	Lung cancer treatment	\$29,000
Injuries	Quadriplegia treatment and rehabilitation	\$570,000 (lifetime)
	Hip fracture treatment and rehabilitation	\$40,000
Low-Birth-Weight-Baby	Respiratory distress syndrome treatment	\$26,500

Table 5

Risk Factors for Leading Causes of Death

Heart Disease	Tobacco, Obesity, Elevated BP, Cholesterol, Sedentary Lifestyle
Cancer	Tobacco, Improper Diet, Alcohol, Environmental Exposures
Cerebrovascular Disease	Tobacco, Elevated BP, Cholesterol, Sedentary Lifestyle
Accidental Injuries	Safety Belt Nonuse, Alcohol, Home Hazards
Chronic Lung Disease	Tobacco, Environmental Exposures

cal activity patterns, drug and alcohol consumption, firearms, and unsafe sexual behavior. Some behavioral risk factors that are related to major causes of mortality are indicated in Table 5.

The impact of behavior on health prospects at their most basic level—life or death—is therefore profound—even without considering its potential for affecting the quality of life. These are no longer novel notions. Even Bill Moyers is writing about it. But it is why behavior is the central challenge for health policy today, and why it is of such concern to the President in the context of health care reform, to the Secretary for our domestic policy agenda, and to *Healthy People 2000*, the Nation's prevention agenda.

Healthy People 2000 has some 22 priority areas and 300 measurable targets for the year 2000, categorized within the broad groupings—health promotion, health protection, and preventive services (see Table 6). The stated level of those specific targets is not particularly important for this session but the importance of behavior to the strategies is. Obviously, from the definition mentioned, the "health promotion" category is focused on behavior change. But the "health protection" category is also dependent on behavioral interventions, and so is the "preventive services" category.

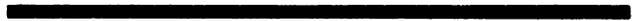
My second major point is: Taking on that challenge is the most complex task yet confronted by science. Science heretofore has tended to unfold within disciplinary vacuums. Mathematics, physics, chemistry, even biology, are fields that have each grown up substantially unencumbered, at least in the analytic sense, by issues or perspectives shaped by factors largely outside of their domain. Pythagoras, Galileo, Kepler, Harvey all had the social and philosophical prejudices of their days to deal with,



Table 6
***Healthy People 2000* Priority Areas**

	# of Objectives by Area
Health Promotion	
• Physical Activity & Fitness	12
• Nutrition	21
• Tobacco	16
• Alcohol & Other Drugs	19
• Family Planning	11
• Mental Health & Mental Disorders	14
• Violent & Abusive Behavior	18
• Educational & Community-Based Programs	14
Health Protection	
• Unintentional Injuries	22
• Occupational Safety & Health	15
• Environmental Health	16
• Food & Drug Safety	6
• Oral Health	16
Preventive Services	
• Maternal & Infant Health	16
• Heart Disease & Stroke	17
• Cancer	16
• Diabetes & Chronic Disabling Conditions	20
• HIV Infection	14
• Sexually Transmitted Diseases	15
• Immunization & Infectious Diseases	19
• Clinical Preventive Services	8
• Surveillance & Data Systems	7
Other	<u>2</u>
Total, including duplicates	334
Discrete Objectives	300

but their observations and experiments could be largely self contained.



Such is hardly the case for behavioral research. Behavioral research, almost by definition, requires an interdisciplinary character. We glean hints from individual studies like those that assess the impact of stimuli during infancy on the development of attitudes and competencies, from those that seek to identify neuro-receptor sites for addictive or mood-altering substances, or from those that attempt to alter the cardiovascular risk profiles of entire communities. But given the fundamental interplay between nature and nurture, none can be seminal in and of itself.

Behavior is simply not a static characteristic of the human beings who display it. It is essentially dynamic and interactive—an interaction of the individual and his or her physical and social environment. Sometimes this interaction is presented as a lifeless kind of link (as between socioeconomic status/poverty/poor education and behavioral risk factors) but such a depiction is too generalized to be very useful. It calls for more specificity.

The interaction of the individual and the environment is further influenced by another dimension of the puzzle of behavior, the individual's developmental stage. Developmental tasks clearly pose special challenges and create unique vulnerabilities that can influence adoption of health-related behaviors at given points in one's lifetime. Early childhood and adolescence are the easiest of the developmental stages to use for examples, but adults also face challenging developmental tasks that can influence their behavioral patterns—mating, child-bearing, parenthood, separation—"letting go"—of children, employment-related achievement/satisfaction, retirement, aging.

Given this labyrinth of interconnectedness, we have, in effect, what might be termed the

paradox of behavioral medicine: that is, unlike other branches of science, the more enlightened we become, the more complex are our solutions. What are the implications for public health policy of demonstrating a clear, convincing and strong relationship between health prospects and one's educational or income status? Having discovered a gene for susceptibility to cocaine or nicotine, what are the implications for screening programs? for insurance purposes? for family planning and prenatal care? Having developed interventions like Norplant or RU-486, what are the implications for welfare policy, for school health, for our judicial systems? I am sure the issues you have already discussed in the preceding one and one-half days of this conference are more complex than even these.

And it's a good thing. This is clearly not the time to shy away from meeting these challenges directly. Hence, Point 3. To competently address that challenge, the research community must simply do more and better in certain key areas of behavioral research.

There are numerous potential participants in this task, but, given last year's reorganization of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), this means in particular the National Institutes of Health. I don't mind saying that, if I had my preferences NIH would have stronger allies in this regard. It was my recommendation—not accepted, mind you—that we take advantage of the ADAMHA reorganization to create a broader Agency for Behavior and Health, with an expanded mandate and capabilities, for both research and services. As you know, the decisions went a different direction, so that leaves the NIH almost alone with that substantial mandate, insofar as the research question goes. It really leaves the NIH in a nearly unique position to

marshall activity on issues that range from the social determinants to the molecular structure of human motivation. To oversimplify the challenge, this means developing a fulsome agenda on four dimensions:

- ▶ identifying and characterizing potential experiential contributors to human behavior
- ▶ identifying and characterizing potential biological contributors to human behavior

- ▶ assessing the nature and results of interactions between experiential and biological contributors
- ▶ assessing how various intervention modalities shape those interactions.

Time constraints do not permit me to elaborate these issues. That is the basic charge to your conference. But I am grateful for your efforts in this regard. They are vital to the evolution of programs and policies of disease prevention and health promotion in this Nation.

Prenatal/Infant/Child

Overview

Suzanne Bennett Johnson, Ph.D.

Unintentional injury is the number one killer of children, accounting for more than half of all deaths in childhood. Consequently, the first initiative developed by the Prenatal/Infant/Child Task Group focuses on promoting safety and preventing injuries.

Exposure to environmental toxins has particular relevance to children since the developing fetus and child may exhibit greater vulnerability to these agents than the adult. Consequently, our second initiative focuses on the impact of environmental exposures on the psychological, behavioral, and medical well-being of the child; methods to screen and identify exposed individuals; and intervention strategies to reduce exposure and to minimize adverse outcomes in already exposed individuals.

