

American Handbook of Psychiatry

**CHANGING THEORETICAL
CONCEPTS IN
PSYCHOSOMATIC MEDICINE**

Morton F. Reiser

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CHANGING THEORETICAL CONCEPTS IN PSYCHOSOMATIC MEDICINE¹

Morton F. Reiser

Introduction

Ever since man first experienced a sense of self-awareness, he has been intrigued with the challenge of understanding the relationship of mind to body, and has worked diligently toward developing empirically based conceptual solutions to the mystifying problems it presents. To this day, the problem eludes solution. The early history of these efforts has been reviewed and this account will pick up the thread of the story toward the end of World War II when experiences in military psychiatry were generating considerable serious interest in dynamic psychiatry and in exploring the interrelationships between mind and body in the etiology and pathogenesis of physical as well as mental disorders. This chapter takes an historical perspective and is presented in three parts. It begins with a review of earlier theories and the empirical context from which they emerged. It emphasizes the important clinical psychiatric observations and attempts to define some of their limitations for theory, while underlining those aspects of earlier data and theory that seem still to be relevant and cogent. Part 2 reviews findings that

for the most part followed the main portion of earlier theory construction, though in fact the time periods overlap, Part 1 roughly covering 1940-1960 and Part 2, 1955-1972. The work of this second period immensely widened our data bases and added important new dimensions to available information about the interrelationship between physiological and psychological aspects of bodily function both in health and in disease. Accordingly, it forces reconsideration of earlier theoretical ideas and calls for drastically modified, if not entirely new, formulations. Part 3 begins with the conclusion that it is not possible at this time to construct a satisfactory and empirically sound general theory of etiology and pathogenesis. Rather, attempts are made in the last part of the chapter to extract a general conceptual scheme for approaching the problem of understanding man in health and disease. Throughout the chapter an effort is made to offer some suggestions as to possible shapes and directions for future work and theory construction, and, wherever possible, to bring older ideas into perspective in regard to present thinking.

Part 1: Earlier Theories

In the first part of the epoch bounded roughly by the years 1940-1960, work proceeded mainly along two lines. First there was combined medical and psychological investigation of selected medical patients. This work aimed at identification and elucidation of the role of psychological conflict (and emotional arousal) in etiology and pathogenesis of medical illness, and in influencing the course of disease, for example, as in inducing remissions or exacerbations or in affecting the rate of progression. Meticulous and detailed combined clinical studies by internists and psychiatrists (Weiss, Engel, Ferris, Wolff, Wolf, Grace, Mirsky, Romano, Levine, Rosenbaum, Saslow, Lidz, and Binger, to name just a few) demonstrated beyond a doubt that many medical diseases first became clinically manifest during periods of psychosocial crisis and that the course of disease can indeed be profoundly influenced by psychological factors. Complications were observed to occur in conjunction with serious psychological stress, disease processes were observed to accelerate during periods of sustained psychosocial turmoil, and remissions were observed in conjunction with periods of relative psychological tranquility. Further it became clear that the doctor-patient relationship by modulating and ameliorating psychological distress of patients could exert beneficial effects on the symptoms and progression of illness, and could at times augment desired pharmacologic effects of drugs (converse effects were

observable as well, albeit with some reluctance on the part of clinicians.) Relationships of this nature are regularly observed in hospitals and clinics when healthcare personnel are interested and when they have been trained to observe and to listen. The limited implications of such observed relationships for theories of etiology and pathogenesis will be discussed below.

The second major line of investigation was more experimental and involved the study of patients at first, and “healthy” subjects later, in the clinical psychophysiological laboratory. Although many variations were developed, the basic experimental design consisted of continuous, or repeated, measurements of (relevant) physiological functions during periods of “base line” or “rest” and during periods when attempts were made to manipulate the patient’s or subject’s emotional state by discussing conflictual topics and/or by exposing him to stimuli designed to elicit specific affects, e.g., anger, anxiety, etc. In this way virtually every tissue and organ of the body innervated by the autonomic nervous system and available for observation or intubation, or accessible to electronic recording from surface or depth electrodes in unanesthetized humans, was shown to be capable of considerable functional variability in reaction to a wide variety of provocative experimental manipulations. The ultimate goal of such experiments was to produce measurable functional changes experimentally in target organs that would mimic or reproduce pathological-physiological patterns of function

associated with specific disease states, e.g., gastric hyperacidity and hypermotility, tachycardia, elevated blood pressure, changes in measures of external respiratory dynamics, etc. In fact, it has been possible to demonstrate repeatedly that a wide variety of impressive physiological changes may be so induced but not with the degree of regularity, predictability, and experimental control required for rigorous support of specific etiologic and/or pathogenic hypotheses. As our experience and sophistication have increased, innumerable technical, methodological, and experimental variations on the basic theme have evolved, but a myriad of highly complex problems (control, instrumentation, data reduction, statistical evaluation, and interpretation) connected with such experiments remain, and their limitations for contributing to the solution of problems of etiology and pathogenesis are indeed still considerable.

The central theoretical issue of the epoch (1940-1960) was specificity. What determines whether a patient falls ill of one disease rather than another (why peptic ulcer instead of rheumatoid arthritis, for example)? More to the point in the context of psychosomatic medicine, do specific psychological factors constitute necessary and/or sufficient factors in determining choice of organ system and disease? Specificity in this sense refers to a different phenomenon from that observed in individual patients whereby a repetitive theme may be repeatedly activated at critical points in the history of the disease, making it a repetitive "core issue" for the particular patient, but not

generalizable to others. In retrospect it is clear that the clinical and laboratory findings of the period under discussion implicated both specific and nonspecific mechanisms, but more attention and interest was directed to the search for specificity.

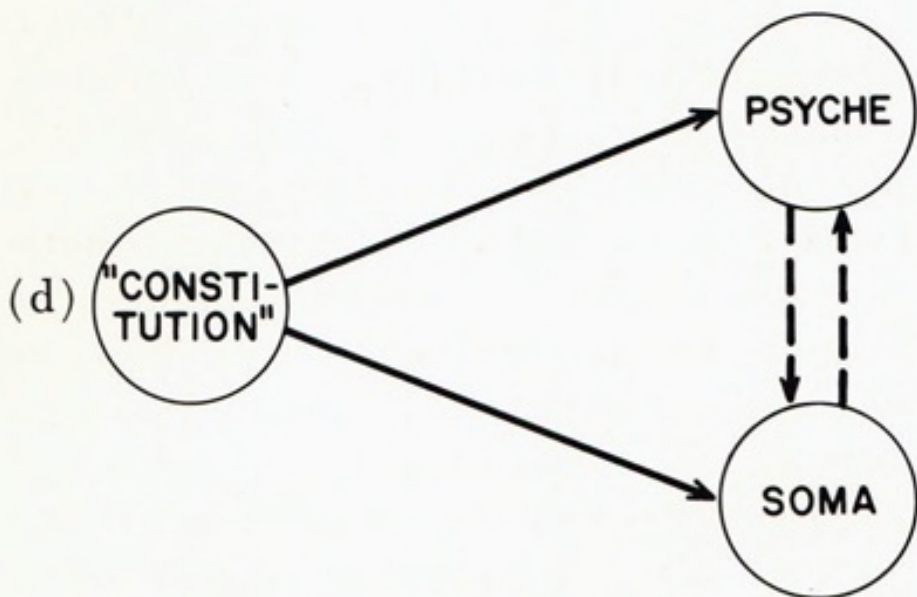
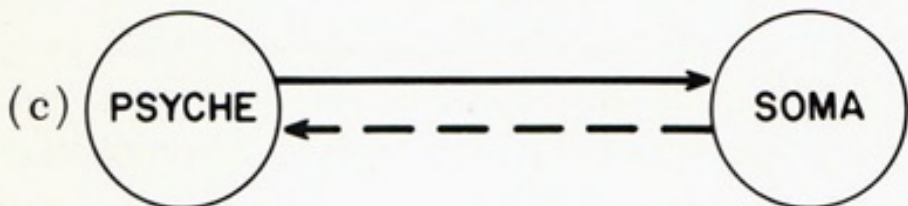
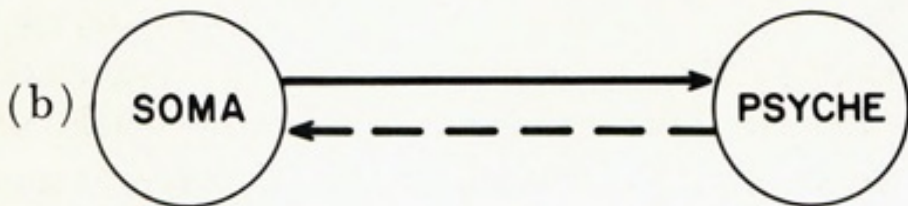
Before undertaking a review of the major theories that represented this point of view, it might be well to mention first some of the more general conceptual issues and problems that complicate the field and frustrate attempts to build and evaluate theory. Regardless of our ultimate conviction that mind and body constitute a true functional unity, the fact remains that as observers, investigators, and theorists, we are obliged (whether we like it or not) to deal with data from two separate realms, one pertaining to mind and the other to body. The science of the mind and the science of the body utilize different languages, different concepts (with differing levels of abstraction and complexity), and different sets of tools and techniques. Simultaneous and parallel psychological and physiological study of a patient in an intense anxiety state produces of necessity two separate and distinct sets of descriptive data, measurements, and formulations. There is no way to unify the two by translation into a common language, or by reference to a shared conceptual framework, nor are there as yet bridging concepts that could serve, as Bertalanffy suggests, as intermediate templates, isomorphic with both realms. For all practical purposes, then, we deal with mind and body as separate realms; virtually all of our psychophysiological and psychosomatic

