

PRESIDENTIAL ADDRESS

Relationships as Regulators: A Psychobiologic Perspective on Bereavement*

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In the spirit of adventure that has been characteristic of our Society, I am going to ask you to join me in a mental journey. The purpose is to try to look at something familiar in a new way. We are going to be looking at bereavement—something you all know a lot about—and I am going to try to get a different perspective on it by using information gathered in very different contexts and by trying to imagine what it is that experiments on infant separation in animals might be telling us about adult human bereavement.

First, I would like to persuade you that there is still a mystery concerning bereavement. Actually it puzzles us on many accounts: is it a disease or a natural function, a temporary insanity or a mobilization of creative energy? The mystery I would like to examine, however, is its place in natural history, its biologic basis, particularly how the experience comes to produce biologic changes in bereaved people.

George Engel asked us, in his presidential address more than 20 years ago (1), is grief a disease? However, medicine at large

and even psychosomatic research has been reluctant to intrude on an event that has been embedded in cultural practices and in the intimacy of family traditions since the beginnings of historic time. Nonetheless, new evidence of biologic changes after major loss and of the health consequences of bereavement are beginning to persuade us differently.

We know something about the cultural history of bereavement and a good deal about its psychology, but relatively little about its biology or natural history. One of John Bowlby's great contributions has been to place attachment and loss in the perspectives of development and evolution (2). This perspective was foreseen by Darwin in his marvelous book, *The Expression of the Emotions in Man and Animals* (3). Darwin suggested that the emotions of adult human grief had much in common with the separation response of children and with the forms of grief existing in other species of animals. However, despite the insight provided by these men, at present we can only see the dim outlines of what the biology of bereavement may turn out to be.

ADULT BEREAVEMENT

In Table 1, drawing from the work of Eric Lindemann (4), Colin Murray Parkes (5), and Paula Clayton (6), the major known features of the human adult response to bereavement are summarized. I have em-

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TABLE 1. Bereavement in the Human Adult

Behavior	Physiology
Acute: Waves of Distress, Lasting Minutes	
Agitation	Tears
Crying	Sighing respiration
Aimless activity-inactivity	Muscular weakness
Preoccupation with image of deceased	
Chronic: Background Disturbance, Lasting Weeks to Months	
Social withdrawal	Decreased body weight
Decreased concentration, attention	Sleep disturbance
Restlessness, anxiety	Muscular weakness
Decreased or variable food intake	Cardiovascular changes
Postures and facial expressions of sadness	Endocrine changes
Illusions, hallucinations	Immunologic changes
Depressed mood	

phasized something that Eric Lindemann pointed out 40 years ago, that there are really two forms of disturbance: the acute, recurrent waves of distress, which last only minutes, and the chronic, more slowly developing background disturbance, which is measured in weeks and months. Table 1 summarizes the symptoms characterizing these two forms of response, with the behavioral and psychologic symptoms listed on the left and the physiologic symptoms on the right. I would particularly call your attention to the cognitive and perceptual disturbance caused by bereavement, with its impairments of concentration, memory, judgment, and decisiveness, including illusions and even hallucinations of the lost person in 12-40% of cases (7). This disorganization of ego functioning contributes to a sense of impending loss of control. We know very little about the physiologic changes. The sleep disturbance has not been characterized in any detail and the evidence for cardiovascular changes is based on epidemiologic data (8). Psychoendocrine research is currently being carried out by John Mason's group at Yale, a continuation of work we

began together many years ago in Washington (9). Two papers have described reduced lymphocyte response in the bereaved (10,11).

It is generally assumed that the acute and chronic symptoms are both parts of the same process, but it is possible that we are wrong in taking this for granted. In this paper I will focus on the chronic background disturbance during which most of the severe biologic changes occur.

