Psychosomatic Medicine: The Scientific Foundation of the Biopsychosocial Model

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Objective: *This article presents major concepts and research findings from the field of psychosomatic medicine that the authors believe should be taught to all medical students.*

Method: *The authors asked senior scholars involved in psychosomatic medicine to summarize key findings in their respective fields.*

Results: *The authors provide an overview of the field and summarize core research in basic psychophysiological mechanisms—central nervous system/autonomic nervous system, psychoneuroimmunology, and psychoendocrinology—in three major disease states—cardiovascular, gastrointestinal, and HIV virus infections.*

Conclusions: *Understanding the core scientific concepts and research findings of psychosomatic medicine should provide medical trainees with a scientific foundation for practicing medicine within a biopsychosocial model of care.*

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In 1977, George Engel challenged the medical profession to reconsider a strict biomedical approach to medical education and care and embrace a "new medical model," the biopsychosocial model (1). Engel argued that humans are at once biological, psychological, and social beings who behave in certain ways that can promote or harm their health. Many interacting factors, from the cellular to the social, contribute to health and illness. A disturbance in any sphere of human functioning affects all of them. If physicians are to realize their potential to promote the healing of patients' illnesses, as opposed to narrow efforts to diagnose and cure diseases, they must understand the nature of these interactions.

Engel was proposing an alternate way to construct clinical reality, another way to see. If physicians understand how a variety of psychosocial factors interact to promote or maintain illness, they can intervene at a variety of levels. No longer constrained to intervening only at a biological level, clinicians can intervene with cognitive, behavioral, and/or emotional strategies as well, knowing that these interventions can have positive effects at all levels of functioning.

Despite a general acceptance of the biopsychosocial model in medical education, U.S. medical education and care are still largely biomedical in focus, and physicians have many deficiencies in biopsychosocial formulations and care (2–4).

Part of the problem may be that medical students are not offered a sufficient scientific foundation for understanding the biopsychosocial model. Since the inception of the modern era of psychosomatic research in the early 1940s, this science has flourished and provided that scientific foundation. Psychosomatic research investigates the multilevel interactions that contribute to health and illness (5), including genetic susceptibility, biological insults (e.g.,

carcinogens and microbes), early childhood experiences, socioeconomic status, personality, acute and chronic stressors, behaviors, life style, social networks, and their combined effects on physiological functioning. The Institute of Medicine (IOM) recently issued a report on enhancing behavioral and social science education in medical school curricula, and emphasized major topic areas in psychosomatic medicine, including mind-body interactions in health and disease (6). Now that the American Board of Medical Specialties has approved the specialty designation of "psychosomatic medicine" for psychiatrists who care for the medically ill (7), there is a unique opportunity to incorporate the science of psychosomatic medicine into medical curricula. Specialists in psychosomatic medicine will likely be tapped to lead the efforts in teaching the fundamentals of biopsychosocial care.

We believe that physicians cannot truly practice within a biopsychosocial perspective without understanding the scientific basis for this perspective. As a resource for medical educators, we offer in this article an overview of major domains, concepts and research findings in psychosomatic medicine that we believe should be integrated into medical school curricula.

We first present an overview of the domains of psychosomatic medicine. Next, we present physiological pathways for intersystem communication among the neural, immune, and endocrine systems—and possible biological mechanisms for the pathogenesis of some diseases. The following three sections offer examples of psychosomatic research in cardiovascular, gastrointestinal, and infectious disease. We then comment on issues related to integrating this science into undergraduate medical education.

The Domains of Psychosomatic Medicine

Because psychosomatic medicine research focuses on the interactions among various traditional scholarly domains (biology, psychology/psychiatry, sociology, economics), it is difficult to categorize the domains of psychosomatic medicine. Figure 1 illustrates one approach to categorization, viewing topics from the vantage point of the most predominant interactions, recognizing that there are biopsychosocial interactions relevant to all of these topics. Each of the domains in the figure contains major examples, and is not intended to be exhaustive. In this article, we focus on the psychological/biological domain, since there may be more need for curricular guidance than other domains which appear to be more fully presented in current behavioral science courses (2, 8). However, it is important to underscore that there is high quality empirical research in all of the other domains that inform students' understanding of biopsychosocial interactions (9, 10). To cite two examples in the social/biological domain, the strength of social isolation as a risk factor for ill health is comparable to high blood pressure, obesity, sedentary lifestyles, and possibly even smoking (11). Also, there is a gradient in the relationship between socioeconomic status and health, with each level of the hierarchy exhibiting less morbidity and mortality than lower levels (12).