Exercise and diet are important predictors of heart disease, diabetes, and some cancers. While these diseases are usually diagnosed in adulthood, dietary and exercise habits develop in childhood. A lifetime of healthy eating and dietary practices should help delay or prevent the onset of these diseases. Consequently, our third initiative focuses on developing healthy dietary and exercise habits in school-age children.

Heredity or environmental exposure places certain children at-risk for the development of certain diseases. For example, children of alcoholic or obese parents are more likely to develop these disorders themselves. Similarly, a variety of medical disorders including diabetes, asthma, and heart disease are known to have a genetic component. Identifying children who are at-risk before they have developed the disease or disorder provides an opportunity for disease prevention. Consequently, our fourth initiative focuses on children who are high-risk for disease but who have not yet developed the disorder.

Across these initiatives, several themes are worthy of note. First, in addition to an interest in child and family, the traditional focus of psychology, there is increased attention to the role of the larger community or environment. Initiatives D-1-1 (Promoting Safety and Preventing Injury in Children) and D-1-3 (Promoting Self-Efficacy to Enhance Healthful Eating and Exercise in School Age Children and Adolescents) make specific reference to community-based interventions. Initiative D-1-2 (Behavior-Based Protection from Environmental Exposures) focuses on environmental agents (natural or man-made) that may be toxic to

humans, and D-1-4 (Preventive Interventions with Defined High Risk Samples) acknowledges the important roles of sociological risk factors such as poverty and culture.

Second, the importance of adequate measurement is central to all four initiatives. D-1-2 (Behavior-Based Protection from Environmental Exposures) specifically mentions the importance of developmentally sensitive measures of the behavioral and psychological impact of environmental exposures. D-1-1 (Promoting Safety and Preventing Injury in Children) acknowledges the difficulty in identifying an appropriate "outcome" variable. Since injury is relatively rare, studies of injury prevention may have to identify appropriate "proxy" measures for injury instead of using actual injury as an outcome variable.

Similarly, the remaining initiatives focus on disease prevention. Since the target of prevention is children and the diseases to be prevented often do not occur until adulthood, actual disease-onset may not be a realistic outcome measure as one would have to wait many years to evaluate the "success" of any prevention effort. Identifying appropriate outcome variables that are linked to ultimate disease onset, but that can be measured during childhood, is a critical component of prevention research.

Third, the importance of sensitivity to developmental issues is a theme common to all initiatives. The importance of developmentally sensitive outcome measures has already been

discussed. However, developmental issues also surface in terms of types of problems to be addressed. For example, certain types of injuries are more or less common during certain developmental periods (D-1-1) and exposure to environmental toxins may have differential impact depending upon the developmental period during which the child is exposed (D-1-2). Similarly, developmental issues remain important when designing prevention efforts. For example, parents may be the more appropriate "targets" for prevention efforts focusing on infants or very young children (D-1-1 and 2) while during the school-age years, child-oriented prevention efforts should be geared to the special and different needs of the elementary versus middle-school versus high-school aged child (D-1-3).

The contributions of gender and race or ethnicity is a fourth theme. Gender and/or race/ethnicity has been associated with type of injury (D-1-1), exposure to environmental toxins (D-1-2), disease onset (D-1-4), and exercise or dietary practices (D-1-3). If they are to be successful, prevention and health promotion strategies must take these biological and socio/cultural differences into consideration.

Finally, the resiliency of certain children to injury and disease despite exposure to high-risk conditions, remains an important area of inquiry. Understanding why certain children do well despite adverse circumstances may provide key insights as to the critical components of prevention and intervention efforts for all children.

Task Group Initiatives

✓ Promoting Safety and Preventing Injury in Children (D-1-1)

Need and Justification

Unintentional injury is the number one killer of children, accounting for nearly half of all deaths in childhood. Motor vehicle accidents are the primary cause of accidental death. Other common causes include drownings and fires. Injuries from falls and accidental poisonings are not a primary cause of death but do result in many nonfatal injuries. (Source: Healthy People 2000) Many of these injuries can be prevented.

Intervention studies should target both the child and the child's environment.

Research Approach/Methodology

Social/environment interventions could focus on parents, school personnel, or community resources. For example, parental interventions could address increasing safety belt use, reducing hot water thermostats, creating safer environments (e.g., securing poisons and toxins, placing a life jacket on a child when near a

pool or water), and providing necessary supervision. Community/school interventions could focus on developing safe play areas, and methods of reducing sports injury. Community wide interventions could focus on one or more safety behaviors (e.g., seat belt and bike helmet use), with the intervention community compared to a control community. The control community could then be targeted for intervention, replicating intervention effects demonstrated in the first community.

Child interventions could focus on enhancing safety oriented behaviors. For examples, interventions could target wearing bike helmets, safe bike-riding practices, and how to handle emergencies when left alone or in the absence of adult supervision. Intervention strategies should be tested in a variety of populations to assess generality and effectiveness.

Outcome variables may include actual injury or proxy measures, such as an increase in the "target" behavior (e.g., increase in use of bike helmets, reduction in hot water heater thermostat settings, increase in safety belt use, etc).

✓ **Behavior-Based Protection from Environmental Exposures (D-1-2)**

Need and Justification

Much information is now available concerning the adverse health consequences of exposure to a variety of environmental agents, including radiation and natural and synthetic chemical toxicants. Some of the many examples include radon, ultraviolet radiation, agricultural chemicals, ozone, noise, indoor air pollutants, lead, mercury, and tobacco smoke. The developing fetus and child exhibit a greater vulnerability to many of these agents, particularly with respect to brain development and cognitive and behavioral functions. Little is known about effective behavioral interventions to attenuate or minimize these exposures. Research needs to go forward on three fronts: further characterization and delineation of such effects; screening populations to identify at-risk individuals, and behavior-based interventions to attenuate the risk and minimize such exposures and thus the adverse health outcomes. Intervention strategies need to be developed and initiated to target women of child-bearing age, pregnant and lactating mothers, as well as children, particularly throughout the period of critical development. These behavioral strategies may become particularly important in cases where risk of exposure is persistent and outside of an individual's control.

A related research area concerns risk perception and its behavioral and psychological conse-

quences (i.e. the "Love Canal Syndrome"). The perception of risk is particularly powerful in parents concerned with their children's well-being and who make significant behavior and life choices based on presumed or real exposures which can profoundly impact their long-term physical and mental health. Given the extensive number of known sites of toxic exposures and pollution in the U.S. and around the world, these are critical research priorities affecting large populations and future generations.

Research Approach/Methodology

The establishment of developmentally sensitive indices of behavior is critical to the progress of this research area.

The development of behavioral interventions designed to prevent or attenuate adverse environmental exposures in at-risk populations must be culturally appropriate to assure acceptance and compliance since many of the most affected populations are racially/ethnically diverse and/or socioeconomically disadvantaged.

In order to evaluate the long-term efficacy of the envisioned behavioral interventions, longitudinal studies with at least 3-5 and up to 12 years follow-up are necessary.