INFANT RESPONSES TO SEPARATION

Table 2 is a summary of infant responses to separation from the mother, taken from studies of several animal species as well as of human infants. Comparison of Tables 1 and 2 will show how prescient Darwin really was. The infant responses to maternal separation closely resemble adult responses to bereavement. Species differences and individual variability (16) do occur, but the broad outline and even some of the details are surprisingly similar for different species. For example, decreased

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TABLE 2. Infant Separation Responses

Behavior	Physiology
<i>Acute: "Protest" Phase, Lasting Minutes to Hours</i>	
Agitation (12-18)	Increased heart rate (19,20)
Vocalization (12-18)	Increased cortisol (21)
Searching, inactivity (12-18)	Increased catecholamines (22)
<i>Chronic: Slow-Developing "Despair" Phase, Lasting Hours to Days</i>	
Decreased social interaction, play (13,14,18,23)	Decreased body weight (18,25)
Mouthing, rocking (12)	Sleep disturbance
Hyporesponsiveness or hyperresponsiveness (14,23,27)	Decreased rapid eye movement, increased arousals (28,29)
Decreased or variable food intake (18,25,26,30)	Metabolic
Postures and facial expressions of sadness (13,14)	Decreased core temperature (19,27)
	Decreased oxygen consumption (31)
	Cardiovascular
	Decreased cardiac rate (19,27), increased vascular resistance (32)
	Increased ectopic beats (20)
	Endocrine
	Decreased growth hormone (33)
	Immunologic
	Decreased T-cell activity (69,70)

body temperature, low heart rates, and a similar pattern of sleep disturbance are found in both infant rats (28,34) and monkeys (29). In the infant, however, the acute distress does not occur in waves as in the adult, but precedes the more slowly developing chronic changes.

Here again, it has been assumed that the acute and the slow-developing changes are part of the same process. In an attempt to determine why this set of behavioral responses evolved, Bowlby (2) and others (14,18) have proposed that both the "protest" and "despair" phases are strategies selected during evolution because of their adaptive value. The arousal of the protest stage tends to result in the mother finding the infant or returning to it, and the inhibition of the despair phase results in safe hiding from predators and metabolic conservation until reunion with the mother becomes possible. In this view, all of the physiologic changes are thought to be cor-

relates of the affective response to the perception and recognition of the loss, just as in adult bereavement.

TWO KINDS OF SEPARATION RESPONSE

Our experiments have caused us to question the tidy view outlined previously. We found that the protest phase in the 2-week-old rat pup, complete with ultrasonic vocalizations, could be readily prevented with a familiar littermate, a surrogate, if it smelled and felt like a littermate, or with the mother, even if she were anesthetized and therefore unresponsive (35). So far this response is like that of young infants of other species (36,37). However, we were observing the slow-developing biologic changes in particular, which to our great surprise continued to occur even when the protest phase was

completely prevented by the presence of effective surrogates (25,27,28,31,38). We were forced to conclude that the slow-developing changes were independent of the acute isolation distress and that the two phases might be caused by different processes (39).

What could produce slow-developing biologic changes without eliciting isolation distress? The clue we found lay in the differences between an active functioning and an unresponsive anesthetized mother. At first, we thought that this effect would be mediated by the infant's perception that something was wrong with the unresponsive mother, which would in turn elicit an affective response that would produce all of the slow-developing biologic changes as an integrated psychophysiologic response. This sequence of events, however, is not what we found. Instead, it was discovered that a single aspect of the mother-infant relationship could entirely prevent one of the physiologic changes without affecting any of the others. Thus, the pattern of slow-developing changes was in reality a composite or assemblage of separate independent processes, each operating over a different pathway. The only reason that all of these changes occurred as a pattern in the separated infant was because all of the individual processes were activated at once by the *withdrawal* of all active aspects of the mother-infant relationship simultaneously.

This idea prompted us to perform several analytic experiments to try to identify and understand the individual processes within the relationship that were withdrawn by the separation. Our group has presented the findings of these experiments from time to time to this Society over the past 10 years.