Intersystem Communication: Psychophysiology and Disease

Because humans evolved as social beings living in an often hostile environment, a variety of psychophysiological mechanisms evolved to maintain health in a variety of contexts. These mechanisms are mediated by the central and autonomic nervous systems, the neuroendocrine and immune systems. These adaptive physiological mechanisms have limitations and can be compromised by adverse social and environmental events. Hans Selye (13) first described how chronic stress can lead to enlarged adrenals, atrophied thymus, tumors, and heart disease in mice. Fifty years later, the psychology and psychophysiology of stress are still not fully understood. What is clear, however, is that psychological stressors can have harmful effects on health. For example, stressors such as ego threat and lack of control are potent stimuli for the hypothalamic-pituitary-adrenal (HPA) axis, and, chronically, can damage the resiliency of neuroendocrine axes (14). There is recent evidence that stress modulates indices of cellular aging (15). A helpful model for understanding the cumulative physiological effects of chronic stress is the allostatic load model. "Allostasis" is the body's adaptive responses to stress, and "allostatic load" the cumulative wear and tear on the body of these responses (16). According to this model, "stressors" are not just psychological but constitute any factor that can dysregulate the stress response systems, including genetics, life experiences, and damaging health behaviors, such as smoking and alcohol use. In the following three sections, we describe basic psychophysiological mechanisms in the central and autonomic nervous systems, the immune and neuroendocrine systems, and their implications for health and illness.

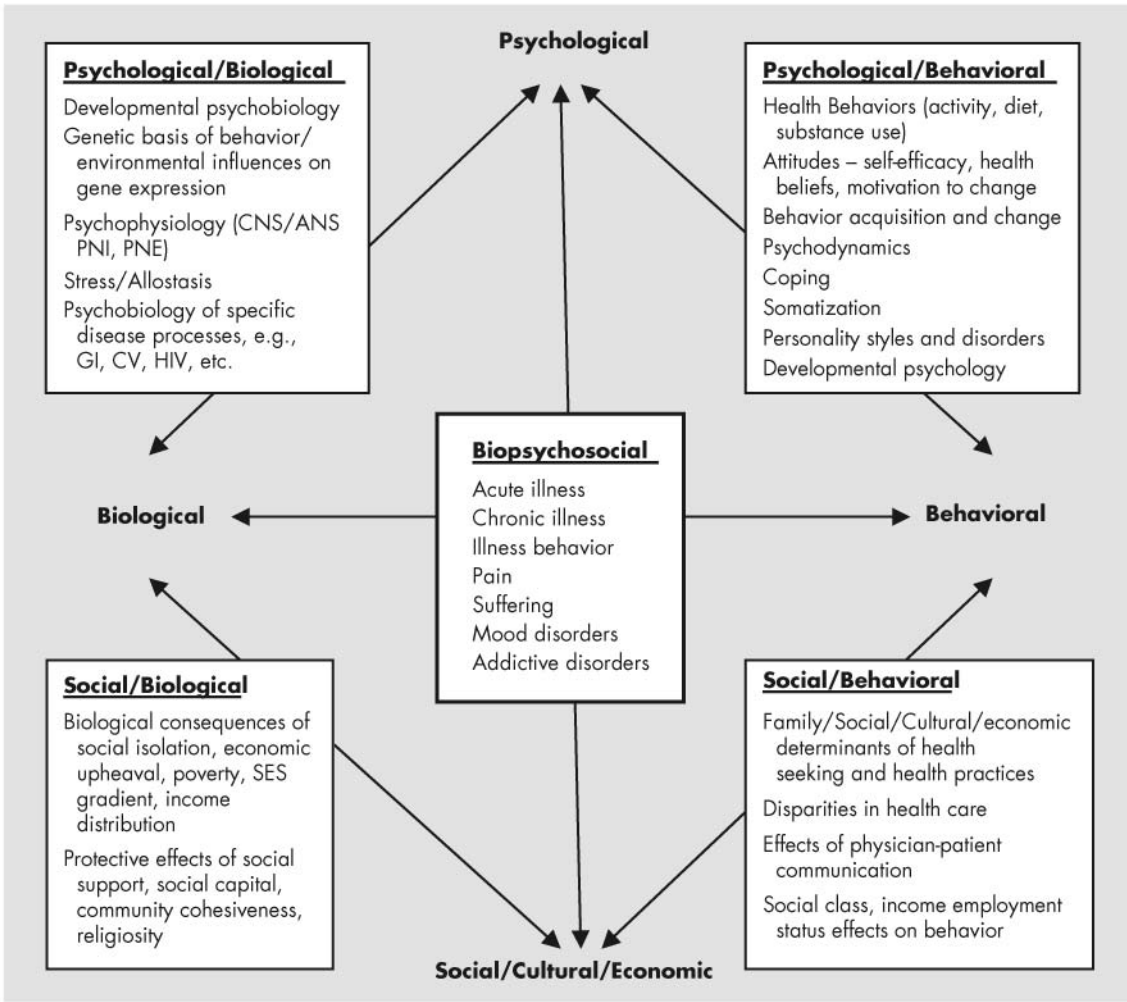
Roles of the Central and Autonomic Nervous Systems in Psychophysiology