data consist in essence of covariance data, demonstrating coincidence of events occurring in the two realms within specified time intervals at a frequency beyond chance. Such findings—our very best ones— tell us nothing in and of themselves about time sequences or causality as ordinarily understood in a linear sequential model. Confronted, then, by covariance findings of this nature, for example an association between a specified dysphoric affect or mood state and the development of a bodily lesion, such as a duodenal ulcer, there are essentially four conceptual schemes that can be evoked to relate the physical to the mental findings (see Figure 21-1). First we might say that there is no more than a coincidental relationship between the psychological and somatic spheres (Figure 21-1 (a)); in essence the duodenum represents a constitutional “weak link in the chain,” hence that part of the body is expected to break down in response to stress of any type. A second model would postulate a somatopsychic sequence stating that the dysphoric state represents a psychological response to the organic lesion (Figure 21-1 (b)). A third model would postulate a psychosomatic sequence stating that the physiological changes accompanying the dysphoric mood are pathogenic and, if sustained, lead to peptic ulceration of the duodenal mucosa (Figure 21-1 (c)). (Both of the preceding models would also allow for secondary reactive sequences in opposite directions, allowing for feedback from psyche to soma in the first instance, or soma to psyche in the second, thus explaining cyclic (escalating) feedback reactions such as pain, anxiety,

spasm, increased pain, etc.) Finally there is a fourth conceptual model which states that the coincident psychic and somatic phenomena in fact represent separate and parallel reflections of a common underlying constitutional factor(s) usually postulated to be related to genetic and early experiential factors (Figure 21-1 (d)). Such a model also allows for secondary reciprocal interplay between the psychic and somatic spheres, as in the preceding two schemes. In essence this is a somatopsychosomatic model.

Figure 21-1.

(a) NO RELATIONSHIP



Conceptual schemes for relating covariant physical and psychological findings in psychosomatic research. (For explanation see text.)

Another source of theoretical confusion can arise from overlooking the fact that there are at least three phases or epochs in the natural history of any disease. These are probably best considered separately when attempts are made to reconstruct pathogenesis. First is the period preceding manifest clinical appearance of the disease. During this period interest centers on predisposing causes, i.e., the various possible combinations of constitutional (genetic and experiential developmental) factors that may be thought of as programming a *capacity for a specific disease* into the organism. The second phase is that of the actual onset or precipitation. Here interest centers on the forces and mechanisms that precipitate the illness. These ordinarily need be in force only for relatively short periods of time, and need not be (and usually probably are not) the same as those involved in generating predispositions; of course the physiological mechanisms involved in different diseases must be quite different from one another. Third is the last epoch, i.e., the period following the establishment of the disease process. Here interest is on those factors and mechanisms influencing the course of the disease, such as remissions, exacerbations, accelerations, and so on, and these again may be expected to be different from those involved in the two preceding phases. For example, once a disease has become established and the individual has become aware of it, knowledge of the lesion and sensations related to it become incorporated into the self-image and are then subject to symbolic

elaboration and incorporation into preexistent conflictual psychological structures. In the somatic realm, as a disease progresses, the role and importance of a variety of influencing factors may change profoundly. For example, the potential of salt to aggravate or accelerate the course of long-standing established essential hypertension in a patient with considerable loss of renal reserve, is very much greater than it is in a patient much earlier in the course of essential hypertension whose renal reserve is still within normal limits. Likewise, in essential hypertension the relative and proportional contributions of neurogenic and humoral factors in maintaining increased peripheral resistance change with time. In duodenal ulcer scarring, pyloric sphincter hypertrophy, sclerosis of blood vessels, etc., all change markedly with time, and play increasingly important roles late in the course of the disease, whereas they may well have been negligible factors earlier in the course. The main point is that both the psychological and the physiological medical data differ in fundamental and important ways, depending upon the phase of the natural history of the disease that is under study, and it clearly may be misleading, and probably quite incorrect, to assume that analysis of the circumstances and mechanisms involved in precipitation of an illness, or in influencing its course (no matter how thoroughly studied and formulated), would necessarily bear any direct relevance for understanding the mechanisms that had been involved in establishing predisposition. A priori, one might very well expect that in

considering predisposing factors, disease-specific influences might very well overshadow nonspecific mechanisms in importance, whereas it is entirely plausible that mechanisms involved in precipitating the onset of disease, and in influencing the course of disease once established, might involve nonspecific mechanisms more importantly. These matters will be discussed further at the end of the chapter.

Turning now to a review of the major theories of the 1940s and 1950s, as noted above, the issue of specificity captured the imagination and attention of the major workers of that period. Generally speaking, the observations of experienced clinicians working at that time strongly suggested that it would indeed be both rational and worthwhile to search for specific elements in the personality structure and psychological life of patients that might participate in etiologic and pathogenic processes and contribute to the choice of symptoms and illness. Not only general clinical experience, but systematic profiles of personality (obtained either by structured interview, or projective and inventory-type psychological tests), led to the inescapable conclusion that patients with certain medical disorders, for example, duodenal ulcer, do in fact resemble one another psychologically more than they do members of the general patient population, or homogeneous groups of patients with other specified diseases. George Engel described the situation very aptly by stating that, if one tells an experienced clinician that he has a patient with ulcerative colitis, the clinician might very well give a surprisingly accurate thumbnail

personality sketch of that patient without ever having seen him. The converse, however, Engel is quick to point out, does not hold, that is, given even a detailed account of the patient's personality, it is by no means possible to predict with any degree of confidence what disease, if any, the patient might have. A major question, of course, is whether the psychological personality features, shared by patients with the same disease, may not be shared because they, in fact, arise in reaction to the disease and hence would be expected to be shared. A more subtle but nonetheless cogent question is whether such shared somatic-psychic features may arise in response to an implicit perception or awareness of vulnerability or predisposition even before the disease becomes clinically manifest. This question is posed in beginning the review of the early specificity theories, since it is of central importance in a discussion of linear sequential cause-effect models, as in fact all of these early theories are. It is now generally appreciated that this critical question is unanswerable in retrospective studies, and probably only partially answerable in most longitudinal prospective studies that are feasible of execution in clinical investigations with human subjects. As will be clear later, with respect to more recent field theories, such as currently obtain generally in human biology, this question is much less important, at least in this particular form.

One of the first and most detailed attempts to relate personality to specific illness was the "personality profile" proposed by Flanders Dunbar.

While its extensive clinical observations were quite accurate, its clinical and theoretical utility turned out to be very limited, and it is now generally regarded as having mainly historical interest and importance.