HIDDEN REGULATORS

In Table 3, I have summarized the work done in our laboratory and in some others that allows us to see what these individual processes may be. This work owes much to my colleagues Herbert Weiner, Sigurd Ackerman, Stephen Brake, and Harry Shair. On the left, the biologic and behavioral systems of the 2-week-old infant rat that show the slow-developing changes after separation are listed: on the right, opposite each functional change, the specific aspects of the mother-infant interaction that ordinarily maintain normal levels of that function are shown. The infant's homeostatic system appears to be relatively "open"; thus, biologic regulation is delegated in part to the mother, even in the 2-week-old pup, which is beginning to eat solid food and can survive on its own (25).

Each of these regulators within the normal mother-infant interaction has its own dynamics and its own transduction mechanisms, about which we are beginning to explore. Some interactions with the mother serve to maintain levels of functions in their systems at a relatively high level during normal conditions (for example, heart rate and oxygen consumption); others normally down-regulate their systems (for example, those underlying behavioral reactivity, arousals during sleep, and sucking). Stephen Brake has shown the degree of specificity that can exist with these regulators: even within one system, that regulating sucking, intraoral stimulation by the mother's teat governs nonnutritive sucking levels, whereas gastric fill from the milk she has supplied regulates the intensity of the pups sucking in *response to milk*.

A great deal more must be learned about

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TABLE 3. Regulators Hidden Within the Mother–Infant Interaction

Infant systems	Direction	Maternal regulators
Behavioral		
Activity level	Increased	Body warmth (25,27,31)
	Decreased	Tactile and olfactory (38,40)
Sucking		
Nutritive	Decreased	Milk (distention) (41)
Nonnutritive	Decreased	Tactile (perioral) (41)
Neurochemical (Central Nervous System)		
NE, DA	Increased	Body warmth (31)
ODC	Increased	Tactile (dorsal) (42)
Metabolic		
Oxygen consumption	Increased	Milk (sugar) (43)
Sleep–Wake States		
REM sleep	Increased	Periodicity, milk and tactile (34)
Arousals	Decreased	Periodicity, milk and tactile (34)
Cardiovascular		
Heart rate (β -adrenergic)	Increased	Milk (interoreceptors) (24,44)
Resistance (α -adrenergic)	Decreased	Milk (interoreceptors) (32)
Endocrine		
Growth hormone	Increased	Tactile (dorsal) (33,42)

the way in which these regulators work and how the infant adapts to their withdrawal. However, the realization that they exist has already had implications for the understanding of developmental processes (45). These biologic regulators may constitute an early stage in the development of what we believe to be *psychologic* regulators within early social interactions, as infants get older and as species evolve. Doctoral dissertation research by Edward Plimpton in Leonard Rosenblum's laboratory (30) has shown that in the monkey (as well as in the rat) the acute and chronic phases of the reaction to early maternal separation can be affected differentially and may be independent processes. Bonnet macaque infants were raised under con-

ditions in which the mother was required to forage for their food, as well as under standard laboratory feeding ad libitum. The situation in which the demand for foraging was high altered the mother–infant interaction in those dyads, creating more evidence of tension, more maternal rejections of infant approaches, and earlier infant independence. When separated from their mothers, these infants showed the same level of protest behavior as those reared under standard conditions, but differed markedly in the more slowly developing “despair”-type behavior, becoming much more depressed and engaging in less complex behaviors during the second week of separation. These findings reveal that differences in the nature and quality of be-

havioral interaction within the dyad can have marked effects on the infant's response after separation and suggest the presence of regulators within the interaction that determine the form of the response after withdrawal by separation. It remains for future work to unravel the psychobiologic processes at work in these interesting effects that so closely parallel and complement our results in laboratory rats.

IMPLICATIONS

Is there anything in this unexpected story about separated infant animals that might help us to look at human adult bereavement in a new way? We must be very careful when we try to generalize across such a vast phylogenetic distance; nonetheless, we know that evolution is conservative, tending to use what is available and adding new features in new species, but retaining much of the old.

It is necessary to try to see what the results in these other species are telling us that might get us to look at human questions in a new way. I have been trying to do so and would like to share some of my speculative thoughts.