An understanding of the structures and functions of the central (CNS) and autonomic nervous systems (ANS) pro-

vides a foundation for appreciating the intricacies of psychophysiology in mind-brain-body-behavioral interactions. The CNS and ANS evolved to maintain homeostasis (i.e., an optimized physiological state) in relation to the internal and external environments, by coordinating a variety of physiological responses to stressors. The interconnections and individual functions of brain structures determine learning, cognition, emotional reactions to and appraisal of interpersonal and environmental stressors. These cognitive and emotional reactions initiate physiological processes that influence health and illness. Quality of parenting and stressors during childhood can influence the reactivity of a variety of neuronal systems to later stressors (9). Knowledge of brain structures and their neurochemistry is essential for understanding normal functioning, as well as pathological states, such as anxiety, depression, and posttraumatic stress disorder, and can be helpful in understanding why certain cognitive therapies are effective. Also, understanding CNS/ANS connections with other organ systems illuminates how a variety of stressors and emotional states might contribute to dysfunction in other organ systems.

Though we understand that most bodily tissues send information to and receive information from the brain, understanding psychophysiology's contribution to pathogenesis is a complex task. It is necessary to identify susceptible

FIGURE 1. The Domains of Psychosomatic Medicine*



PNI = psychoneuroimmunology; PNE = psychoendocrinology; GI = gastrointestinal; CV = cardiovascular
*An earlier version of this figure appeared in Psychiatric Times (2006; 23:1, 6–8, 38)

organs, brain regions involved, linkages between them, and mechanisms of dysfunction. Some organ systems implicated include cardiovascular, gastrointestinal, immune and endocrine, and the brain itself.

Neural connections between the CNS and visceral organs pass through the ANS (17, 18), which has both efferent (brain to body) and afferent (body to brain) parts. The efferent is divided into sympathetic and parasympathetic parts, with the sympathetic typically involved in active behavior, and the parasympathetic mediating vegetative functions. Although less well understood, the afferent part appears similarly constructed (19). The hypothalamus and pituitary gland are the main mediators between the CNS and endocrine systems.

Emotional changes are related to pathological bodily changes (e.g., there is evidence suggesting a pathogenic role for anger, hostility, and irritable mood in disease) (20). Although all brain regions are potentially involved in psychosomatic processes, some are essential because of their involvement in emotional and ANS functioning: frontal and cingulate cortical areas (21) and limbic system (22), including the amygdala (23) and basal ganglia (24).

If brain regions associated with emotions play roles in psychosomatic processes, the neural pathways that mediate these effects may also contribute. The efferent ANS, particularly via enhanced sympathetic nervous system activity, is implicated in the psychophysiology of cardiovascular disease and HIV. The afferent ANS and visceral sensory processes that play roles in the psychophysiology of disease have been less extensively investigated, but some research has been suggestive. Pavlov et al. (25) demonstrated that visceral functions could be conditioned via interoceptors. Biofeedback research demonstrates that, under some conditions, humans are aware of visceral functioning (26). Visceral sensory information can affect thought, emotion, and behavior, even outside of awareness. Neuroimaging studies have identified brain areas implicated in visceral sensation (27): solitary tract, parabrachial nuclei, locus ceruleus, hypothalamus, amygdala, other limbic structures, and prefrontal, cingulate, somatosensory, and insular cortices (28). Neuroimaging studies are elucidating how CNS and ANS are associated with emotions and symptoms of bodily distress (29–31). Understanding visceral afferent and efferent mechanisms provides an underpinning for understanding the role of psychophysiological processes in hypertension, cardiovascular reactivity, and heart disease, gastrointestinal disorders, infectious disease, neoplasias, stress reactions, and anxiety and depression.

Psychoneuroimmunology

Evidence of brain-immune system interactions exists at several levels of organization. The brain communicates with the immune system via the autonomic nervous system and neuroendocrine outflow from the pituitary. Primary and secondary lymphoid organs are innervated with sympathetic nerves that release a variety of neuropeptides, the stimulation (or interruption) of which influence immune responses. Lymphocytes carry receptors for a variety of hormones (e.g., cortisol, beta adrenergic, human growth hormone, thyroid hormone, insulin, glucagons, parathyroid hormone, histamine), which suggests that the cellular interactions that mediate humoral and cellular immunity can also be modulated by the neuroendocrine environment in which these responses occur. Conversely, the production of neuropeptides and hormones by lymphocytes and the release of cytokines by an activated immune system are capable of influencing neural and endocrine function. It is hardly surprising then, that Pavlovian conditioning or the neuroendocrine changes associated with the perception of and the behavioral and emotional responses to stressful life experiences would be capable of influencing immune functions. Ader (32) comprehensively reviews evidence of brain-immune system interactions.