✓ **Promoting Self Efficacy to Enhance Healthful Eating and Exercise In School Age Children and Adolescent Females (D-1-3)**

Need and Justification

Lifetime exercise and dietary healthful behaviors are important to establish during early childhood. Physical activity and dietary behaviors have been identified as two of the priority health promotion areas in Health People 2000. These two health areas are the foundation for the prevention of several major chronic health problems.

Data from studies indicate that fat makes up more than 36 percent of calories in the average American diet and obesity is on the increase in children and adults. "Evidence of the multiple health benefits of regular physical activity continues to mount. Regular physical activity can help to prevent and manage coronary heart disease, hypertension, noninsulin-dependent diabetes mellitus, osteoporosis, obesity, and mental health problems. On average, physically active people outlive those who are inactive. Regular physical activity can also help to maintain the functional independence of older adults and enhance quality of life for people for all ages. Unfortunately, few Americans engage in regular physical activity despite the potential benefits." (Healthy People 2000, pp.94-95.) Girls, in particular, show a decline in activity levels beginning in early adolescence. At this time, they also begin to exhibit concerns about weight.

Schools provide important opportunities to teach healthful individual behaviors as well as promotion of environmental, organizational, and

policy changes related to diet and exercise behaviors. Areas that could be targeted for intervention include school lunches, physical education classes, and education about the importance of nutrition and exercise. Interventions should be age appropriate and might include strategies to promote self efficacy, teaching activities that appeal to a particular gender (e.g., dancing for girls) or racial/ethnic groups as well as emphasizing lifetime sports skills (e.g., biking, walking, swimming, hiking).

A sense of self efficacy is important to developing and practicing health promoting behaviors including physical activity and dietary patterns. Self efficacy can be facilitated by teaching school age children and adolescents to control specific physiological responses via training methods such as biofeedback. While this training has been applied principally to enhance sports performance or for specific medical treatments, it also may be useful in promoting healthful behaviors related to diet and exercise as part of the school health curricula.

Research questions to be addressed include:

- ▶ Does teaching school children to modulate an easily measurable physiologic response result in increased personal responsibility for positive eating and exercise behaviors in early elementary age students or middle or high school female students? Is it feasible to deliver this type of intervention to groups of students during school classtimes as part of the curriculum?

- ▶ What specific intervention strategies are most successful over time to enhance healthful eating and exercise patterns for K-3 students and middle or high school females?
- ▶ How can interventions be tailored most effectively to varying developmental stages, learning styles, interests, and ethnic groups of grade K-3, middle school or high school students?
- ▶ What are predictors of permanent changes toward more healthful eating and exercise behaviors for K-3 students and females at the middle or high school levels?

Research Approach/Methodology

Two different age groups should be studied:

1. Kindergarten through grade 3, males and females
2. Middle or High School age female students

Intervention research studies, individual grants, and multisite studies may be appropriate.

✓ **Preventive Interventions with Defined High Risk Samples (D-1-4)**

Need and Justification

There has been increasing precision in the definition of high risk populations of children for a wide variety of diseases and health problems. There are three broad categories of risk criteria that can now be used to define appropriate target groups.

▶ *Biologic*

Progress in both the location of single genetic loci and set of related genetic alleles that are associated with specific diseases allows for clear definition of target groups. Furthermore, mechanisms of inheritance have become more clearly understood. Even for genetic disorders without defined genetic loci, increased estimates of probability of inheritance have been established. Beyond genetics, an increasingly large set of physiological and metabolic markers have been identified that can be used to quantify level of risk.

▶ *Environmental*

Both familial and sociological risk factors such as poverty, single parenthood, parental psychopathology and substance abuse, and family violence are associated with increased risk for certain diseases or poor health outcomes.

▶ *Ethnic and Cultural Considerations*

It is increasingly well understood that specific ethnic groups have defined additional

levels of risk for certain illnesses. This includes both specific genetic vulnerabilities (i.e., sickle cell anemia) and cultural obstacles to access appropriate primary health care.

Research Approach/Methodology

One strategy is to target for intervention children of parents with a known familial disorder such as alcoholism, obesity, asthma, heart disease, and diabetes. Early designation of children at-risk would allow for the development and testing of intervention protocols that are both developmentally salient and disease specific.

While appropriate design of the interventions must vary based on the nature of the disorder and environment, two critical elements are necessary:

1. a randomized, controlled design;
2. a prospective longitudinal strategy that spans a sufficient duration of time to capture the emergence of the onset and course of illness.

Key independent variables should include familial adaptation and comorbid behavioral and emotional disorders.

Adolescent/Young Adult

Overview

Mindy Fullilove, M.D.

Adolescence is a period characterized by rapid personal development and change. Behaviors established in childhood are rethought and reworked as the young person begins to establish an identity separate from the family of origin. With physical and emotional growth and development come new possibilities for exploration and experimentation, as well as new responsibilities for work, school and family.

Adults need to be a part of the adolescents' world, guiding youth into appropriate and productive adult roles. However, in US society, the current organization of work and social roles has decreased adult contact with adolescents and increased the importance of the peer group in guiding development through these formative years. The central problem for adolescents in the US is that a rapid and powerful developmental process propels behavioral change in relative isolation from adult guidance.

To address this issue, the Task Group proposed a series of four research initiatives:

1. interrelationships between adolescents and the larger environments in which they live;
2. adolescents making "choices" in their lives;

3. communication between adults and adolescents; and
4. peer-based interventions for secondary prevention among adolescents.

We believe this research agenda would accomplish a number of goals. First, we attempted to broaden the current research concerns. We were particularly concerned with the lack of attention to larger social forces. Recent publications on social class and health have emphasized the enduring impact of social status. Much more information is needed in this area. Second, we attempted to apply established concepts to new problems. We are convinced that peer-based interventions are effective in reaching adolescents. Applying such interventions to secondary prevention is a fruitful avenue for new initiatives. Third, we attempted to deepen our current understanding of adolescents' lives. The initiatives on choice and communication build on established research traditions where additional studies are likely to provide new and meaningful information. With changing times, old theories and paradigms must be reexamined to see if they apply under new social and environmental conditions.

Task Group Initiatives

✓ Environmental Interventions to Improve Adolescent Health (D-2-1)

Need and Justification

Individual behavior is influenced by a host of factors in the physical and social environment, such as laws and regulations that govern behavior (formal social control); social and peer pressures to act in a particular manner (informal social control); the availability of noxious or beneficial foods, tools, toys and other materials; social upheaval or conflict; and environmental changes, including natural disaster or climatic changes. For example, in the United States the prevalence of smoking has declined in response to a wide range of environmental changes, such as increased tax (so-called "sin taxes"), and decreased social acceptance. Careful examination of the response of smokers to these social interventions has shown that both formal and informal mechanisms of social control are important for the establishment and maintenance of healthy behaviors.

Adolescents, as a group, appear to be particularly sensitive to many environmental factors. Research has established the importance of the social control exerted by adolescent peer groups, which are, in turn, shaped by larger social forces such as television, advertising, and social fads and fashions. The effects of many other environmental factors remain poorly understood. This initiative supports new research directed at understanding the role environmental factors play in shaping health-promoting behaviors among adolescents. Research

paradigms employing an "ecological" perspective are needed to address the complex interactions and interrelationships between events and conditions in the environment and adolescent health.