A second important theoretical framework emerged from the extensive research program headed by Harold Wolff and his collaborators. The full scope of his investigations can only be appreciated by consulting some of the major original publications such as *Human Gastric Function*, the classic study of a patient with a gastric fistula by Harold Wolff and Stewart Wolf. In essence Wolff postulated that stress diseases arise as part of the human physiological reaction to stress, i.e., “forces or individuals that jeopardize the life or love of a human being . . . which interfere with the realization of his aspirations and needs or block the exercise of his potential. These threats are reacted to by mobilization of an individual’s defenses.” [p. 1059] Thus, the bodily reactions were regarded as having been set in motion as adaptive, protective, or defensive or offensive responses, depending upon the subject’s nature, his past experience, and the situation. “They are more or less effective and more or less costly to the individual, depending on these and other factors, such as the nature and integrity of the structures participating in the protective reaction.” [p. 1060] Wolff and his co-workers postulated patterns of defensive reactions which, they felt, were specifically associated with defensive responses, in particular organ systems, and affecting specified functions such as eating, ejection-riddance, etc. The psychological formulations were based

upon personality features and behaviors that were directly observable with minimal or no inference, and that pertained primarily to conscious layers of the patient's personality function and life experiences. Further focus was on psychological observations that could be carried out simultaneously with detailed study and observation of the patient's clinical status, and with measurement of the function of affected organ systems in the physiological laboratory. Naturally, the formulations looked and sounded quite different from those of contemporary psychoanalytic investigators (as will be noted below) but in retrospect, it can be seen that the specificity formulations of Wolff and of Franz Alexander, in particular, are in fact quite compatible in regard to the central themes, though they differ considerably in respect to the level of mental functions emphasized, in the amount of inference involved in constructing theory from observation, and in the dynamic richness and scope of the formulations, as well as the ease with which such formulations could be apposed to (or fitted with) concurrent measures of clinical status and organ function. For example, the following statement by Harold Wolff regarding "protective patterns of defense involving eating: the stomach and the duodenum," can be compared to Alexander's formulations (quoted later) concerning the specific psychological contributions to disorders of the same organs. Wolff states:

One of the earliest aggressive patterns to manifest itself in the infant is that associated with hunger and eating. In later life, this pattern may reassert itself in certain individuals when they feel threatened; at such times of

danger, feelings of anger and deprivation, of longing for emotional support, or of need for being "cared for," may be repressed by the equally insistent assertion that the individual is strong, independent, capable of doing alone, or standing 'on his own feet,' either through actual deprivation of emotional support or an unwillingness to accept it. This feeling state shows itself in the stomach as one of readiness for eating; hypersalivation may also occur. The gastric hyperfunction associated with these feelings is manifested by increased blood flow, motility, and acid secretion. Under such circumstances the mucous membrane was found to be unusually fragile. The hyperdynamic state of the stomach was found to be associated with symptoms, namely heartburn and localized epigastric pain, relieved by food and soda whether or not ulceration was present, [p. 1064]

Later, two of Wolff's students, Grace and Graham, formulated a derivative hypothesis which they named "specificity of attitude" hypothesis. This hypothesis states that there is associated with each psychosomatic disease a specific attitude toward the life events that precipitate the first appearance or later exacerbations of the disease. Attitude was defined as: "(1) How a person perceives his own position in a situation—what he feels is happening to him, and (2) What action, if any, he wishes to take." [p. 159] It was postulated that attitudes are different for different diseases but that all persons with a given disease would have the same attitude. For comparison with the Wolff and Alexander formulations, the attitude leading to duodenal ulcer was described by Graham as "felt deprived of what was due him and wanted to get even (didn't get what he should, what was owed or promised, and wanted to get back at, get revenge, do to him what he did to me)." Thus, Graham and his co-workers extracted from a broader formulation a distilled

statement about attitude which then could be tested quite explicitly by a variety of techniques, including induction of attitudes under hypnosis, while measuring appropriate bodily system responses, as well as by postdiction from interview material by blind raters— postdiction which would match patients with diseases by detecting evidences of “specific attitudes” in the interview material.

Franz Alexander and his associates in 1932 began a series of psychoanalytic studies of patients suffering from chronic organic ailments in which emotional conflicts were thought possibly to play an etiologic role either as primary or contributing factors. Alexander’s studies utilized mainly the investigative method of psychoanalysis and proceeded on the basis of a fundamental distinction between “visceral neurosis” and conversion hysteria which he first articulated in 1939. Freud, in his studies on hysteria with Breuer in 1895, had demonstrated that specific unconscious contents could be symbolically expressed in the body language of somatic symptoms through the mechanism of conversion. In 1910, Freud also noted that there could be mechanisms other than conversion whereby unconscious attitudes might alter physiological functions without symbolizing any definite psychic meaning, but did not further specify their possible nature. Alexander formalized the distinction between hysteria and the “visceral neuroses,” a term he used in referring to those disorders which were identified with the field of psychosomatic medicine. He pointed out that whereas in conversion

hysteria symptom formation acts to resolve unconscious conflict, in the visceral neuroses, the basic conflict remains unresolved; he postulated that the chronic affect associated with unresolved conflict, even though repressed or suppressed, would nonetheless be accompanied by its (appropriate) physiologic concomitants. Alexander theorized that the physiological changes accompanying the chronic emotions associated with unresolved conflict were the physiological changes then that would give rise, first to altered function in the appropriate organ systems and, if long enough sustained, to alterations in structure and disease. Thus, for each of the seven diseases that he and his colleagues studied, a formulation of specific conflict was derived from the clinical data produced in the course of psychoanalytic treatment and/or investigation. For comparison with the preceding formulations, Alexander's formulation regarding duodenal ulcer is quoted below:

The central dynamic feature in duodenal peptic ulcers is the frustration of dependent desires originally oral in character. The craving to be fed appears later as a wish to be loved, to be given support, money, and advice. This fixation on early dependent situations of infancy comes in conflict with the adult ego and results in hurt pride, since the infantile craving for help is contrary to the standards of the adult, to his wish for independence and self-assertion. Because of this conflict, the oral craving must be repressed. Oral receptiveness when frustrated often changes into oral aggressiveness, and this also becomes repressed because of guilt feelings it provokes. Both oral dependent and oral aggressive impulses may then be frustrated by internal factors—shame and guilt.

The most common defense against both oral dependent and oral acquisitive impulses is overcompensation. The latently dependent or acquisitive person overtly appears as an independent, hard-working

individual who likes responsibility and taking care of others. He responds to challenges with increased activity and ambition, works hard and assumes greater and greater responsibilities. This in turn increases his secret longing to lean on others. To be loved, to be helped is associated from the beginning of life with the wish to be fed. When this help-seeking attitude is denied its normal expression in a give-and-take relationship with others, a psychological regression takes place to the original form of a wish to ingest food. *This regressive desire seems to be specifically correlated with increased gastric secretion.* (Italics mine.)

Not all patients suffering from duodenal ulcer overcompensate for their dependent desires with an outward show of 'go-getting' activity. Many of them are overtly dependent, demanding, or disgruntled persons. In such individuals, the dependent tendencies are frustrated not by internal repudiation, but by external circumstances. But even in these overtly demanding patients, a definite conflict about dependent cravings can be discovered. The crucial psychological finding in all ulcer patients is the frustration (external or internal) of passive, dependent, and love-demanding desires that cannot be gratified in normal relationships.

Onset of illness occurs when the intensity of the patient's unsatisfied dependent cravings increases either because of external deprivation or because the patient defends against his cravings by assuming increased responsibilities. The external deprivation often consists in the loss of a person upon whom the patient has been dependent, in leaving home, or in losing money or a position that had given the patient a sense of security. The increased responsibility may take the form of marriage or the birth of a child or the assumption of a more responsible job. [pp. 15-16]

The other six diseases studied by the Chicago psychoanalytic group of Alexander, were bronchial asthma, rheumatoid arthritis, ulcerative colitis, essential hypertension, neurodermatitis, and thyrotoxicosis. For each specific psychodynamic constellation, there was postulated also a specific related "onset situation" i.e., the life conditions preceding illness that affected

patients emotionally at the time of onset (by reactivating old conflicts); and a third factor which Alexander designated an X factor by which he meant a constitutional vulnerability of a specific tissue, organ, or system. This then was a multiple factor model in which each of the three factors was considered a necessary but not sufficient cause, with the development of manifest disease depending upon presence and activation of all three in appropriate combination. In Alexander's words, the operational hypothesis of this work could be reduced as follows: "A patient with vulnerability of a specific organ or somatic system and a characteristic psychodynamic constellation develops the corresponding disease when the turn of events in his life is suited to mobilize his earlier established central conflict and break down his primary defenses against it. In other words, if the precipitating external situation never occurs, a patient may, in spite of the presence of the predisposing emotional patterns and of organ vulnerability, never develop the disease." [p. 77]

This then was a linear psychosomatic theory (Figure 21-1 (c)). A central feature to note is the postulation that the pathogenic physiological changes involved were conceived of as physiological concomitants of emotion, such as are encountered in mature adult organisms and patterned on the fight-flight physiology of Cannon, namely sympatho-adrenal and/or parasympathetic activation. For example, essential hypertension was seen as resulting from chronically suppressed and repressed rage with concomitant sympatho-

adrenal activation and elevation of blood pressure, such as might be seen in acute rage attacks; gastric hypermotility and hypersecretion of acid were seen as the physiological concomitants of vagal stimulation accompanying repressed and suppressed longing for love (equated with longing to be fed). These psychophysiological characteristics of the theory appear as well in the formulations of Harold Wolff and his co-workers.