Behaviorally conditioned alterations of immune function provide one of the more dramatic lines of evidence linking the brain and the immune system. Animals reexposed to a conditioned stimulus previously associated with immunomodulatory (including antigenic) stimuli show conditioned suppression or enhancement of humoral and/or cell-mediated immune responses, and unreinforced exposures to the conditioned stimulus result in extinction of the conditioned response (33, 34). By capitalizing on conditioned immunosuppressive responses, the onset of lupus in genetically susceptible mice was delayed using a lower cumulative amount of an immunosuppressive drug that was otherwise ineffective in altering progression of the autoimmune disorder (35). The biological impact of conditioning has also been demonstrated in reducing the severity of adjuvant-induced arthritis (36–38) and promoting the survival of allogeneic tissue transplants (28, 39–41).

In animals, stressful life experiences can disrupt immune function and increase susceptibility and/or mortality to experimental tumors (42) and a variety of infectious agents (e.g., herpes simplex virus, influenza, Coxsackie virus, Sindbis virus) (43–45) or allow an otherwise inconsequential exposure to a pathogen to develop into clinical disease (46, 47). In contrast, some of these same stressors have no

effect or can decrease susceptibility to other immunologically mediated disease processes (48–50). The effects of stressful life experiences on immune function depend on the nature of the behavioral circumstances; the nature of the antigenic stimulation and the temporal relationship between them; the immune response and the time at which it is measured; a variety of host factors; and the interactions among these variables (51).

In humans, immune function may be altered by affective states and by major and minor acute and chronic stressful life experiences (52). Although characterized by a high variability within and between studies, depression, for example, is generally associated with a reduced level of immunocompetence (53, 54). Reliable changes in cellular immunity are even associated with such ubiquitous stressors as academic examinations (55). Major life changes like separation and divorce and other chronic stressors have also been associated with immunologic impairments, including a depressed antiviral response to an influenza immunization (56), diminished cell-mediated control over a latent virus (57), and delayed wound healing (58). In contrast, distress-reducing interventions like relaxation, massage, or even guided imagery may enhance some aspects of immune function in some individuals under certain conditions (59). The clinical significance of such changes, however, remains to be elaborated.

The neural and endocrine changes associated with changes in behavioral states and the network of connections between the brain and the immune system provide multiple pathways through which behavioral processes could influence immune defenses. The existence of these bidirectional pathways reinforces the hypothesis that immune changes constitute an important mechanism through which psychosocial factors could influence health and disease.

Psychoneuroendocrinology

Psychoneuroendocrinology is the study of interactions between mind, brain, and endocrine function. The HPA (hypothalamic-pituitary-adrenal) axis and one of its endproducts, cortisol, are major areas of study. Cortisol exerts multiple effects on physiology, with a primary role in glucose homeostasis and homeostatic responses to stressors (60). While gross deviations in cortisol levels have clearly pathological effects, as in Cushing's Syndrome, repeated elevations of stress hormones may lead to dysregulated stress responses and risk for disease (61). Chronic stress does not have a monolithic effect, rather several phenotypes of HPA axis dysregulation may result: hypercortisolism or less frequently, hypocortisolism (62), each with different likely health consequences. This section emphasizes hypercortisolism, the most common phenotype of dysregulation.

Animal studies show chronic stress promotes visceral fat, risk factors for heart disease and frank atherosclerosis (63–65). An important pathway that explains this stress-disease relationship, at least in rodent models, is increased cortisol secretion which can stimulate appetite for sugar and fat, and promote visceral fat accumulation (64). Adrenergic activity is also clearly important in stress-induced atherosclerosis (65).

In humans, research suggests similar underlying mechanisms, but causal evidence is scant. History of childhood sexual abuse is linked to increased reactivity of the HPA axis, whereas posttraumatic stress disorder (PTSD) has often been related to low levels of cortisol (62). Low birth weight, associated with low socioeconomic status and high stress (66), may contribute to HPA axis hyperactivity and development of the metabolic syndrome in adulthood (67). Exaggerated HPA axis activity is associated with both visceral fat and a preference for sweet high fat food in women (68, 69). Several studies show associations between chronic stress or HPA axis dysregulation (both hyper- and hypocortisolemia) with aspects of metabolic syndrome, such as elevated fasting insulin or visceral fat (67). In people with diabetes, stress tends to exacerbate hyperglycemia, and stress reduction may improve glycemic control for some patients (70), perhaps by improving HPA regulation.

Chronic hypercortisolemia is associated with atrophy of the hippocampal pyramidal neurons (crucial in regulation of emotion and memory), although how this effect is mediated remains unclear. In subordinate rats, hippocampal cell damage and death have been correlated with high levels of cortisol (71). In humans, hippocampal atrophy has been found in disorders associated with the dysregulation of the HPA axis, including recurrent major depressive disorder (72), Alzheimer's disease (73), PTSD (74), and Cushing's Syndrome (75). However, evidence that cortisol plays a causal role in the hippocampal atrophy in humans is still lacking, and in at least some cases, reduced hippocampal volume appears to be a predisposing factor, as shown in a study of PTSD (76).