Research Approach/Methodology

A wide range of research approaches is recommended, including experimental studies, natural experiments, policy studies, and descriptive studies. The following examples are proposed to give an idea of the scope of studies proposed:

1. In many inner-city communities, there is limited access to healthy foods such as fresh fruits and vegetables, or low-fat protein sources. This has particular relevance for adolescents, as they need to establish healthy eating habits that will protect them throughout life. Changing access to healthy foods may have a dramatic effect on eating habits. One way to change access is the introduction of farmer's markets, which bring fresh fruits and vegetables from family farms located in the nearby rural areas. Operated in conjunction with the promotion of positive nutrition patterns, farmer's markets might improve dietary habits, and lower rates of obesity and heart disease.

2. Federal legislation is pending to prohibit the sale and distribution of tobacco products to youths 18 and under. Implementation of this law would be enforced by state governments and compliance would be assessed by the Federal Government. Non-compliant states might lose block grant funding. To study the impact of this pending legislation, a natural experiment is proposed which will test the following hypotheses:
 - ▶ under-age smoking will decrease more in high-compliant than in low-compliant states; and
 - ▶ the distribution in retail markets will be more reduced in high-compliant than in low-compliant states.
3. In the 1960s, urban renewal projects restructured existing inner-city communities. In some instances the replacement housing intensified segregation by income. Those restructured communities with high proportions of poor residents (30-40% of residents below poverty level) are at great risk for negative health outcomes. Studies might examine differences in social interaction and other health-related behaviors in income-integrated and income-segregated communities.

✓ **Development of Disease Prevention Strategies Based on Behavioral Choice in Adolescents (D-2-2)**

Need and Justification

Adolescents and young adults make health behavior choices that are influenced by a variety of factors, including peer norms, familial values, availability and accessibility of alternative behaviors, and evaluation of the consequences of performance of the behavior. An important perspective for disease prevention and health promotion is to intervene using methods designed to promote better choices by manipulating access to more healthful alternatives as well as training in cognitive/behavioral methods to improve problem solving and making choices more consistent with long-term health. Significant progress has been made in understanding some of the variables that explain decisions of health behavior. Among the factors that have been involved are: maturational variables, immediate versus delayed consequences of the behavior, perceived and actual availability and accessibility of alternatives, and cognitive processes involved in decision making.

Behavioral choice theory emphasizes the complementary role of cognitive, behavioral and environmental variables as factors that can influence choice. For example, attempts to teach children to choose low-fat versus high fat foods requires availability of low-fat foods, and at least equal accessibility to these foods. Likewise, changing activity patterns from sedentary to active may require increasing availability and support for vigorous activities while accessibility for sedentary activities is decreased. To modify alcohol intake it may be very important to offer alternatives that have equal or greater reinforcement qualities.

An important aspect of this model is the availability of well-defined techniques and procedures for decision making and problem-solving. These methodologies makes this approach especially appropriate for primary or secondary preventive behaviors.

Research Approach/Methodology

The main paradigm for these studies should be randomized trials that modify choice. These include standardized methods for teaching children problem solving using the steps of identifying problems, generating solutions, weighing outcomes of the solutions, developing a plan and evaluating the outcome of implementing the plan. In addition, interventions can be designed to modify the availability or accessibility of alternatives to increase the probability of choosing more healthy rather than less healthy behaviors.

The studies should include predictor variables to indicate for which subjects problem solving and decision/making methods are most appropriate. In addition, process variables should be included to understand how and why interventions are working.

In implementing problem solving and decision making methodologies, it is particularly important that non-coercion methods be tested that promote perceived control over decision making. It is also important that investigators be sensitive to the unintended negative consequences of decision making when appropriate health decisions are made in social situations,

but these decisions are in conflict with the decisions or demands of their partners or peers.

Innovative research issues to be addressed include:

- ▶ effectiveness of alternative modes for delivery of these interventions such as the use of interactive computers.
 - ▶ generalizability of decision-making and problem solving across types of problems.
 - ▶ extent to which skills acquired at particular ages are generalized across ages.
- ▶ understanding the extent to which positive and negative social influences impact decision-making and problem-solving behavior and therefore outcomes.
 - ▶ factors that influence the adaptability of decision-making behaviors under a wide variety of positive and negative situations.
 - ▶ development of problem-solving techniques for a variety of populations, including people at high risk for specific behaviors due, in part, to poor decision-making skills.

✓ **Research on Communication Strategies to Improve Disease Prevention and Health Promotion (D-2-3)**

Need and Justification

The mass media play a crucial role in defining our culture, including the behavioral norms that affect public health. Indeed, "lifestyles sustained by mass media entertainment and advertising influence life expectancy much more than medical technology" (Gerbner, 1990:53). Young Americans are exposed daily to hours of TV and other mass media entertainment and advertising messages. At the same time, the mass media may be used to convey information about the health hazards associated with alcohol consumption, drug use, and smoking as well as to promote healthier lifestyles through public service messages, social marketing campaigns, and "cooperative collaboration" between TV producers and health promotion experts.

Initial health promotion efforts used information-oriented health communication approaches. Their ineffectiveness has led toward "affective education" strategies based on Evans' "social inoculation" theory (Evans *et al.*, 1978) that is designed to provide young people with information, counterarguments, and techniques with which to resist peer pressure.

Accumulation of knowledge about the effects of advertising, media programming and health promotion efforts has been hampered by research design flaws, narrow conceptualizations, and data availability limitations. These shortcomings indicate the continued need for methodologically sound research that can demonstrate the potential and limits of mass communications which might affect health attitudes and behaviors, particularly among adolescents

and young adults who are establishing long-term behavior patterns. Further research is needed to:

1. Assess the extent to which behaviors associated with health risks (e.g., violence, smoking, and use of alcohol and other drugs) are a result of messages conveyed by the mass media; and
2. Develop and evaluate social marketing and other mass communication strategies to prevent unhealthy behaviors and promote the adoption and maintenance of healthy ones.

Research Approach/Methodology

Potential areas of research might include:

1. Basic research on how the effectiveness of the message is related to: the person delivering it (e.g., the effects of celebrity status, age, ethnicity, class on audience receptivity); the content, style, and orientation of the message (positive versus negative); and the medium and language used to deliver it.
2. Examinations of the ways in which messages are interpreted and acted upon by youth, particularly those in high risk environments.
3. Studies of the actual effects of media messages on behavior, including research to evaluate the effectiveness of

existing or newly-initiated health promotion campaigns.

4. Studies of the effects of targeting messages to reach various audience segments based on race/ethnicity, age, socioeconomic status, and gender.
- 5) Ways to more effectively involve multiple sources that combine the mass media and other interventions such as organized discussion groups and visible enforcement of deterrent laws against sales to minors.
- 6) Examinations of the relationships between advertising expenditures or advertising policies and sales of alcohol and cigarettes.
- 7) Studies that apply techniques of commercial marketing to social marketing to develop more effective counteradvertising and health promotion efforts.