In retrospect, these early specificity formulations appear rather narrow and oversimplified; to a large degree this may be the result of preoccupation with what we now realize to be a relatively narrow and limited sector of the field. While giving little more than lip service to multiple-factor concepts, these early writers limited their attention to predominantly intrapsychic issues and proximate interpersonal transactions in the psychological realm, and to peripheral autonomic effector mechanisms and end-organ systems in the physiological realm, while relatively little attention was paid to external social systems, to central nervous system mechanisms, or to cellular and molecular biological phenomena. In other words, the formulations may have been premature in the sense that they will have turned out to be incomplete and overinclusive rather than intrinsically incorrect.

Other psychoanalytic investigators of the same time period, particularly Grinker, Schur, and Deutsch, were impressed not only with the ubiquity in “psychosomatic” patients of core conflicts around pregenital issues (as

Alexander had been) but also with the extensive and impressive evidence of regression and primitivization of ego functions in these patients, particularly at the time of the life crises associated with precipitation and/or aggravation of the disease and during periods of prolonged active illness. Impressed by the resemblance of pathological physiological function in “visceral neurosis” to the labile relatively unmodulated patterning of physiological responses in infancy and very early childhood, they speculated about its possible significance. Their (essentially epigenetic developmental) theories regard the pathological physiology of psychosomatic diseases as being patterned according to the physiology of infancy and early childhood and postulate the physiological anlagen (X factors) to be constitutional (genetic and early experiential), possibly or probably fixed or programmed into the organism by coincidence (conditioning), and later reinforced in the mother-infant and child-family interactive relationships during development. Two of the investigators of that era, Margolin and Szasz, also were impressed with the primitive “regressive” nature of the physiology, and Szasz spoke of “regressive innervation.” These theories stand in sharp contrast to Alexander’s theory in two ways: (1) they utilize transactional field rather than linear models, and (2) they postulate the physiological components to be more primitive and less well regulated than the adult patterns evoked in Alexander’s theory. Grinker postulated an infinite series of progressive stages of differentiation of body systems from psychosomatic unity at birth to the

highly complex differentiated and integrated adult organism. He saw a breakdown in adaptation involving progressive dedifferentiation of varying degrees regressively back through stages of psychosis and various psychosomatic disorders all the way to primitive disorganized and overwhelming panic states (roughly equivalent to the neonatal conditions of total response). Schur conceptualized the progressive maturation from infantile "psychosomatic unity" as occurring in two spheres: (1) progressive desomatization of reactions to danger in the physiological sphere (a gradual refinement from general chaotic uncontrolled total-body responses to the finely modulated, discrete and homeostatically balanced responses of the adult, such as "signal anxiety"), and (2) progressive refinement from primary process thinking to secondary process-controlled thinking (mediated and modulated by small discrete quantities of "delibidinized and deaggressivized" energy) in the psychologic sphere. He emphasized that the ego reacts simultaneously to danger in two ways: evaluating danger and responding to danger. If failure of defensive ego functions under stress and reactivation of unconscious conflict occur, he postulates that danger signals are increasingly evaluated along progressively more (primitive symbolic) primary-process modes and also that there is a concomitant (but not necessarily entirely synchronous) "resomatization" of the response. As the resomatization proceeds to primitive levels, old infantile patterns of bodily response can be reactivated and result finally in disease (the specific organs and processes

involved having been predetermined by constitutional factors). He considered that alterations in “ego state” in reaction to stress were of utmost importance in permitting and/or promoting emergence of primitive pathophysiological patterns of function that could then lead to disease. Deutsch also emphasized return to infantile, or primitive developmental points of physiological “fixation” and was, at the same time, quite impressed with the primitive body language (symbolism) encountered in psychosomatic patients and included important elements of pregenital conversion as well as conditioning and genetic endowment in his thinking about specificity of organ and symptom choice. Needless to say, none of these theoretical systems is amenable to empirical testing (given the present “state of the art”) but they do bear an interesting conceptual compatibility with many of the newer biological findings to be reviewed later.

A few psychoanalytic clinical investigators, such as Garma and Sperling have continued the conceptual tradition begun with Groddeck that considers psychosomatic visceral disorders to arise mainly on the basis of symbolic conversion mechanisms. The observations and rich clinical data about symbolic significance of bodily symptoms and changes are not in question; they are prominent in the data whenever clinicians work at psychological depth with medical patients. But these theories regarding pathogenesis are neither empirically testable at present, nor are they readily reconciled conceptually with recent developments in the biology of disease, nor as noted

earlier is it possible in a retrospective historical study to distinguish whether such psychological meanings occur as reactions to the presence and knowledge of illness or whether they antedated illness and may have contributed to its genesis.

The work and the theories of several investigators of this epoch have been reviewed in considerable detail not only because they are considered to be important and representative (and responsible for stimulating a highly productive era of psychophysiological research); but also because many of the main ideas contained in them should ultimately be brought into proper perspective and reconciled with more recent findings and theoretical models. This period produced an enormously rich yield of carefully detailed and documented observations, and of derivative formulations. Many of the *clinical observations themselves* have been confirmed and replicated many times over and by this time have been incorporated into the general body of information about clinical medicine. Many of the psychodynamic formulations, particularly Alexander's work, have been supported as valid *psychological* findings and formulations by other investigators (Mirsky, Weiner, Dongier, Wittkower et al., Wallerstein et al., see below). On the other hand, original *psychosomatic* formulations regarding the direct role of specific psychodynamic factors in etiology and pathogenesis of disease have not fared as well in attempts to validate them in careful and often highly sophisticated and elaborate clinical research. Yet at the same time there has been enough

partial empirical support to preclude their being summarily dismissed. It seems certain that future theories will have to account for the observations, and it is also likely that the general shape of the major hypotheses may still be discernible in future formulations albeit with different emphases and perspectives, when information from broader data bases and newer systems and transactional theoretical models are taken into account.

Part 2: Modern Developments, 1955-1972

As noted earlier, the work of the first part of the epoch 1940-1960 concentrated mainly on intrapsychic mechanisms, peripheral autonomic and humoral mechanisms in control of target organs and organ systems, and phenomena that seem to bear directly on the issue of specificity, with less attention being paid to broader interpersonal and social ecological factors, to the role of the *central nervous system* (CNS) in mediating between cognitive emotional and peripheral neurovegetative effector mechanisms, to cellular and molecular biologic processes, and to mechanisms of genetic transmission. And there were relatively few studies concerned with dissecting mechanisms and relative contributions of genetic transmission, neonatal, early infant, and child development in determining “constitutional” predisposition, and with the role of nonspecific bodily responses in medical pathogenesis. All of this has changed radically with the tremendous expansion of information that has occurred in the human life sciences and neurobiology since the mid 1950s. Technical breakthroughs in electronics and instrumentation, along with the rapid development of computer science, have now made it possible to investigate biological processes that previously had been inaccessible to experimental analysis, and to obtain answers to questions that were previously out of reach. Currently there is a much fuller appreciation of the

fact that understanding states of health and disease requires understanding of biological, psychological, and social parameters to be complete. More investigators and theoreticians are appreciative of the obligation to address the complexity of interacting factors and mechanisms in these three spheres as they contribute to the development of an actual phenotype from a genotypic blueprint. This broadened understanding has made it clearer than ever that mind and body cannot be regarded, or dealt with, as separate much longer despite our bondage to Cartesian dualism. Corollary to this is the recognition that subclassification or distinction of psychosomatic from other disorders is rapidly losing (perhaps has already lost) its meaning and utility. The next section will review selected sectors of clinical and related neurobiological research that have contributed to newer perspectives in the field. It is not intended to be a fully comprehensive review, but rather to concentrate on selected fields of study and data that have had major impact on our perspectives regarding relations between mind, brain, and body. Important new work and perspectives in the social, epidemiologic, and transcultural aspects is not included here. For this the reader is referred to Chapter 25.