Another important area of research is the bidirectional relation between mood disorders and hormones. Endocrine disorders of the thyroid, gonadal, and especially the HPA axes are associated with depression, and, conversely, depression is associated with dysregulation of these hor-

mones. Initial studies suggest that antiglucocorticoid strategies may improve depression (77). Life event stress is known to precipitate episodes of major depression. Taken together, these findings suggest a plausible role for stress-induced HPA axis dysregulation in the pathogenesis of major depression (78). Although a great deal remains to be understood about the effects of stress on health and disease, the relationships between stressful life experience, HPA axis dysregulation, metabolic syndrome, and hippocampal volume begin to illustrate the interplay between physiology, psychology, and the social world.

Disease Models

Cardiovascular Disease

There has been extensive study of interrelations among biological, psychological, social, and behavioral factors in cardiovascular disease morbidity and mortality. Cross-sectional and longitudinal investigations demonstrate that high levels of stress, low levels of social support or social isolation, low socioeconomic status, personality factors, and negative emotions, such as anger or hostility, depression, and anxiety are associated with increased cardiovascular disease morbidity and mortality (79, 80). These associations remain significant after controlling for conventional cardiovascular disease risk factors, such as smoking, physical inactivity, and deleterious lipid profiles. However, psychosocial factors may display interactive effects with standard risk factors in promoting cardiovascular disease.

Psychosocial factors have been linked to a variety of pathophysiological mechanisms that could influence both the long-term development of cardiovascular disease and trigger acute clinical events (79, 80). For example, the psychosocial factors discussed above have been associated variously with enhanced sympathetic nervous system activation (e.g., increased blood pressure, heart rate, cardiac output, total peripheral resistance) and impaired parasympathetic (vagal) activity, particularly upon exposure to psychological stress, increased circulating levels of catecholamines and corticosteroids, enhanced blood coagulation and fibrinolysis, endothelial dysfunction, coronary vasospasm, components of the metabolic syndrome, and various inflammatory markers (79–82).

A series of investigations in nonhuman primates is relevant to the issue of long-term cardiovascular disease pathogenesis. In these studies, behavioral dominance and social instability (in males), subordination (in females), and heightened cardiac responses to stress were associated variously with the development of enhanced coronary artery atherosclerosis, indexes of transient endothelial injury, hypercortisolemia, and ovarian dysfunction. Select associations were abolished by beta-adrenoceptor blockade, suggesting sympathetic nervous system mediation (80, 83). In humans, stress-induced blood pressure responses have been associated prospectively with the development of hypertension, left ventricular hypertrophy, carotid atherosclerosis, coronary heart disease, and stroke (84–86).

Regarding the acute elicitation of clinical events, anger has been identified as a trigger of myocardial infarction (87). Negative emotions in daily life have been shown to elicit myocardial ischemia (88). Mental-stress-induced myocardial ischemia, in turn, has been shown to predict future clinical events in patients with coronary artery disease, perhaps via a lowered threshold for ventricular fibrillation. Negative emotions have also been linked to sudden cardiac death (89). Depression is highly prevalent following myocardial infarction or cardiac surgery and strongly predicts subsequent morbidity and mortality (90, 91).

The role of lifestyle modification (e.g., smoking cessation, diet, exercise) in improving cardiovascular health is well established. However, psychological interventions, such as relaxation therapy, stress management, and other cognitive and behavioral therapies, may independently improve psychological distress and physiological functioning, and reduce morbidity and mortality in patients with cardiovascular disease (80, 92). Though initial intervention trials have not all been successful, there is reason for optimism for the future of this research (93).

Psychosocial factors may also play a critical role in participation in and adherence to treatment regimens such as cardiac rehabilitation. Cardiovascular disease has also been shown to affect quality of life and cognitive function negatively (94). Thus, there are plausible mechanisms underlying the assertion that interventions to enhance biopsychosocial care could assist in the prevention and treatment of cardiovascular disease and help to preserve patients' quality of life and level of functioning.

Gastrointestinal Diseases

The onset and course of nonulcer dyspepsia and irritable bowel syndrome—functional gastrointestinal disorders—are strongly conditioned by psychosocial factors, such as personality (95) and life stress (96). Patients show characteristic patterns on functional brain imaging (97) and spectral ECG analysis (98), while psychologically based interventions are efficacious (99, 100). Mechanisms that may account for these associations include effects on

gastrointestinal motility mediated by a visceral nervous system laden with immune reactive cells, a lowered threshold for perceiving adverse visceral sensations (101); and behavior changes including aerophagia and substance consumption (cigarettes, alcohol, caffeine, and nonsteroidal anti-inflammatory drugs [NSAIDS]). The relations between functional gastrointestinal disorders and psychosocial factors are not straightforward, however. The impact of severe symptoms on quality of life can inflate apparent associations, while nonpsychosocial factors, such as luminal flora (102), low-grade inflammation (103), and food sensitivities (104) play important and complex roles. Psychological factors contribute to the determination of whether an individual will develop long-lasting irritable bowel syndrome following acute infectious gastroenteritis (105).