We know that in adult animals and humans, homeostatic regulatory systems remain under environmental control to a certain degree. For example, young women that live together for a period of time develop synchrony in their menstrual cycles (46). The sensory receptors for this social regulating influence are not known for the human, but for other species showing the same phenomenon are known to be olfactory mediated (47).

Thus, it may not be too far-fetched to ask whether it is possible that some of the

changes following human bereavement might not result from withdrawal of specific sensorimotor regulators hidden within the many complex interactions of the relationship that has ended.

Are there any studies that might provide some evidence in answer to this question? Two lines of work have occurred to me, the studies done in the late 1950s and early 1960s on sensory deprivation and more recent work in the field of chronobiology. In both types of experiments, subjects are not bereaved in the usual sense of the word, but social interaction is either withdrawn or altered in its schedule over a period of hours or days. If there is any validity to our notion, subjects in these experiments should show some of the slow-developing, more chronic symptoms of adult human bereavement, without, of course, any of the acute grief responses.

SENSORY DEPRIVATION

Based on centuries of observations by explorers, mystics, shipwrecked sailors, and prisoners in solitary confinement and spurred on by the success of Russian and Chinese brainwashing techniques in the early 1950s, a number of groups began to study the acute effects of reduced environmental stimulation on human subjects. These lines of research were brought together in a symposium on sensory deprivation, held in 1958 at Harvard Medical School (48). Subjects were generally confined in dark, lightproof, soundproof single cubicles, often with a portable refrigerator, toilet, and urine collection bottles, and monitored electrophysiologically. Gauntlet-type gloves were worn to reduce hand sensation and associated activity and

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noise. Subjects remained in these cubicles for periods as long as 4 days in some studies and as short as 4 hr in others.

Table 4 summarizes the changes reported in these studies. These changes are strikingly similar to the chronic "background" symptoms reported in the classic studies on bereavement by Lindemann (4), Parkes (5), and Clayton (6) (Table 1). The acute episodes of grief are missing, as is depressed mood, but the cognitive and perceptual disturbance has much in common with that seen in the bereaved: diminished concentration and memory, difficulty in ordering thoughts and making decisions, diminished confidence in personal judgment, recurrence of "unbidden images," and illusions, particularly hallucinations—all resulting in fears of loss of control. Of course, in bereavement the mental content and the nature of the illusory perceptions are primarily related to the lost person, whereas in sensory deprivation the material has a highly variable and primitive, "primary process" quality.

Hallucinations occurred in as many as 25 of 29 subjects in one sensory deprivation study (49), reminding one of the clinical reports of hallucinations in nonpsychotic elderly people who rapidly develop cataracts (50). In the latter patients, increasing the level of light caused the abnormal perceptions to subside temporarily, and cataract removal was curative. Hallucinations were more frequent during sensory deprivation, the greater the degree

of enforced inactivity, suggesting an element (regulator) that might be specifically related to a particular symptom. The anorexia and weight loss of sensory deprivation are also worth noting. There was loss of interest in the abundant and palatable food and in one study, subjects lost weight at an average rate of 2.03 kg in 3 days (51).

What these studies certainly tell us is how dependent we are on everyday environmental stimuli for the proper functioning of our minds. The loss of customary environmental stimulation seems to reproduce several of the cardinal symptoms of the bereaved. Of course, the bereaved are not deprived of nearly as many sources of sensory stimulation as the subjects in this study. However, when one person becomes enormously important to another, unrelated events and interactions have relatively little impact; thus, the loss of this one source may actually constitute a massive deprivation of relevant environmental input. In addition, the social withdrawal and self-enforced inactivity of the bereaved may contribute to the sensory deficit and may intensify the symptoms.