Longitudinal “Predictive” Studies of Persons at Risk

This section deals with studies of predisposing (physical and psychological) factors and of precipitating (psychosocial) factors in

longitudinal studies of populations identified as being at risk for a particular disease by virtue of possessing known biological markers. The best known of such studies are those of Mirsky and co-workers on duodenal ulcer which further refined the Alexander concept. Mirsky identified the physiological (genetically-determined) condition necessary, but not sufficient, for the development of duodenal ulcer; that is, the hypersecretion of pepsinogen into the blood. He postulated that this inborn trait, through its influence on the mother-infant relationship, would also play a central role in personality development and in determining the type of social-conflict situation that would later be pathogenic for the individual in adult life. This, then, is a circular rather than linear theory, i.e., it suggests somatopsychosomatic sequences rather than linear psychosomatic ones. It is supported by empirical data gathered in a study on duodenal ulcer by Weiner, Thaler, Reiser, and Mirsky in which independently studied psychological data were used to predict (using Alexander's formulations of core conflict specific for peptic-ulcer) which, of a large number of potential ulcer patients (as determined by pepsinogen level), would actually develop the disease under the psychosocial stress of basic military training. These data, as noted earlier, lend validity to the psychodynamic formulations that Alexander and his colleagues derived from psychoanalytic studies of patients with duodenal ulcer. At the same time it should be emphasized that these studies by Mirsky et al. do not address the question of what the physiological mechanisms may be that lead to actual

ulcer formation in the duodenum, and thus do not bear directly at all on the psychophysiological psychosomatic hypotheses advanced by Alexander et al. Similarly, partial support of Alexander's psychodynamic formulations about thyrotoxicosis is provided by the work of Dongier and Wittkower, and of Wallerstein et al., which demonstrates an association in euthyroid subjects between a high propensity of the thyroid to incorporate I and the psychological personality characteristics described by Alexander et al. in patients with thyrotoxicosis. The relationship, if any, of this physiological trait and thyroid disease is not clear, and as Weiner has pointed out, the psychological traits may be linked with a tendency toward involvement of the thyroid gland in diseases affecting its secretory function (in either an upward or a downward direction).

In an unfinished statement written shortly before his death, Alexander took into account the findings of Mirsky and others on these newer demonstrated interrelationships of biological, psychological, and social factors in etiology and pathogenesis and indicated some readiness to modify his theoretical model:

These three variables—inherited or early acquired organ or system vulnerability, psychological patterns of conflict and defense formed in early life, and the precipitating life situations—are not necessarily independent factors. It is possible that constitution at least partially determines both the organ vulnerability and the characteristic psychological patterns. At present little is known about the interdependence of these two variables. There is strong indication,

however, that the correlation between constitution and characteristic psychiatric patterns is not a simple one. Constitution alone without certain emotional experiences of early life, particularly the early mother-child relation, may not produce a consistent pattern. [P. 17]

The power of such risk studies (which are possible only when biological “anlagen” such as pepsinogen are known) can be further amplified when applied to studies of *discordant disease incidence in monozygotic and dizygotic twins*. Katz and Weiner point out that risk strategy could be applied in gout (utilizing hyperuricemia to identify subjects at risk); it might also be applicable for the study of rheumatoid arthritis, utilizing certain immune proteins as indicators of risk. Another appropriate application might be in coronary artery disease where there are multiple factors (such as obesity, cigarette smoking, exercise habits, heredity, hypertension, blood lipids, etc.) that are known to affect the risk of myocardial infarction in additive and combined ways (see Chapter 26). In longitudinal risk studies of coronary disease, it would seem worthwhile to study in detail both the nature of the precipitating circumstances, and the psychological personality characteristics of subjects. Such data might then be useful in helping to clarify: (1) the relative roles of specific vs. nonspecific ubiquitous psychosocial stress situations (like bereavement, see below) in precipitation of myocardial infarction; and (2) the relation of “predisposing” psychological characteristics, such as the Type A personality of Friedman and Rosenman, to incidence of myocardial infarction. Does “Type A personality” lead to disease

by making the person's life stressful, or is it rather a parallel psychological manifestation of an underlying predisposing constitutional factor that also leads to coronary artery disease? (Figure 21-1 (d).)

Mortality and Morbidity of Bereavement

Studies on the mortality and morbidity of bereavement exemplify the emergence of data emphasizing *the importance of nonspecific effects of psychosocial stress on physical health*. Rees and Lutkins reported in 1967 on the study of a small community in Wales in which a cohort of 903 close relatives of patients who had recently died were identified as experimental subjects. A group of 878 control subjects from the same community matched for age, sex, and marital status were also identified. The health of the experimental and control subjects was followed for one year following death of the relative or selection as a control subject. During the year of bereavement the death rate in the bereaved subjects was *seven times* that of the controls! A related, and perhaps even more impressive finding was that the risk of death was twice as high if the relatives had died outside the home (including in the hospital) than when they had died in the home. A study of widowers in Britain by Parkes, Benjamin and Fitzgerald yielded similar results and showed that the majority of deaths in the first six months of widowhood could be accounted for by coronary artery disease in subjects of the appropriate age group. A controlled study by Bennet following the

Bristol flood (July 1968) in Britain demonstrated in the twelve months following the flood an increase in morbidity and a 50 percent increase in mortality in subjects whose homes had been flooded compared to those whose homes had not been so affected! The earlier findings of Engel and Schmale, demonstrating the high frequency with which real, threatened, or symbolic object loss and separation precede development of illness of any type, are quite consistent with the findings of these British investigators. Taken altogether, the data convincingly demonstrate that bereavement, object loss, and the associated reactive affective states may have profound reverberations in the physical sphere, affecting even the capacity to sustain life itself. The affective and psychological characteristics of these states span a wide spectrum: natural bereavement, aggravated or serious bereavement, depression of various types, and include states that Engel and Schmale feel deserve special designation as "helplessness and hopelessness" associated with attitudes of "giving up" and "given up." Engel postulates that there may be a fundamental biological stress or danger response state in addition to "fight-flight" which he has named "conservation withdrawal." He points out that the metabolic changes associated with such a response would be anabolic, as opposed to the catabolic activation responses of the "fight or flight" reaction described by Cannon, which was used as the exclusive physiological referent for earlier psychosomatic theories. Engel considers that the physiological changes he postulates to occur in "conservation

withdrawal” would act in an entirely nonspecific manner by rendering the organism less resistive to *a variety* of pathogenic factors. While the physiology of conservation withdrawal as such has not been documented, there is much evidence that psychoendocrine phenomena may well play an important role in clinical events of this kind (see below).

Psychoneuroendocrinology

Psychoneuroendocrinology constitutes the third major section for discussion here. This field of study serves as a major link between clinical and basic research endeavors. While its main relevance pertains to nonspecific mechanisms in pathogenesis and precipitation of a wide variety of illnesses, it may also have some interesting and provocative indirect implications for the issue of specificity as well. Studies in the psychoneuroendocrine sector probably more than any other single sector have (1) contributed to our growing recognition of the overwhelming importance of nonspecific mechanisms in development of disease; and (2) provided a beginning of vitally important insights into the fascinating and intricate (still incompletely understood) mechanisms by which the CNS is able to mediate between higher mental functions (and psychological responses to psychosocial events) on one hand, and maintenance of metabolic processes and integrity in body tissues and systems on the other hand. It has, in fact, provided us with an overwhelming sense (incomplete in fine detail) of the highly complex

integrated linkages between the limbic forebrain system and (1) the autonomic nervous system (which extends outward to innervate peripheral tissue); and (2) the pituitary (via the hypothalamus) and through it, the entire endocrine system, thus making it possible for the hormones to act as circulating extensions of the nervous system. These relationships and linkages are summarized and discussed fully in Chapters 22, 23, and 24 by Weiner, Hofer, and Mason, respectively. The discussion here will highlight only some issues that are of interest in the context of this particular chapter.

First is the fact that alterations in endocrine function occurring in experimental animals in response to psychosocial stresses have been shown to influence host resistance to a variety of pathogenic organisms and to affect the viability and rate of growth of implanted neoplastic tissue. In this connection it should be noted that there is also considerable evidence that central neurophysiological mechanisms may participate more directly in these psychosocial stress effects on host resistance by influencing immunological reactions, including tissue sensitivity to histamine and levels of circulating antibodies (see Chapter 29 by Schiavi and Stein). It appears then that the hormones, separately and in combination as described by Mason (see Chapter 21), may play a role not only in stress and hormone-dependent diseases, but also in infectious and neoplastic processes as well.