Research methods and approaches might include the use of focus groups in developing and refining messages; experimental, longitudinal, and multi-method community-based field studies; and econometric and time-series analyses of aggregate data.

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✓ **Peer-based Interventions for Health Promotion and Disease Prevention in Adolescents and Young Adults (D-2-4)**

Need and Justification

Primary prevention programs have targeted adolescents and young adults who have not yet embarked on health-damaging behaviors. Other prevention programs have focused on adults who have diagnosable conditions that are already taking a toll on health.

Individuals who have initiated health damaging behaviors, such as drug or alcohol abuse or poor nutritional habits, but who have not yet developed an established pattern or lifestyle that places them at continuing risk, constitute a population that may be particularly amenable to changing health behaviors before experiencing the health consequences later in life.

This initiative proposes to test peer-based interventions in populations who are at greatest risk for developing chronic maladaptive lifestyle problems. Although little attention has been focused on this population, it is precisely at this point in the risk-behaviors continuum that a window-of-opportunity for health promotion and disease prevention strategies may prove most effective.

Research has shown that for adolescents and young adults, peer-based preventive interventions are often more effective than didactic or other traditional approaches. Moreover, peer-

based approaches to secondary prevention and harm reduction have considerable promise and potential for significant impact on interrupting the establishment of risk behaviors that set a trajectory which can have serious health implications.

Research Approach/Methodology

To test the efficacy and effectiveness of peer-based interventions, comparative studies are needed. These studies should be carried out in a variety of settings, including schools and universities and the community targeting out-of-school youth, such as community centers, clinics, detention facilities and prisons. Particular attention should be made to match the age, gender, ethnicity, SES of the peer educators to that of the target population.

These studies also provide an opportunity to identify determinants of health protective behaviors. Individuals who, while living in settings where others adopt high risk behaviors, do not initiate these behaviors, are of particular interest. The characteristics of these individuals and the determinants of their decisions, including influences from role models, norms and personality, should be studied as they may provide new directions for health promotion and disease prevention.

Midlife Adult

Overview

Carl Kendall, Ph.D.

The Task Group discussed four options for focussing research on disease prevention and health promotion:

- ▶ Evaluation of Social Policies as Preventive Interventions
- ▶ Interventions to Enhance AIDS Prevention Behaviors
- ▶ The Role of Social Norms in Health Promotion and Disease Prevention
- ▶ Interventions to Enhance Early Detection and Screening Behaviors

The topics raised by the group identified both behavioral and policy research questions and proposed a mix of quantitative and qualitative research methods to answer these questions. Within the context of this discussion and related to the varying disciplinary commitments of Task Group members, a number of different methodological and theoretical approaches were emphasized.

With respect to method, it was recognized that the conference had a constructed focus on the general knowledge of clinical trials design and methods used in clinical trials. There was concern expressed within the group that such a

design approach is too rigid and limited an application for complex social and behavioral phenomena (for complex physical phenomena as well.) For example, in addition to the issues of blinding, learning effects, auto-correlation and ethics raised in the conference, many social, cultural, contextual factors cannot be reproduced for the trials, either in a "clinical" setting or in the field; even if this were possible, the relevance for such factors to the real world performance would be suspect.

In developing the conference initiatives related to disease prevention/health promotion in adult midlife, a number of points were highlighted:

- ▶ To maintain that controlled trials need to be exclusively used ignores two factors. First, many programs fail in moving from the trial to real world applications. Second, this approach associates "cause" with what can be identified in a given controlled trial. We know our measurement tools are limited in assessing outcomes, including community, structural and internal psychological effects.
- ▶ Solutions for the limitations of social and behavioral science methodology, or of natural science methodology, can only be the product of additional research and

exploration. Several promising paths are developing. First, a much broader set of field experimental tools are available in quasi-experimental designs. These designs, in any given setting, may be the only choice for researchers:

- one path involves bridging the dichotomy between qualitative and quantitative methods to the benefit of a more complete and comprehensive analytical approach;
- another path involves the new and exciting work on complexity, in which non-linear dynamic modeling involving simulation of multiple agents with simple rule-based behaviors create complex, unpredictable structures which mimic the performance of complex systems such as the stock market, and provide more adequate explanations of phenomena than do linear models.

Eclecticism in method, then, should be a primary goal of social and behavioral sciences at the NIH. Eclecticism in the service of carefully defined problems and goals will yield greater payoffs and enhance the reputation and status of the social and behavioral sciences.

The group also spent some time discussing theoretical approaches and associated contro-

versies. Human behavior is associated with myriad factors: the physical and biological environment, internal biological and psychological states, experience, culture, social structural factors, peer and non peer networks and other elements of the social environment. Theory which is meant to account for this behavior—even to be merely adequate—needs to encompass these factors. One obstacle to achieving this at the NIH is the distinction made between "basic" and "applied" research, especially the lack of recognition that behavioral and social sciences encompass and depend on both types of research for scientific advancement.

Social and behavioral sciences have been successful in realizing the importance of testing ideas, hypotheses and theoretical constructs not only in the laboratory, but in real world interventions. Increasingly, these disciplines are working to make mechanisms of action as explicit as possible for interventions in a way that also facilitates multidisciplinary dialogue.

As the study of complexity is demonstrating, to be at the boundary between a stable system and chaos is an exciting opportunity, where many real world phenomena, previously unexplained, can be more convincingly explored. That these findings can have practical benefits for health and human welfare could only enhance their value. The following initiatives generated by the Task Group reflect this perspective.

Task Group Initiatives

✓ Evaluation of Social Policies as Preventive Interventions (D-3-1)

Need and Justification

Social policy changes have the potential for having major effects on health-related behaviors. As an example, increasing cost through taxation, restricting access and availability of tobacco products, and limited public areas in which smoking is permitted have a variety of effects on smoking behavior, with important health consequences.

The importance of the role of public policy in health promotion and disease prevention is underscored by the forthcoming national health plan, with its hoped-for emphasis on universal coverage. Intrinsic to universal coverage is medical, economic, and moral pressure for preventive intervention at both the service delivery and public policy level.

Yet there is comparatively little systematic research about the components of public policy which are most efficacious in achieving positive health outcomes. Examples of areas in need of study include:

- ▶ regulation of tobacco and alcohol, recommendations for optimal fat, sodium and fiber content in the diet. More than a third of preventable deaths in this country are attributable to tobacco use, the leading cause of death (400,000 per year);

- ▶ death from accidental and self-inflicted causes, the leading killer of young people in the US. Gun control legislation is currently a matter of major public policy concern. There is evidence that suicide rates are lower in states with more restrictive access to guns;
- ▶ domestic violence, another major public health problem, with long-lasting medical and psychiatric consequences;
- ▶ the health consequences of community policies which promote social integration and maintenance of support systems;
- ▶ public safety laws, such as those requiring the use of passenger restraints and motorcycle helmets, which affect rates of morbidity and mortality, but are dependent upon utilization. Providing protected bicycle and walking paths in cities promotes healthy exercise behavior;

It is obvious that public policies have intended and unintended health consequences, both worthy of systematic analysis.