SOCIAL ENTRAINMENT
OF BIOLOGIC RHYTHMS

The second set of studies do not entail such extensive sensory deprivation, but rather a specific sort of hidden regulatory process involved in controlling circadian and other rhythms. As you know, all of our biologic systems have a 24-hr functional rhythm, as do psychologic functions such as attention, memory, and even tolerance to pain (52). These rhythms are organized in a complicated web of cycles

TABLE 4. Symptoms after Sensory Deprivation

Fluctuating concentration and attention	Decreased body weight
Restlessness, anxiety	Sleep disturbance
Difficulty ordering thoughts	Muscular weakness
Decreased food intake	
Illusions, hallucinations	

that overlap to various degrees, creating a fabric of interweaving functional waveforms. Recent chronobiologic research, as reviewed by Moore-Ede et al. (53), has revealed that the pattern of this fabric is maintained by a hierarchic system of oscillators that culminates in two separate circadian pacemakers in the hypothalamus. These biologic clocks organize the functional rhythms under their control, but the pacemakers require daily synchronization to match their rhythms to our schedule. The environmental events that can synchronize or entrain rhythms, vary somewhat from species to species, and were given the name *Zeitgebers* by Aschoff in the early 1950s.

Under conditions of absent or insufficient *Zeitgebers*, two things happen. First, the major pacemakers run free at a period of about 25 hr, thus disengaging biologic rhythms from the 24-hr daily cycle. Second, after a period of days, the two major oscillators desynchronize from each other and major rhythmic biologic functions lose their constant phase relationships to each other. There is growing evidence that this internal desynchronization is harmful to homeostatic and adaptive functioning (54).

Thus, the nature of environmental events that can entrain our biologic clocks is obviously of considerable importance. Recent evidence shows that light-dark and ambient temperature cycles are the primary *Zeitgebers* for insects; for mammals, particularly primates, periodic and regularly occurring social interactions may be the relevant daily cues (55).

What might all of these findings have to do with bereavement? It seems possible that one of the important regulators that may be withdrawn by bereavement are the events that served to entrain and synchronize the biologic clocks of the survivor. If

the synchrony of the rhythmic cycles of all of our internal systems is dependent upon environmental events that include interactions with another person, loss of these interactions may lead to desynchronization.

If this line of thought has any validity, we should be able to find two kinds of supporting evidence: 1) that social interactions are indeed capable of synchronizing biologic rhythms in the human; and 2) that lack of synchrony is in fact associated with some of the chronic symptoms seen in the bereaved.

What reasons do we have to believe that social interactions can function as *Zeitgebers* for humans? First, recent experiments (56) show that when individuals are isolated from daily cues in special environments and housed together in groups, each group develops its own circadian period to which all members of the group become entrained. If one subject is moved between groups, he gradually resynchronizes his biologic rhythms to the new group's period. Second, in another experiment done by Wever (57,58), singly housed subjects were studied in rooms insulated from the everyday world around them, except for the lighting system, which was on an automatic 24-hr cycle. A system of bells was used to signal the time at which urine samples would be picked up for metabolic studies. These bells were the subject's one remaining link to the people outside his apartment. Initially it appeared that the morning "lights-on" signal was sufficient to entrain the subject's rhythms to 24 hr. However, when the bells were discontinued as a control procedure, the subject's circadian rhythms slipped away from a 24-hr rhythm, despite the morning "lights-on" signal, and ran free at close to 25 hr. These experiments led Wever to infer that

even symbolic events, such as the bells, that stand for social interactions may be sufficient for social entrainment in humans.

Next, we may consider the symptoms reported to occur in situations that involve loss of synchrony between circadian rhythms and the 24-hr day, jet travel across time zones and a change in work shift. Again we find the appearance of many of the major chronic symptoms of bereavement (Table 5). In one study (59) individuals required to remain in their hotel rooms after flying across six time zones were found to take longer to recover than those required to leave their hotel rooms and interact with the people of the new location, thus suggesting the importance of social entrainment processes for adjustment to a new environmental time schedule.