A second important feature is the phenomenon of *reciprocity between*

the effectiveness of ego defenses and the level of activation of stress hormone systems (mainly the sympathoadrenal system and the pituitary-adrenal axis). This was first demonstrated in man in a classic study by Sachar et al. in patients with acute schizophrenic excitement. Subsequently it has been shown to operate in a wide variety of both acute *and* chronic conditions (as noted in several of the chapters that follow). The demonstration of this phenomenon has proved to be of fundamental theoretical significance and brings us a giant step closer to understanding the way in which *intrapsychic phenomena may be interposed between psychosocial vectors on the one hand and alterations in body physiology on the other*. Ego defenses may protect against excessively brisk endocrine activation by functioning effectively; conversely vigorous endocrine activation may take place when ego-defense functions in the psychological sphere are inefficient or totally inadequate. The clinical significance of these findings is further enhanced when it is realized that the pathogenic effects of the adrenal steroids may be mediated not only by their influence on peripheral tissue metabolism, but also in less obvious but nonetheless highly important ways by *their effects on CNS function* (to be discussed below).

Third, the endocrine system, like the autonomic nervous system, shows evidence of a waxing and waning of its level of activity in association with regular biologic rhythms— principally the circadian diurnal rhythms, but also longer seasonal rhythms, the menstrual ovulation cycle in females, and

certain ultradian rhythms such as the 90-min. REM cycle in sleep. Ordinarily these multiple rhythms, each with different periods, are considered to be in some way synchronized or accommodated to each other. Curtis has reminded us that the potential for psychopathological and pathophysiological effects, when desynchronization between these multiple biologic rhythms takes place, is just beginning to be appreciated and studied. A number of investigators, including Sachar, Roffwarg, Heilman, and their associates, have demonstrated important differences in patterns of endocrine function during different stages of sleep. They have also shown that there are alterations in these patterned relationships in patients in active episodes of psychotic depression. Of related interest are the observations described in this volume by Hofer (Chapter 23), and by Williams and Karacan (Chapter 35), to the effect that autonomic-nervous-system function varies dramatically in different stages of sleep, e.g., the marked increase in variability of some autonomic functions during REM periods has led to considerable interest in possible pathogenic effects, e.g., in certain cardiovascular conditions such as coronary insufficiency with nocturnal angina. Friedman and Fisher and Kripke have adduced evidence that an ultradian ninety-minute rhythm persists throughout a twenty-four-hour period and is not just confined to sleep although its (behavioral) manifestations are different during waking hours. The fact that these sleep and related waking ninety-minute rhythms are, or may be, linked with fluctuations in levels of consciousness (and

possibly with changes in patterns of homostatic physiologic regulation) is especially provocative when recalling Schur's formulations regarding the significance for medical pathogenesis of "altered ego states"—a psychological term that refers at least partially to altered states of consciousness. It should be recalled also that Breuer and Freud, in their original "Studies on Hysteria," postulated an altered "hypnoidal state" of consciousness as providing the biologic substrate for actual symptom formation.

This sector of work has been (and bears promise of continuing to be) an especially fruitful area for collaboration between psychiatric clinicians and clinical physiologists. Stressful periods of life provide opportunities for *intensive parallel and simultaneous application of depth psychological techniques with neuroendocrine techniques*, and for attempts to arrive at integrated formulations concerning the biological significance of the changes observed. The psychoanalytic technique is particularly well suited for elucidating critical and important details of the psychological aspects, since it provides opportunity for repetitive finely detailed studies at those very times when major changes in balance of intrapsychic forces and in levels of consciousness and ego state are occurring. Since earlier theories, for the most part, took physiological "mechanisms" for granted, it would be desirable to conduct new studies now (such as those carried out by Knapp et al.) in which psychological observations are made in conjunction with observations of these complex biological mechanisms. This will be required before

empirically sound improvements can be made in the realm of theory.

Finally it should be noted that Henry, Axelrod, and collaborators have demonstrated increases in adrenal weight and marked increases in adrenal tissue content of the biosynthetic enzymes of norepinephrine in response to an intense psychosocial stress in mice (the same stress that simultaneously leads to development of sustained hypertension and renal pathology in the experimental animals). The enzymes involved in synthesis and metabolism of catecholamines in the CNS have also been shown to be influenced by the hormones of the adrenal cortex (see Weiner, Chapter 22), and it even seems possible that psychoneuroendocrine stress responses may in some way be involved in CNS regulation of biogenic amine metabolism, and thus participate in development of those major affective disorders that are considered possibly *to reflect disturbances in biogenic amine systems*.

Autonomic Conditioning

The fourth section, instrumental conditioning of autonomic responses, is reviewed in Hofer's chapter on the autonomic nervous system. These studies, pioneered by DiCara and Miller and associates, hold major and fundamental significance in regard to etiology and pathogenesis of medical illness. Older specificity theories evoking early life "conditioning" as a factor in constitutional predisposition were limited in the scope of possible visceral

changes that could be conditioned to those that could be evoked by an unconditioned stimulus as long as the Pavlovian paradigm of classical conditioning was considered the only form applicable to the autonomic nervous system. The demonstration that instrumental conditioning of the autonomic nervous system can occur means that virtually any change in the functional repertoire of the viscera bears the potential for “shaping” and augmentation by instrumental learning. Hofer discusses how this might operate during development, to influence later predisposition to disease. These findings also make it evident that there are, in fact, important functioning afferent pathways to the brain from autonomically innervated structures, and that feedback effects on the brain from the viscera via the autonomic nervous system pathways are far more important than was previously thought. Study of these pathways and mechanisms should clarify and elucidate many of the previously somewhat mysterious somatopsychic effects encountered in clinical medicine, and, as Hofer points out, may have far-reaching fundamental implications for understanding the interrelationships of the CNS and the autonomic-nervous-system function in integrating behavior and bodily function.

Developmental Psychophysiology

A fifth section deals with research in developmental psychophysiology, which is of course highly cogent to the questions regarding the role that early-

life experiences may play, along with conditioning and genetic endowment, in determining “constitution.” The most important findings in this field derive from experimental studies on laboratory animals that reach maturity in a short period of time, thus permitting later adult effects of early-life experimental behavioral manipulations to be observed within convenient time periods. For example, Levine and collaborators have developed extensive data on the effects of subtle early manipulations such as “handling” on important parameters of adult behavioral (e.g., excitability) and physiological responses to novel stimulation and stress (responsiveness of the pituitary adrenal system). Levine has also studied long term behavioral influences of sex hormones administered during critical periods of infantile development, elucidating some important developmental aspects of hormonal effects on complex adult patterns of sexual and aggressive behavior. Ader and Friedman, in extensive programmatic studies, have developed several animal models of disease susceptibility in which experimental manipulation of infantile experience (such as solitary vs. crowded conditions of raising) has been shown to influence subsequent adult susceptibility or resistance to a number of pathogenic challenges, including various pathogenic microorganisms and viruses, as well as a number of behavioral manipulations known to be stressful. Their data clearly demonstrate marked effects on “host resistance” in both directions—augmentation or decrease of resistance depending upon the nature of the

early life experimental manipulations, and upon the pathogens and/or stresses employed. Hofer and collaborators have studied maturation of physiological mechanisms regulating heart rate and rhythm in rats, and have demonstrated asynchrony of maturation of sympathetic and vagal systems, and have identified developmental epochs of possible significance as “critical periods” (perhaps even as anlagen of adult pathological response patterns, such as the fatal bradycardia known to occur in certain adult rodents under threat of severe attack). By combining longitudinal developmental studies with techniques of selective breeding, the distinct possibility exists for elucidating the interaction of genetic and experiential factors in determining predispositions or specific susceptibilities of organ systems to specified types of disorders, and even to differential responsiveness to specific pharmacologic agents as Corson has shown in hyperkinetic dogs. A highly important aspect of the work of Henry et al., mentioned above, consists of the fact that it clearly demonstrates the influence of differential conditions of early rearing and experience upon later susceptibility to developing hypertension and associated adrenal changes in mice exposed to the psychosocial stress he employs. This work is truly noteworthy in that it addresses the entire span of the biological, psychological and social aspects of the experimental disease model; it provides important details of the social stress employed, of behavior, of pathological physiology, of organ pathology, of changes in endocrine and metabolic enzyme systems, and of early

developmental parameters as well!