Research Approach/Methodology

Proposals may involve the development and testing of appropriate methodologies for assessing the impact of policy change. Implementa-

tion of these methodologies could then systematically evaluate the effects of existing differences in salient public policy across well-chosen comparison areas, or study of the effects of change in policy in one area. Other examples could include effects of funding changes for

public services, such as mental health, emergency medical care, educational, police and court services, on measures of health care utilization, morbidity and mortality. Proposals could also involve relevant studies of public policy and its health effects in other countries.

✓ **Interventions to Enhance AIDS Prevention Behaviors (D-3-2)**

Need and Justification

The development of effective strategies for prevention of HIV infection is dependent on increasing knowledge regarding behaviors, their determinants, and mediators related to the risk of HIV transmission, including sexual behaviors and use of drugs and alcohol in all age groups. Some behaviors may also be related to disease progression in HIV-infected individuals.

The Global Program on AIDS of the World Health Organization has identified numerous successful prevention projects world-wide. Unfortunately, many of these programs have not been rigorously evaluated. NIH supported prevention research has demonstrated some key components of successful behavior change intervention and generated important site and population specific data. However, research which tests interventions across multiple populations in diverse geographic settings is needed. The NIMH, in collaboration with components of other federal agencies, has initiated a multi-site, multipopulation prevention trial to identify theory based interventions which can be readily adapted by public and private agencies.

The research proposed here complements the NIMH study by proposing multimethod and systematic exploratory approaches to developing and testing new health promotion and disease prevention interventions. The interventions will utilize current knowledge provided by behavior-

al medicine, behavioral epidemiology and advances in qualitative and ethnographic research on AIDS risk behaviors to develop community-based strategies for behavior change. Study emphasis will be placed not only on primary prevention proposals but also on relapse prevention and health behavior maintenance. Because the proposal supports many small studies, this research can focus on promising new interventions not ready for full-scale trial and not included in the NIMH study. A special focus of the study will be on understanding why behaviors occur, including their genesis and maintenance. In short, the research will support more of a basic science approach to these behaviors than is possible in large-scale field trials.

Research Approach/Methodology

Because substantial activities in this field are currently ongoing, a two-stage process is proposed. First, an expert panel of intramural and extramural scientists will be convened. The panel should include activities and representatives of the communities most affected by the epidemic. The purpose of the panel is to review ongoing activities to avoid duplication, and to identify gaps and promising new approaches not found in other ongoing research. The topics and approaches identified by the expert committee will provide the basis for a trans-NIH RFA.

✓ ***The Role of Social Norms in Health Promotion and Disease Prevention (D-3-3)***

Need and Justification

Changing social norms in facilitating or impeding behavior change have been recognized as central to successful research on smoking cessation, hypertension, heart disease and AIDS prevention programs. Several Federally-sponsored AIDS prevention programs are utilizing approaches—based on prior research conducted by the NIH—that attempt to influence social norms. However, the mechanism by which changing social norms influence behaviors is not well understood. Understanding these processes would improve our efforts to incorporate health enhancing behaviors into daily life for all Americans through daily routines, improved diet and exercise, smoking cessation, and stress management both at home and in work settings. To be effective, interventions to bring about these changes will involve influenc-

ing policies and environments, including community perspectives on healthy behavior.

Research Approach/Methodology

Research approaches should include assessing natural experiments, targeted interventions and exploratory studies. Currently many countries and states are engaged in policy reform to improve health. Additionally, many work sites are currently developing policy guidelines directed towards promoting healthy behavior and life styles in the workplace and at home. Few of these interventions are being evaluated from the perspective of how health policy influences social norms. Data gained from these opportunities, if systematically collected and analyzed, will permit rapid development of this field.

✓ **Interventions to Enhance Early Detection and Screening Behaviors (D-3-4)**

Need and Justification

Recent NIH-sponsored research indicates that significant proportions of the population are not availing themselves of early detection and screening programs. These groups include women and minority groups, particularly persons of lower socioeconomic status. In addition, for cardiovascular diseases, there is evidence that women and minority populations are less likely to receive early diagnostic tests and therefore their disease is detected at later stages. A number of factors have been found to contribute to this inadequate care-seeking behavior, including lack of access to care and cost of

care, attitudes of health care providers, cultural norms and beliefs, lack of knowledge about these procedures, among others. Therefore, interventions are needed to enhance care-seeking behavior in these underserved groups.

Research Approach/Methodology

Randomized controlled studies are needed to test the effectiveness of specifically tailored and targeted behavioral interventions to reach high risk populations. Interventions using approaches that can be utilized in a wide range of settings, such as clinical settings, schools and workplaces are encouraged.

Senior Adult

Overview

David Mechanic, Ph.D.

Several general principles were implicit in all of the issues discussed. The first concerned the fact that we are dealing with an extraordinarily heterogeneous group, not only socially and culturally, but within the "senior" age category as well. We are considering people from 60 to 100; even though it's convenient to talk about "seniors", we are talking about an age range in which people differ tremendously across many dimensions, e.g., physical and mental functional capacities.

Secondly, different birth cohorts age in different ways and at different rates, and so with changing birth cohorts, we are really talking about a moving target. People at age 60 or 70 or 80 at one point in time may be very different in their health characteristics as compared with people of the same age at some other point in time. We must be sensitive to this issue both in how we look at various analytic factors and also in how we propose to intervene.

The third general principle concerns the lifespan issue itself: there is considerable continuity among earlier and later periods across the lifespan, even though we, for convenience, have divided lifespan into "sectors". We have to be sensitive to that continuity, as indeed actions taken at a much earlier point have consequences later on.

The first of our initiatives deals with the question of whether it is useful to consider intervening on health behavior for elderly people. A variety of studies have shown that, contrary to general opinion, intervening with the elderly in terms of cigarette smoking, maintaining well being, maintaining social contact, has had very positive effects.

In the area of hypertension or blood pressure control, for example, there was an assumption that it was normal for elderly people to have higher systolic hypertension and many people took the view that treating elevated systolic hypertension was pointless and counter-productive. A sophisticated, controlled clinical trial showed that the treatment of systolic hypertension in the elderly was indeed functional for enhancing health and life. So, we are beginning to reverse these old biases about the pointlessness of intervening in the elder years. However, there are many areas which lack a strong data base and we really don't know what the impact would be in trying to intervene in areas like diet or cholesterol control or other areas. In those areas where we do know that certain kinds of intervention make a difference, it is important to try and understand what factors enhance the likelihood of those interventions/behavior changes occurring, and what are the barriers to those kinds of behavioral

changes. We also believe that for some of these areas it is time for careful controlled trials to analyze different ways of inducing these behavioral changes in elderly populations.

The second initiative relates to the fact that senior adults are dependent upon the kinds of formal and informal structures that exist in their communities and this affects the way in which households are constituted, the kinds of helping patterns that exist either formally or informally, the kinds of volunteer networks that exist in communities. This initiative deals with trying to identify and study the impact of different kinds of community organizational factors and social support factors that promote independence and continue the successful functioning among the elderly within the community.