In "organic" gastrointestinal diseases, the mix of psychological, infectious, behavioral, and physiological elements differs in detail but not in essence from the "functional" disorders. For example, psychological influences on the pain threshold may affect gastroesophageal reflux symptoms (106). Similarly, the association of peptic ulcer with Helicobacter pylori (HP) does not negate a role for psychological factors, since at least one ulcer in four develops in the absence of HP and only one HP-infected person in five develops an ulcer. In prospective studies, shared stressors increase the risk of peptic ulcer (107), and psychological vulnerability and perceived stress raise ulcer incidence in defined cohorts (108).

Ulcer formation is facilitated by stress-related increases in gastric acid secretion (109), and net acid delivery to the duodenum, which in turn facilitates HP infection, may be further increased by motility changes and by impaired food buffering due to irregular meals. Behavioral concomitants of stress, such as cigarette smoking and NSAIDs, can reduce the efficacy of mucosal immune defenses. Other plausible mechanisms for stress effects on ulcer include impaired wound healing (58) and circulatory changes. Psychological distress hinders the healing of peptic ulcer (110), and worsens its long-term course (111), whereas patients who develop an ulcer while under temporary stress are unlikely to go on to chronic or refractory symptoms (112). The efficacy of current medical treatment for peptic ulcer has, however, decreased the practical importance of psychological approaches to therapy except in unusual cases.

The inflammatory bowel diseases are currently believed to represent a heightened immune reaction in the gut wall to luminal contents, abetted by excessive antigen leakage across the mucosa, alterations in the resident flora, immune hyper-reactivity, and/or NSAIDs. Since stress has the potential for increasing intestinal permeability (113), changing the bacterial flora (114), dysregulating immune function, increasing analgesic use, and decreasing behavioral adherence to prophylactic regimens, and since relapse of chemical colitis is promoted by stress in animal models (115), apparently by impairing the mucosal barrier to antigen penetration (116), it is not surprising that psychological factors can influence endoscopic rectal inflammation in inflammatory bowel disease patients (117–119).

Clinical exacerbation has been found to be facilitated by life stress in ulcerative colitis (117) and by depressive symptoms in Crohn's disease (120, 121), though life stress is unlikely to cause disease onset (122). Psychological factors strongly influence the health-related quality of life of inflammatory bowel disease patients (123, 124), especially in vulnerable patients (125). Psychologically oriented interventions aimed at modifying the course of inflammatory bowel disease have thus far shown disappointing results when applied to unselected patients (126, 127). Efficacy may yet be demonstrated among patient subgroups with high distress levels and high levels of activity, and psychological counseling can in any case be valuable in coping with these diseases.

Human Immunodeficiency Virus Infections

Since stress influences the immune system in healthy populations, it is plausible that stress and other psychosocial factors may compound immune abnormalities in HIV-infected persons. Research shows that stressful life events, depression, personality and coping style, social support, spirituality (128, 129), and stress management techniques (130) are associated with immune system alterations and/or clinical disease course in HIV-infected persons.

HIV-positive men and women who remain healthy despite low CD4+ cell counts have relative preservation of natural killer cell cytotoxicity (NKCC) (131). Stress-induced impairments in NKCC and cytotoxic T cell functioning may allow latent virus reactivation to go unchecked, leading to HIV replication and progression to AIDS (132). This may also increase the risk of virally related cancers, such as Epstein-Barr Virus-associated Burkitt's lymphoma and human papilloma virus-associated cervical cancer (133). Because several of these viruses are known to have immunosuppressive effects, in and of themselves, reactivation of these viruses could have implications for compounding HIV-induced immune system decrements and possibly disease progression.

Psychosocial factors are hypothesized to influence these aspects of immune system surveillance via several adrenal hormones—including cortisol and catecholamines. Cortisol modulates lymphocyte proliferation and NKCC enhances HIV replication in vitro, and may favor a shift from Th1 cytokines (e.g., gamma-interferon) to Th2 cytokine (e.g., IL-10) production (134), which may work against adequate surveillance of HIV and other viral infections. HIV-infected persons display physiological changes consistent with elevated resting levels of cortisol, as evidenced by muted cortisol responsivity to cold pressor (135) and corticotropin-releasing hormone (CRH) challenges (136), and a flattened circadian rhythm for the secretion of cortisol and other HPA hormones (137). Elevated cortisol levels predict accelerated immune decline and development of AIDS in HIV-positive persons (128).