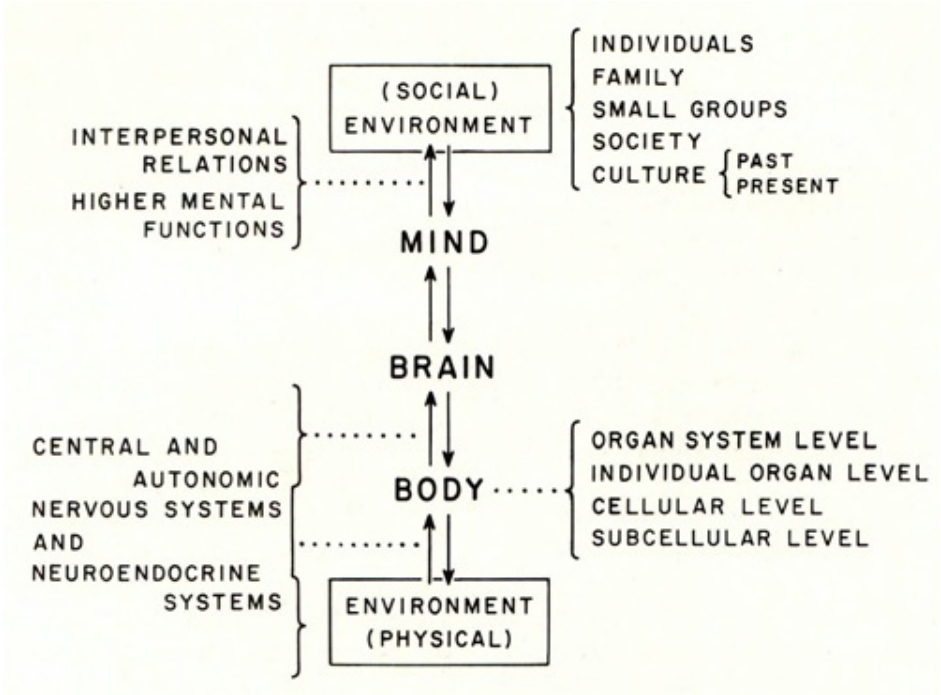
In summary, psychosomatic research has gradually evolved from early case and clinical psychophysiological experiments, to include extensive basic and clinical research that addresses issues ranging from discrete cellular functions at one extreme to transcultural comparisons at the other. Whereas the earliest contributions came mainly from medical psychiatric and psychoanalytic clinicians and from experimental psychophysiologicals, an extremely wide range of neurobiological and behavioral scientists are now actively engaged in work related to the field of medicine. A great deal of research is increasingly directed to a study of the mechanisms whereby the brain subserves, regulates and coordinates higher mental and social functions on the one hand, and widespread physiological functions throughout the body on the other. These have become possible because of the technical and methodological breakthroughs that have occurred in the life sciences, in neurophysiology, in endocrinology, in computer science, and in the social and behavioral sciences as well.

Part 3: Toward a Theory

Considering the findings reviewed in the preceding section, it seems reasonable to think of man as existing in a “bio-psycho-social” field as illustrated in Figure 21-2. This depicts an open transactional system that allows uninterrupted bidirectional flow of information and energy transactions extending from the deepest and most minute recesses of the body (intracellular metabolic processes) to the social field, encompassing cultural forces, even historical forces that contributed to shaping the culture. In the center is the brain which both subserves mental functions and influences (and is influenced by) body function. On the one hand, the higher mental functions, which include mechanisms for regulating interpersonal relations, mediate the individual’s transactions with his social environment including family, social groups, and society at large. On the other hand, the brain also in some fashion (mysteriously) “transduces” nonphysical immaterial aspects of the social field (that is, symbolic meanings) into physical-physiological events within the CNS, and these in turn initiate physiological changes throughout the body. At the same time brain function itself is, in turn, influenced by physiological changes occurring in the periphery of the body. These two-way interchanges of information and energy between the central nervous system (brain) and the periphery (body) are negotiated by the central and autonomic nervous systems and the

neuroendocrine systems. This transactional continuity extending from subcellular metabolic processes throughout the body via the brain to the social environment makes it understandable that major life experiences, such as bereavement, can influence even the capacity to sustain the life process itself. A *unique* feature, not explicitly depicted in the diagram, is that the brain, which occupies this interface position between mind and body, *is at the same time itself an organ of the body*, subject to influence by the very same alterations in the body's internal environment that it, in fact, helps to generate. Viewed in this way, the brain can be thought of as a possible "target organ" in sustained and profound stressful reactions. It may not be entirely fanciful to speculate that some forms of functional psychosis may in fact represent "stress diseases" in which the brain is the "target organ."

Figure 21-2.



The Bio-psycho-social field. (For explanation see text.)

Considering the apparent complexity of relationships and the incompleteness of our knowledge concerning the mechanisms involved, we do not yet seem to be in a position to construct a satisfactory general theory of etiology and pathogenesis that would account in a parsimonious fashion (as a good theory should) for the variety of ways in which psychosocial forces may be involved in the development of bodily illness. All the same, some implications for the general shape and character, and for some components,

of a future theory can be drawn. If etiology and pathogenesis are conceived of as stepwise processes, and the natural history of disease is considered in respect to the separate phases (the phase preceding manifest disease, the phase of precipitation, and the phase of established disease), it appears that varying admixtures of specific and nonspecific mechanisms are involved, the relative proportions depending upon the stage of pathogenesis and phase of the disease process.

In *phase 1*, the period preceding the development of manifest disease, the important issue to be understood is if—and if so, how—a predisposition to a specific disease may be programmed into an individual who is later to be affected. Here we face a complex of elements ordinarily referred to as “constitution.” It appears likely that specific programming could involve (1) peripheral tissues in patterns or characteristics of organ function or tissue response, e.g., rate of pepsinogen secretion; (2) the CNS in modular central-nervous-system circuits (see Chapter 19 for a review of central-nervous-system circuits influencing various organ systems); and (3) both peripheral and central: parallel tissue-response pattern *and* central-nervous-system circuits, with appropriate autonomic and endocrine effector linkages.

For many diseases it is clear¹ that necessary but not sufficient programming information is transmitted in the genes; but since the transmission pattern seems to be one of incomplete penetrance, other factors,

such as early experience very probably interact and contribute in fundamental ways to determination of “constitutional” predispositions, and it appears that this could occur in several ways.

Developmental physiology suggests that there may be “critical periods” representing crucial stages in maturation when neurovegetative systems responsible for regulation of important visceral functions (such as heart rate and rhythm, peripheral resistance, etc.) may be particularly amenable to sensitizing or conditioning, and sensitive or open to influences by experiential events. Particularly intriguing is the possibility of autonomic conditioning (visceral learning) occurring during such “critical periods,” and eventually shaping a predisposition stored in central-nervous-system circuits for highly specific (pathogenic) visceral innervative patterns that could become activated (and pathogenic) under appropriate conditions later in life. The credibility or face validity of such an idea is enhanced by considering the possibilities for continuing reinforcement and further shaping provided by the continuing transactions between infant and mother, and later between child and family, that take place throughout development. Mirsky in his formulations about duodenal ulcer, has described how a basically genic constitutional predisposition in an organ, if expressed in behavior (e.g., as an excessive need to be nurtured and nourished in the case of gastric hypersecretion), may influence the mother’s behavior in response to the infant. This in turn would modify subsequent behavior in the infant (perhaps

by frustration and intensification of need) which would then feed back to the mother's behavior etc., etc., gradually creating a nidus of "core conflict" in the developing personality which would be specifically and inextricably related to the genic constitutional predisposition. At the same time in the course of development, reactive or protective ego defenses would develop around this vulnerable part of the personality system, and the nature and potential imperfections in this defensive matrix might very well determine the kind of psychosocial stress situation that could be expected to overwhelm the defenses and activate the conflict. Regardless of whether a constitutional predisposition originated in genic transmission and/or autonomic conditioning and/or classical conditioning (by repetitive fortuitous coincidence of stressful events with periods of illness), an epigenetic developmental sequence similar to this might well be expected to take place and eventuate in an individual with specifically patterned interrelated biological, psychological, and social vulnerabilities. Thus the emphasis in regard to this preillness phase of disease seems to weigh heavily in favor of specific preprogramming, with the evidence suggesting that both genetic *and* early developmental factors are involved and in complex interrelated ways. But the data do not permit us to do more than speculate about the possible nature of the interrelationships and the specific mechanisms whereby such effects might actually be induced.