The third initiative deals with the fact that health promotion and disease prevention among the elderly is very much dependent upon "interveners", particularly primary care physicians, who share many of the biases noted above. The same biases about the elderly are promulgated by the mass media. Many doctors have

attitudes about the elderly that are counter-productive and inconsistent with the existing data base. This initiative deals with ways of intervening in both the training and continuing education of physicians that make them more aware and more sensitive to what is possible in terms of health promotion with the elderly and to consider various techniques for trying to produce more positive attitudes and behaviors among people who are in a position to support the prevention of disease and promotion of health for elderly persons.

The fourth initiative focusses on one particular problem among elderly persons—individuals who are isolated because of their geographic location, or because everyone in their social network has died or is no longer available to them, or because of cultural or language barriers. This initiative seeks to identify ways of bringing preventive and health promotion services to individuals who are less accessible because of the above "barriers" and seeks to identify and test interventions to overcome problems associated with isolation.

Task Group Initiatives

✓ Interventions for Promoting Health In Later Life (D-4-1)

Need and Justification

Many of the behavioral and social risk factors associated with morbidity and mortality among the general population have been shown to have continued health and functional effects in late life. There is now impressive epidemiological evidence that cessation of smoking, moderate physical activity, and social involvement are sufficiently health enhancing to warrant intervention studies in the elderly. Three lines of research are recommended:

1. Epidemiological research to demonstrate the impact of other, less well studied behavioral and social risk factors (e.g., dietary intake, different types or intensities of physical activity, doctor-patient interactions, and work environments). Special attention is needed on how these potential risk factors change over time and the health effects of such changes as people age.
2. Health behavior research is needed to identify factors that encourage recommended health behaviors and social environments, as well as on the barriers to change. Interventions directed at both the older population and health care providers/health care systems need to be developed and tested. Such research would inform the design of community intervention trials among elderly populations in various social contexts.

3. Social and behavioral research is also needed on medical self care behaviors, including delays in seeking preventive screening and prompt and appropriate care among elderly populations, and the factors that reinforce maladaptive health and illness behavior. Appropriate use of self care also should be studied. Research on new approaches and technologies for dealing with compliance problems associated with age-related problems (e.g., memory, sight, mobility) is especially promising.

Research Approaches/Methodology

A variety of research approaches are needed to address these research questions. Among these are epidemiological investigations of the prevalence of a wide range of health behaviors in the elderly and their effects of morbidity, mortality, and functioning. Longitudinal studies that initially sampled younger populations are particularly valuable sources of data as subjects age (e.g., the Alameda County Study which started in 1965). Quantitative and qualitative analyses are needed on factors that inhibit behavior change and that promote adoption of particular health behaviors. Controlled intervention trials are also needed to test the health impacts of a wide range of individual and community interventions for initiating and maintaining health enhancing health practices and lifestyles. An especially fruitful research approach is to focus

on how interventions, developed and tested in younger populations, can be applied to the older population, with special emphasis on high risk older populations (e.g., low SES, oldest old, rural elders).

✓ **Social and Physical Characteristics of Health Promoting Environments for Older Persons (D-4-2)**

Need and Justification

We know a good deal about the characteristics of behaviors that promote health and effective functioning in late life. These include good health habits, physical and social activity, and sense of personal efficacy. Some interventions have been developed to facilitate these health promoting attributes in institutionalized populations. Adequate knowledge is lacking of how the social and physical characteristics of non-institutional environments affect the maintenance of health and functioning in later life. However, a more general body of relevant theory and evidence exists in community and ecological psychology and sociology. For example, community size and residence patterns within a community influence the nature and the extent of social interactions. Other research has demonstrated that characteristics of work, school, and home environments impact significantly upon intellectual functioning and sense of control in children, adults, and older people.

In recent years, many older persons have moved, more or less voluntarily, to new residences or communities. Wide variations in preferences for living arrangements exist by age, SES, marital status, and ethnicity. Research is needed to understand the kinds of community and residential arrangements that facilitate the development and maintenance of health and healthy behaviors in later life and how these may vary for people of different social backgrounds and circumstances.

Within communities, we need to understand the existing social arrangements, or the lack there-

of, that help sustain the elderly in their preferred residential settings, keep them linked to the community, and the mechanisms through which such integration into the community helps to maintain and even enhance their general well-being. Many communities have developed promising programs (e.g., cross-age helping programs such as foster grandparents) that require more rigorous evaluations and a better understanding of the underlying dynamics.

Among the researchable questions are:

1. How different living arrangements (e.g., living alone or in shared or cooperative housing) affects older people's social support, instrumental help, economic resources, and ability to function outside of institutions.
2. The influence of age-segregated housing on health and functioning of older people.
3. How various community characteristics (e.g., provision of transportation, respite care, opportunities to participate in community decision-making) influence older people's use of health care, their social participation, or their intergenerational relationships.

Recommended Research Approach/ Methodology

A variety of research approaches are required. Population-based survey and epidemiologic

studies are needed of the types of residential and living environments of older people, including availability of and participation in special programs for older persons, and how these relate to health and well-being. More focused studies are also required of particular communities or programs or residential arrangements within communities. These would include

focused, indepth studies employing ethnographic and ecologic methods and quantitative evaluation research to assess the impact of programs and residential arrangements. An important element of such research should be individual and group differences in preferences for social interactions and the consequences of such preferences.

✓ ***Educating Health Providers, the Media, and the Public about Disease Prevention and Health Promotion in Older Persons (D-4-3)***

Need and Justification

Both the media and health providers have misconceptions about the potential of disease prevention and health promotion for older adults. Stereotypes that older adults are homogeneous (e.g., frail and sick) need to be overcome. In fact, today there are greater numbers of healthy, fully functional older people in our society than ever before. The primary need of this group is not for medical care, but for maintenance of their healthy state.

Health providers remain the most important source of health recommendations for older adults, yet research indicates that older adults often do not receive advice to stop smoking, get regular exercise, or seek early detection of the

common diseases of the older years, e.g., mammograms in women.

Research Approach/Methodology

Studies would explore and test educational interventions with providers (with particular emphasis on primary care physicians) about the disease prevention and health promotion needs of older adults. The studies would also test methods to change providers' behaviors with regard to disease prevention and health promotion for older adults. This research would include such strategies as development of guidelines for care, tailoring of the health care system to maintaining continuity of care, and improvement of providers' skills in communicating with older adults.

✓ **Health Promotion for Isolated Older People (D-4-4)**

Need and Justification

Older people whose life situation includes solitary living arrangements, disabilities, or isolated geographical location, experience special barriers to involvement in the health promoting programs and social interactions that enhance well-being. Research is needed to identify and overcome these barriers that include, for example:

- ▶ Isolating environmental arrangements (e.g. living alone, rural residence);
- ▶ Economic barriers to participation in activities, to obtaining transportation, or to access for treatment;
- ▶ Language differences that shut older people out of available programs;
- ▶ Absence of kinship and social support;
- ▶ Dangerous living situations (e.g. inner city) and the fear of violence;
- ▶ Physical disabilities that confine older people;
- ▶ Emotional and mental disabilities that result in social isolation and withdrawal (e.g. depression).