The sympathetic nervous system is also activated during stressful circumstances, and lymphocyte beta-adrenergic receptors may transduce the effects of behavioral stressors to down regulate lymphocyte and NK function via cAMP. Chronic sympathetic nervous system (SNS) activation with release of norepinephrine may alter lymphocyte trafficking, cytokine production, and cytotoxicity and facilitate HIV replication (138). HIV-positive men with signs of autonomic nervous system activation show less suppression of HIV plasma viral load and poorer CD4 + T cell recovery on highly active antiretroviral therapy (HAART) (139).

Cognitive behavior stress management (CBSM), the most widely studied psychosocial intervention in HIV-positive populations, includes cognitive restructuring and training in relaxation, and coping and interpersonal skills. These may reduce anxiety, depression and social isolation by lowering physical tension, increasing a sense of control and self-efficacy, and building interpersonal skills necessary to maintain adequate and effective social relationships. These psychological changes are hypothesized to improve ability to regulate peripheral catecholamines and cortisol via changes in the sympathetic nervous system and HPA axis regulation. Stress management interventions increase self-efficacy, decrease perceived stress and burnout (140), reduce substance use (141), and decrease levels of SNS and HPA hormones, and improve immune functions (130). Studies of HIV-positive persons assigned to CBSM demonstrate less activation of HPA axis-mediated stress responses (142), better immunologic control of certain viral pathogens (143), increases in markers of immune system reconstitution (144), and decreases in HIV viral RNA in peripheral blood (145) up to 15 months after intervention. Many of these biological changes were associated with reductions in depression and increases in relaxation and social support during intervention (143, 146).

Comment

We have summarized basic psychophysiological mechanisms, and have chosen to focus on psychosomatic interactions in cardiovascular, gastrointestinal, and HIV-related diseases as illustrative. However, there are biological, psychological, behavioral and social interactions in all diseases. We could have easily illustrated these interactions within the context of cancer, end-stage renal disease, chronic obstructive pulmonary disease, or the common cold.

Psychosomatic medicine is inherently an integrative science, which partially explains its lack of emphasis in medical education. The current emphasis on molecular biology and genetics favors a reductionist approach in medicine and biology and strives to understand a living organism by breaking it down to its smallest components. However, adding up all of the information presented by the basic science disciplines does not allow for understanding the integrative whole of human functioning. Human health and disease can ultimately only be understood within the context of interactions of all the disciplines, and it is here that the science of psychosomatic medicine resides.

How are the divisions and barriers in U.S. medical education to be surmounted? How are medical students to understand the myriad interconnections among the social environment, behavior, emotions, physiology, and genetics in the genesis of illness and disease? Training medical students to think about illness and disease from a multilevel perspective must begin in the early medical school years. If, for example, in immunology courses they learn about how the immune system can be influenced by the endocrine system, and, in turn, in physiology and behavioral science courses learn how stress can activate the endocrine and immune system, the template is established for students to continue to think about the implications of these connections as they enter their clinical years. Problem-based instruction is particularly suited to realizing the multilevel analyses that psychosomatic medicine demands. The Professional Education Committee of the American Psychosomatic Society recently outlined a comprehensive, longitudinal curriculum in psychosomatic medicine, addressing issues related to educational design and implementation (8). The core of that curriculum is outlined in Appendix 1. Appendix 2 presents tips for teaching students and residents.

Psychosomatic medicine's emphasis on the interconnections between systems and disciplines offers a unique and vital contribution to the future of medical education. Implementing an interdisciplinary approach in both basic and clinical science curricula is critical to enhancing students' scientific understanding of human health and disease. A firm foundation in psychosomatic medicine should help students understand why they must inquire about patients' backgrounds, current lives, health habits, stressors, moods, hopes, and fears. Physicians trained in this scientific foundation can offer patients explanations of how stressors and life experiences can be related to their somatic symptoms. Patients who understand something of the psychophysiology of irritable bowel, anxiety, depression, addiction, and other disorders may experience less guilt or shame about having these disorders, and may more readily accept pharmacological and psychotherapeutic help. An understanding of psychosomatic medicine should enable physicians to practice medicine within a biopsychosocial model of care, and to design interventions that will help heal their patients' illnesses as well as cure their diseases.