**WITHDRAWAL OF
SENSORIMOTOR STIMULATION**

Evidence from the studies on sensory deprivation and chronobiology indicate that we are surprisingly dependent on the lev-

TABLE 5. Symptoms Accompanying Loss of Synchrony between Circadian Rhythms and 24-hr Day

Symptoms after Jet Travel across Time Zones
Decreased vigilance, attention span
Decreased appetite
Sleep disturbance
Malaise, fatigue
Symptoms after Change in Work Shift
Decreased vigilance
Cognitive impairment
Insomnia
Weakness, fatigability
Depression, hostility

els and patterns of stimulation in our everyday lives for maintaining and regulating the complex organization of our mental and physical functioning. We are not directly aware of the role that this stimulation plays until it becomes insufficient or its patterning is radically changed. Then, we notice that our concentration and attention are impaired, our perception is somewhat distorted, we do not sleep well, our appetite is reduced or subject to sudden cravings, and we are periodically overcome with fatigue. In its extreme form, we feel that we are falling apart mentally. We see and hear things that are not there.

The similarities between these symptoms and the chronic background symptoms of bereavement are striking. The interpretation of the results of these studies is that the subjects are suffering from withdrawal of patterns of sensorimotor stimulation that had been exerting an imperceptible regulating action on the subjects' minds and on their internal biologic systems.

Might these same sorts of regulating actions be going on in close human social relationships such that bereavement also produces a set of withdrawal responses? This reaction could be possible when one of two persons who have been living very closely together dies. However, what about the situation in which the two grew up together, but now see each other only occasionally, living many hundreds of miles apart, and the death is announced over the telephone? Do the chronic background symptoms of bereavement occur to the same degree in this case, in which the loss is not one of actual interaction but of hopes, expectations, and memories? I know of no studies on this question, but it would certainly be interesting if the acute waves of

distress occurred to the same degree in this situation of "bereavement at a distance" but the chronic background symptoms were much less pronounced. Evidence on this point would give us an idea of the relative importance of the withdrawal of sensorimotor aspects of a relationship in the acute and to the chronic symptoms of bereavement.

INTERNAL REPRESENTATIONS

Human relationships are conducted at the mental or symbolic as well as at the sensorimotor levels. Our lives are lived as much within the internal world of mental representations as among the actual people themselves. This enables us to endure temporary separations without full-scale bereavement responses. Therefore, the inner experience of our relationship with another person, the memories, the expectations, and the way we bring our perception of their reactions and responses into our everyday lives through fantasy, are at least as important to consider as the actual interpersonal interactions themselves.

Could these elements of our inner life come to serve as biologic regulators, much the way the actual sensorimotor interactions with the mother function for the infant animal in our experiments? And could this link internal object relations to biologic systems? I think this may be possible. Certainly, associative or Pavlovian conditioning is a well-known mechanism by which symbolic cues and even internal time sense can come to control physiologic responses (60).

Thus, it seems possible that the regulating action of important human relationships upon biologic systems may be transduced, not only by sensorimotor and

temporal patterning of the actual interactions, but also by the internal experiences of the relationship as it is carried out in the mind of the person involved. A loss that is believed to be permanent is sustained at both levels of organization, so that both representational and actual interactions are affected by the event.

People whom we have known for a long time are represented in our minds by a multitude of memories and expectancies, running the whole range of sensory imagery and involving cognitive, emotional, and action derivatives. These representations appear to be laid down in memory during social interactions as distillates of actions performed and experienced, imbued with the dominant motivational setting and with preexisting fantasies. These individual units of experience are integrated into something like a network of attributes and invested with affect, resulting in the formation of an "internal object representation." Ordinarily the whole network is reexperienced as a unified entity when only one attribute is elicited, but it can be temporarily broken down into constituent units (for example, during psychotherapy). In bereavement, once the reality of the loss is accepted, the integration begins to loosen and individual representational units recover their separate existence in the mind of the survivor, so that, as Freud described it, "the work of mourning is carried out piecemeal" (61). Proust, however, gave us the clearest view of this process when he wrote in this famous passage about his own inner experience following the death of his lover, Albertine (62):

If all of a sudden I thought of her room . . . her piano, her motorcar . . . (every) one of the things which she had used, seemed to be giving me a fresh translation, a

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different version, to announce to me for a second time the news of her departure . . . it was not one, it was innumerable Albertines that I must . . . forget.