To promote health and prevent disease among socially-isolated populations requires bringing them into a social context in which they can benefit from information, activities, and already-developed disease prevention and health promotion programs. Such services are increasingly available to more integrated older people.

Research Approach/Methodology

Research to reach isolated and at risk older people must first characterize the circumstances (living arrangements, disabilities, or location factors) that remove them from resources to maintain health and prevent disease. Criteria must be established to distinguish those living alone, but **not** isolated, from others who are at risk because of isolation.

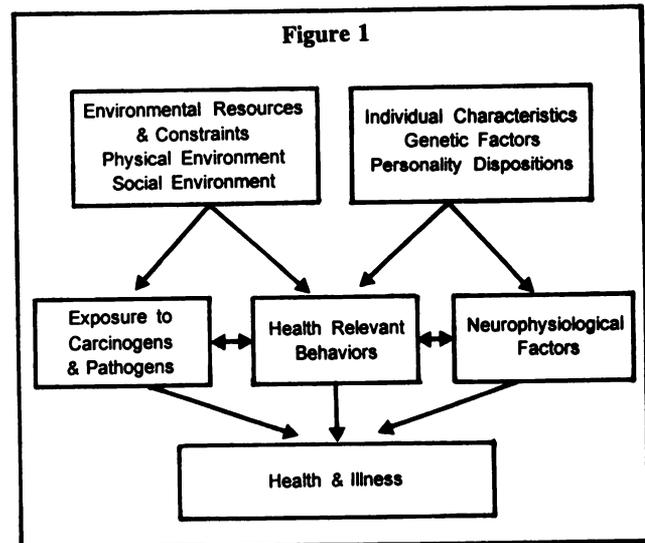
Demonstration programs are needed to bring such older people into fuller social and supportive networks. Creative programs may include, for example, establishment of a hot line for community residents, outreach activities by community and church groups, alerting community workers (mail carriers, police, etc) to bring isolated older persons to the attention of relevant community resources. Quasi-experimental designs using comparison/control communities would determine the effectiveness of such programs in enhancing health and quality of life for senior citizens.

Synthesis

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The ultimate objective of behavioral medicine research is the prevention of disease and the promotion of health. This is the rationale given by behavioral medicine for research studies exploring basic mechanisms to trials testing theoretical models and interventions. Research moves into the disease prevention/health promotion arena to either provide data on the environment or community in which behavioral medicine efforts are often applied or to conduct tests of behavioral medicine interventions. The public domain in which disease prevention and health promotion activities are examined concerns dynamic relationships involving physical and social environments; characteristics of individuals including genetic influences, perceptions, psychological factors, and physiological patterns of reactivity; health behaviors; and health outcomes. When arranged in a model, as shown in Figure 1, these relationships provide a helpful rubric for identifying the themes for disease prevention and health promotion research across the life span.

The four task groups, representing the life span, developed initiatives that focus on different relationships within this dynamic model. For example, the physical environment can be the source of environmental agents, including radiation and pollutants, which can impact health directly or can exacerbate risk generated by genetic predispositions or health behaviors. One initiative calls for interventions that can be designed to prevent or attenuate environmental exposures in children. The physical



environment is also the site of hazardous conditions that result in injuries and accidents, the leading cause of death among children. A number of initiatives across the four task groups call for research to investigate these conditions, to study their individual characteristics, and to intervene to prevent their adverse consequences.

Social environments, such as the family, schools, senior residences and the community can be the target of disease prevention and health promotion efforts. The task groups proposed initiatives to examine the influence of social norms on behavior and to identify the processes underlying this influence. Specifically, research is needed that would investigate how norms are created and analyze how they are manipulated by social forces, such as the media, to increase such risk behaviors as smok-

ing and alcohol use. These same processes and social forces, when thoroughly understood, could be used to promote behavioral risk reduction.

Social norms operate at other points in the health promotion and disease prevention arena besides their role in encouraging or discouraging risk behaviors. For example, the Senior Adult task group initiatives point out that social norms influence attitudes among physicians and the public about the potential benefit of promoting positive health behaviors in senior adults. These public and health professional perceptions can become avenues or barriers to health promotion among various segments of the population, across the life span.

The social environment is also the forum for policies that impact behavior. Health professionals, including those in behavioral medicine, are called before policy-making bodies to provide guidance. Research, including that described in the task groups' initiatives, could be used to inform this advice and guidance. Initiatives point out the need to study how policy changes serve as 'natural experiments' that influence health behaviors. For example, increases in tobacco taxes have profound effects on tobacco use. Other such natural experiments expected in the future, including gun control and needle exchange, provide valuable opportunities for study. Changes at the level of the social environment, as shown by the model, can have profound influences on individual characteristics, as well as health behaviors and outcomes.

Community-based interventions are given prominence in a number of the initiatives. These interventions call for approaches to change such health behaviors as diet and exercise that are based on social marketing theory,

diffusion of innovative practices, the use of peer educators, and existing channels of communication. The initiatives acknowledge the extent to which environmental settings, with certain physical and social characteristics can constitute barriers to the development and practice of health behaviors. Examples include the limited access to such resources as fresh fruit and exercise facilities in urban settings, and social isolation among older adults. To the extent that such barriers are identified and overcome, the effects of disease prevention and health promotion efforts can be magnified throughout the community.

At the level of the individual, a theme across a number of the task groups, focused on the development and natural history of decision-making regarding health behavior choices. Research is needed to help explain why health education efforts, even when based on health belief models, have limited impact on behavior change. Among the questions that need to be addressed are to what extent, and by what mechanism, do peers or media messages influence health behavior choices. A number of initiatives focus on identifying individuals who are at elevated risk for adverse health outcomes and, as such, are candidates for disease prevention and health promotion interventions.

Elevated risk is variously defined as taking into account genetic characteristics, personality predispositions, physiological patterns such as excessive reactivity, previous behavioral practices, and social factors such as poverty in crowded, violent neighborhoods. Thus, individuals in various settings within communities could be screened to identify those with a family history of hypertension, who have a certain hypertension-prone personality predisposition, who show excessive adrenergic responses to stressors, who are overweight, and who live in higher-stress neighborhoods.

A number of initiatives express the need for interventions designed for those at risk for chronic or infectious diseases. Examples include interventions to increase the frequency of healthy eating and exercise in order to reduce cardiovascular risk, and programs to reduce the practice of behaviors that increase risk for transmission of the human immunodeficiency virus which causes AIDS. The initiatives highlight the need to tailor these interventions to target groups defined not only by age and gender but by other important socio-cultural factors, including social status, education and ethnicity.

The common theme of many of the disease prevention/health promotion initiatives is to investigate the complex processes that influence risk. This theme requires research that is multifactorial and that examines interactions among the biological, psychological, behavioral, social and environmental factors that, as shown in the model, determine health. It is apparent that the research sought by these initiatives will go beyond advancing our knowledge about the underlying processes that influence health outcomes. Implicit in the initiatives is an interest in designing interventions based on this new knowledge and testing the efficacy of these interventions in the pursuit of improving public health and quality of life across the life span.

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