APPENDIX 1. Components of a Comprehensive Longitudinal Curriculum in Psychosomatic Medicine for Medical Schools

A. Teach Core Content

1. Core topics in psychophysiology: CNS/ANS, psychoendocrinology, psychoneuroimmunology, stress responses, allostasis
2. Common clinical syndromes: chronic fatigue, panic disorder, fibromyalgia, functional bowel disorders, headache, back pain, anxiety, depression. Cover psychophysiology as well the impact of emotions and stress on disease pathogenesis, onset, maintenance, and recovery.
3. Psychosocial epidemiology: the impact of socioeconomic status, social support, job stress, and culture on health and illness.
4. Psychosocial aspects of acute and chronic diseases: AIDS and other infectious diseases, cardiovascular diseases, renal diseases.
5. A behavioral science curriculum: one that includes essential behavioral and psychodynamic principles in medical care, psychopathology, personality types and disorders, psychiatric diagnoses, and behavioral theory and treatments. It should also include psychological and behavioral principles and techniques that can be applied by medical clinicians, as well as knowledge of therapeutic techniques used by behavioral medicine specialists.
6. A longitudinal curriculum in doctor-patient communication: one that includes basic skills, such as data-gathering, patient education, and communicating empathy, as well as advanced skills, such as giving bad news, communicating with patients with terminal illnesses, recognizing and treating anxiety and depressive disorders, alcohol counseling, and others.

B. Integrate and Reinforce Teaching in Both the Preclinical and Clinical Years

1. Teachers in physiology, biochemistry, microbiology, pathology, community health, clinical skills, and other preclinical courses should have segments of their curricula or topics in specific lectures that present basic psychosomatic concepts. These presentations should be complimentary and designed to enhance student understanding. Behavioral science clinicians should have a role in teaching activities on inpatient wards, ambulatory care settings, and in conferences in all clinical rotations, including surgery and ob/gyn.

C. Pay Programmatic Attention to Medical Students' Personal and Professional Growth and Well-Being

D. Pay Attention to Educational Process

1. Written goals and objectives should be developed for each educational endeavor.
2. Development of high quality teaching materials
3. Development of standardized procedures for oral presentation, clinical evaluations and documentation that explicitly require gathering, integrating and using psychosocial data. These procedures would be required in all clinical rotations and teaching activities.
4. Faculty development to ensure consistency and quality of teaching
5. A comprehensive assessment that includes:
   a. Student evaluations of the teaching,
   b. Assessment of student knowledge and skills, using content examinations, structured faculty observations, and/or standardized patient exams
   c. Assessment of the impact of the curriculum on student attitudes toward psychosocial aspects of care, and on students' personal growth and well-being
   d. Assessment of the outcomes of such teaching on patient care.

E. Identifiy potential barriers to implementing this curricular reform and creating strategies for overcoming these barriers.

Adapted from: Novack DH: Realizing Engel's vision: psychosomatic medicine and the education of physician-healers. Psychosom Med 2003; 65:925–930

APPENDIX 2. Pointers for Teaching Psychosomatic Medicine to Students and Residents

Overall Goals of Teaching

1. Learners should be able to identify the biopsychosocial factors contributing to illness onset and maintenance. Trainees should be able to make multiaxial diagnoses of medical problems, similar to DSM-IV diagnoses (147).
2. Trainees should be able to suggest a combination of biological, cognitive, behavioral and social interventions that will contribute to relieving the current symptoms, address patients' concerns, enhance their understanding and adherence, and lead to behavioral changes that will prevent recurrences of illness.

Strategies

1. Join with preclinical teachers of physiology, and offer to teach in Introduction to Clinical Medicine courses, illustrating how basic psychosomatic concepts and research findings enhance understanding of clinical medicine.
2. Work with Internal Medicine and Family Medicine colleagues, and attend inpatient rounds at regular intervals. Demonstrate the value of integrating discussion of social, emotional, and behavioral issues into all discussions of patients' illnesses. On rounds, briefly interview random inpatients to illustrate how psychosocial factors are playing a role in the patient's illness. Gently point out the fallacy of dualistic thinking (i.e., when residents discuss a ''psychiatric overlay'' to a patient's illness).
3. Ask trainees to prepare for rounds by reading key psychosomatic literature. Ask trainees to summarize salient points of the articles and say how they will use the learning in their patient care.
4. During rounds, do brief role-plays of patients that illustrate approaches to diagnosing and understanding biopsychosocial interactions in illness, and how to approach these problems effectively. Allow ''tag team'' interviewing, getting comments and input from others in the group to advance the process.
5. When doing consults on medical patients, periodically invite the students and residents from the inpatient team. Ask them their understanding of the nature of the patient's illness, and how psychosomatic factors relate to illness presentation and maintenance. Guide them through a diagnostic interview. Ask trainees about why or why not they addressed or avoided certain topics. Often trainee misunderstandings, attitudes, and personal biases affect their communication with patients. These can be honestly and respectfully addressed within the team discussions.
6. Address common problems in communication in clinical care. Use checklists for evaluation and feedback of trainee skills.
7. Use effective teaching principles and strategies.
8. Inquire about trainee's well-being. Depression and other mental health problems are common in medical trainees and may diminish their effectiveness with patients. Identifying and addressing well-being issues can help team dynamics and patient care as well as the individual trainee.

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A more comprehensive list of references is available from the first author.

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