Thus, evidence from the psychology of grief supports the idea that multiple representations of the lost person exist, and in grief, unlike normal states, they tend to fragment and are dealt with separately by the bereaved individual. It is possible that each of these individual units of representation may be related to particular biologic responses, much the way certain memories make us blush.

In older children and adults, these internal representations may serve as active but symbolic surrogates that prevent the release of withdrawal responses after separation through their associative connections with biologic systems. This may be what allows some people to survive relatively long periods of isolation from others. The tendency to rely on sensorimotor pathways is strong, however, and re-emerges with more prolonged separation. I have heard that for "solo" sailors on long voyages, the boat becomes personified in their minds and they find themselves attuned to her every movement, as if her sensorimotor stimulation had replaced that of social interactions.

When we are convinced that we have experienced a permanent loss and not simply a separation, however, one aspect of our interaction with our internal representations is irrevocably changed: our expectations. We cannot anticipate doing things with the person ever again, or even hearing what he thinks or feels about anything. Certainly he will not return at a certain time of day. It is the experiencing of these multiple expectancies that elicits the repeated waves of distress that constitute the acute form of the bereavement response outlined in Table 1. We may also suppose

that it is in these expectancies that the regulator functions of the internal object relationship reside.

Mourning involves the repeated experiencing of these expectancies and their painful revision according to the "command of reality" (61). Is it possible that this revision includes or results in the dissolution of their associative link to biologic systems, so that the internal representation gradually ceases to be an effective regulator? This idea would fit well with the disorganization so characteristic of the mourning period and with the reorganization that ensues when the person successfully turns to new people and new pursuits as he emerges from his grief.

PHYSIOLOGIC EFFECTS OF SOCIAL RELATIONSHIPS

If we are on the right track at this point, we should be able to find evidence that the presence of human social relationships can modify physiologic responses in the participants and have important effects on health outcome. Here we are on firmer ground, thanks to members of this Society such as Sidney Cobb (63), Bill Greene (64), Margaret Singer (65), and others, because these researchers have documented the prime importance of social support for health and delineated specific aspects of social transactions, such as the intensity of "engagement-involvement," as important modifiers of physiologic responses. We now know that variations in the doctor-patient relationship and even the experimenter-subject interaction can have more intense effects on physiologic responses than the medications given by the doctor or the experimental variables introduced by the researcher.

This work has prompted another set of questions, which ask more specifically how social relationships may exert these effects. For infant animals sensorimotor systems predominate; for human adults, however, the elements of meaning and motivation are surely crucial, as well as other abstract elements such as predictability and the degree of control exercised by the participants.

Many people who have tried to approach this problem have been impressed with the importance of seemingly minor aspects of social interaction (66). The non-verbal signals, mannerisms, tones of voices, gestures, facial expressions, brief touches, and even the timing of events and pauses between words may have physiologic consequences—often outside the awareness of the participants. I am reminded of John Mason's study (67) of B-52 bomber crews, whose individual members all tended to show similar levels of adrenal cortical output while they worked closely together. How can such a hormonal regulatory effect be transmitted? This question is a challenge for the future.

CONCLUSION

Finally, I would like to return to the experiments with infant animals, not because they can ever answer basic questions about human nature, but because they may have given us a new perspective on the problem of human bereavement and alerted us to possibilities that we might not otherwise have imagined. First, they

suggest that in response to loss, several different processes may be at work having different biologic mechanisms. In particular, the acute affective responses may be distinguished from more slowly developing disturbances of biologic and psychologic organization. Second, they suggest that we look carefully at the relationship before the loss took place and try to understand more precisely who and what has been lost, rather than beginning our investigation with the disruption of the emotional tie or bond between the two individuals, as if bereavement were simply a stress that was suddenly imposed. Third, the studies on infant animals show us that complete homeostasis is a later development than we had thought and suggest that independent self-regulation may not exist, even in adulthood. Social interactions may continue to play an important role in the everyday regulation of internal biologic systems throughout life. Finally, they make us consider the possibility that some of the changes following bereavement, particularly the chronic biologic changes, may be caused by withdrawal of the multiple regulators woven into the fabric of the relationship before the loss.

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