A rather different set of questions arise in considering the phase of

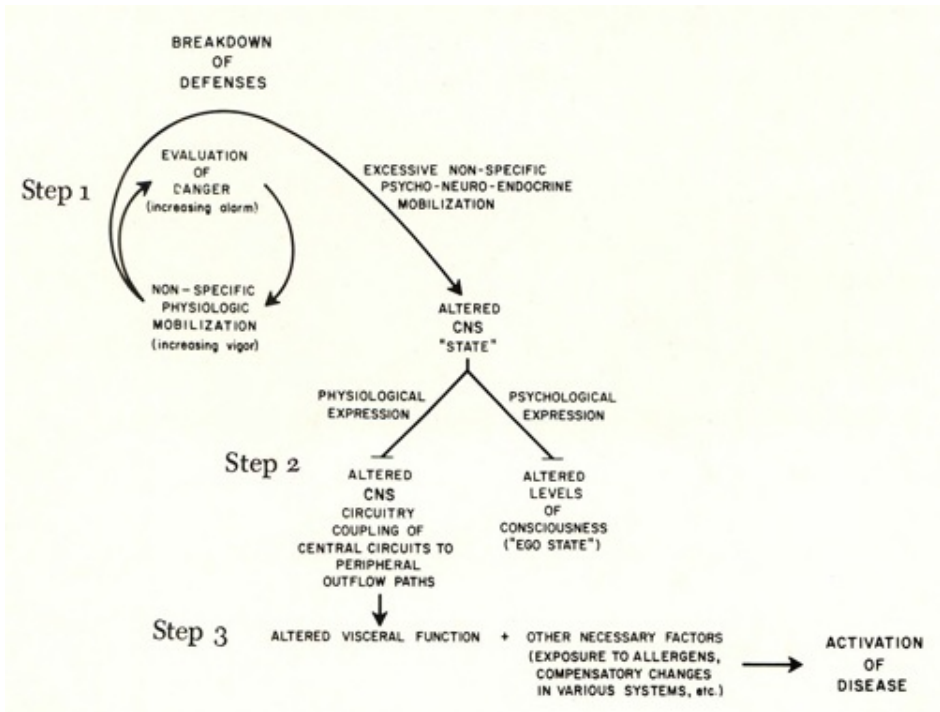
precipitation of active disease. Here the problem is one of understanding how psychosocial stress is to be related to activation of illness. In approaching these questions, primary emphasis shifts to the nonspecific factors reviewed in Part 2, i.e., the nonspecific effects of the psychoneuroendocrine stress responses on "host resistance" through effects on immune mechanisms, and through interfering with synchronization of circadian, ultradian and seasonal rhythms, etc. As noted earlier, the nature of the psychosocial stress situations that might be expected to overwhelm psychological defenses and allow for reactivation of conflict in any given individual would be related to his history, and to his personality organization, more precisely to the nature of whatever unresolved core conflicts remain active in him, and require continuing defensive activity. If under stress his defenses fail and his adrenal cortical and other endocrine activity is affected, he might, for example, be less resistant to infection, and develop a clinical infection more readily on exposure to an infective challenge that he would resist under more favorable circumstances. Such nonspecific reactions affect all people and their effects seem to be ubiquitous in medical practice.

But what about that relatively small group of persons supposed to be preprogrammed or predisposed as described above? *In such individuals the proximal pathogenic vector is not thought to be external (as in the case of pathogenic organisms) but rather internal, i.e., a predisposition, albeit previously latent and inactive.* In what way, if any, could the intrinsically

nonspecific changes attendant to psychoneuroendocrine stress response be related to activation of such a process? Or to put the question differently: in what way, if any, could the changes ultimately induced in the body by the endocrine response be favorable or permissive to actual expression of the previously inactive but potential pathogenic mode of function? The findings suggest that this could happen in a number of ways. Neurovegetative and endocrine changes in response to psychosocial stress have been shown to affect higher mental processes such as cognition, and could in this way influence perception and evaluation of danger signals and anxiety proneness. It could be hypothesized then that sustained pressure from active psychological conflict, with weakening of defenses, might set into motion a cyclic reaction whereby psychological processes involved in evaluation of danger would become increasingly more primitive and symbolic (regressive) as a consequence of the physiological responses they evoke, and that the physiological responses would become increasingly more vigorous as danger signals were evaluated with increasing alarm (Figure 21-3, step 1). One could speculate further that exposure of the brain to vigorous and continuous changes in circulating hormones (changes in the amounts and rates of rise and fall of individual hormones, in profiles among various hormones, in rhythms, etc.) could so affect patterns of central-neurophysiologic regulation that preprogrammed but inactive pathogenic circuits would become active and make connection with appropriate efferent fibers to the viscera, and

thereby induce altered visceral function (Figure 21-3, step 2). I have speculated previously that such hypothesized altered CNS conditions might be manifested behaviorally in the form of subtly altered states of consciousness (altered “ego states” in psychoanalytic terms as described by Schur; or “hypnoidal” states as hypothesized by Breuer and Freud). Such a notion is fully compatible with clinical observations of patients with high levels of free anxiety, and with a number of experimental observations: (1) at least one known state of consciousness (REM sleep) is well known to be associated with markedly altered (less well regulated, more “primitive”) patterns of autonomic function; (2) some serious illness episodes (e.g., myocardial infarction, status asthmaticus, hemorrhage from duodenal ulcer, etc.) are known to be precipitated or exacerbated in sleep; and (3) it has been shown that the ultradian ninety-minute rhythm seen in sleep (REM cycle) may continue throughout the twenty-four-hour period and be manifest in behavior (e.g., increased eating behavior) during waking hours.

Figure 21-3.



Hypothesized steps in precipitation of disease in conjunction with psychosocial stress.

Finally, in order to activate the specific pathological physiology involved in pathogenesis of a particular disease state (Figure 21-3, step 3) the altered visceral function produced in step 2 (as outlined above) would need to be combined with other factors essential to the particular disease (such as exposure to allergens, pathogens, compensatory and secondary changes in the same and other systems, e.g., circulatory adjustments, etc.) Of course

these would be entirely different for each disease, depending upon the nature of its pathological physiology and pathology.

This conceptual schematization of *phase 2* (precipitation) of disease emphasizes a series of *nonspecific* psychoneuroendocrine changes that may operate to aid in inducing illnesses of all sorts in all people, but which also might facilitate or induce in a smaller group of people so predisposed an altered state of CNS function permissive for activation of specific preprogrammed pathogenic patterns of visceral innervation. In other words, a nonspecific response would prepare the way for emergence of a more specific pathogenic process, with the specific predisposition having been laid down by interaction of psychologically meaningful early experiences with genetic endowment in a series of epigenetic somatopsychosomatic transactions throughout development.

In *phase 3* of disease, i.e., that in which the disease has already been established, it is likely that both nonspecific and specific mechanisms as described above would operate separately or in combination to influence the course and induce exacerbations or complications. But two modifications should be added. First, with increasing progression of disease and diminution in organ reserve, it is entirely possible and plausible that nonspecific changes might very well play an increasingly significant role with time, since less and less functional reserve in organs and resilience in homostatic mechanisms

would be available to moderate the disruptive effects of nonspecific stress responses. Second, with time, perception of the disease and its meaning become increasingly elaborated within the individual's self-image and increasingly incorporated into ongoing mental life, particularly in the conflict sphere (Hartmann). Accordingly, symbolically meaningful ideas would with increasing frequency and importance be associated with periods of activated or aggravated pathogenic physiologic responses. It would be expected then that idiosyncratic symbolic meanings connected with the disease would, with increasing frequency, become enmeshed in important issues in the patient's psychosocial field, and in ongoing intrapsychic conflicts as well. This would result in heavy emphasis on symbolic meanings associated with the disease, its signs and symptoms, in the patient's associations in psychoanalysis or psychotherapy, thereby creating the (probably false) impression that the disease had originated as a symbolic conversion mechanism.

In presenting these admittedly fanciful speculations in the final part of this Chapter, I have attempted mainly to have them reflect back to earlier theories while remaining consistent with the ever increasing wave of new empirical data, and to offer them as guides to possibly fruitful areas for research and as rough forecasts or previews of the nature and shape of (components of) future theory which is yet to be developed on a sound empirical basis. In any event, it seems reasonably clear to me that understanding the brain and its relation to the body on one hand, and to the

mind and social environment on the other, will probably ultimately provide the key to the riddle; i.e., full understanding will come from discovering how the brain orchestrates, integrates, and at points transduces across the biological, the psychological, and the social realms. In keeping with this view, Part Two of this volume begins with central regulation of autonomic-nervous-system function, followed by discussion of the autonomic nervous system itself, and then by reviews of psychoendocrinology and the data pertaining to the psychosocial parameters of illness in man. Finally come the separate chapters dealing with specific organ systems and diseases.

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Notes

1 This Chapter introduces the second part of the Volume and refers extensively to material covered in chapters that follow, particularly Chapters 22, 23, 24, 25, and 26. To avoid unnecessary duplication, many of the bibliographic references listed in those Chapters have not been repeated. Readers interested in a thorough follow-up of literature sources, therefore, are advised to consult those Chapters and their bibliographies as well as the bibliography of this one.