

Section of Psychiatry

President Desmond Pond FRCP

Meeting November 8 1966

Paper

A Psychological Setting of Somatic Disease: The 'Giving Up - Given Up' Complex

by Professor George L Engel MD¹
(Departments of Psychiatry and Medicine,
University of Rochester School of Medicine,
Rochester NY, USA)

The notion that physical illness may supervene when people suffer grievous losses or are subjected to serious discouragement is an old one which repeatedly appears in the writings of the clinicians of the nineteenth century and earlier. For example, Samuel Black, reporting on two cases of angina pectoris before the Medical and Chirurgical Society on January 23, 1816, cited 'ossification of the coronaries' as the 'primary and original cause' of the disease, but also invoked 'the powerfully pernicious influence of strong mental emotion, or of depressing passion' as a contributing influence. He vividly describes the seizure of the Rev McCormick during an emotion-laden leave-taking of his beloved friends and flock when assigned to a new but distant parish; of Mr Marron, whose attack followed a consecutive train of calamity culminating in the loss of all of his children; and he refers to Dr Parr's patient whose seizure occurred immediately after imprisonment on account of debt (Black 1816).

Since 1946 the Rochester group have been studying patients with somatic disease in order to learn something of the life settings in which illness develops. A recurring theme seemed to be that onset of illness coincided with a period when the patient was also attempting to deal with some real or threatened loss or separation from a key object or goal in life *and* was experiencing feelings

of an inability to cope, variously voiced as 'discouragement', 'despair', 'giving up' or 'depression' (Engel 1955, Greene *et al.* 1956, Schmale 1958, 1965). Two distinctive affects, *helplessness* and *hopelessness*, were identified as characteristic responses to the perception by the patient that the loss was irretrievable (Schmale 1958). With *helplessness* the subject feels powerless to overcome the loss of gratification, but perceives the environment to be responsible and expects the environment to take over and provide the missing gratification; with *hopelessness* the subject assumes he is responsible for the loss of gratification and cannot be helped even if the environment takes action.

The discovery of a profound withdrawal reaction among human and other mammalian infants upon separation from a familiar environment or with inadequate mothering (Darwin 1872, Kaufman & Rosenblum 1967, Seay & Harlow 1965, Spitz 1945, 1946) and the demonstration that such responses could be instantaneously provoked by a minor stress (appearance of a stranger) in a susceptible baby and be accompanied by marked physiological changes (Engel & Reichsman 1956, Engel *et al.* 1956) suggested both phylogenetic and ontogenetic origins for the psychological state noted among adults.

These data on animals and infants led us to suggest two primary biological defence systems, 'flight-fight' and 'conservation-withdrawal', each with its underlying mediating neural organization and each serving an adaptive function in the face of environmental threat (Engel 1962). For the mammalian infant the greatest biological danger is separation from the nurturing female. The 'flight-fight' system mediates the active response whereby the animal struggles to maintain or re-establish contact or escape from an external danger. The 'conservation-withdrawal' system comes into play when the active response is fruitless and it serves to conserve energy, reduce

¹Research Career Awardee, National Institute of Mental Health, US Public Health Service. Supported in part by grants MH 14151, MH 00750, MH 11668 and MH 7521 from the National Institute of Mental Health

contact with the environment, and minimize the risk of detection by predators. We presume these basic biological defence systems to involve distinctive and appropriate physiological and biochemical patterns as well as to provide a matrix within which learning and psychic development take place, but they may predispose in later life to idiosyncratic vulnerabilities to loss, with activation of the corresponding biochemical and physiological systems.

The high incidence of various losses at the onset of illness reported by patients and/or their families retrospectively, 80% according to Schmale (1958, 1965), has called for a more precise delineation of the relevant psychological state. For purposes of identification we refer to it as the 'giving up - given up' complex and identify six characteristics, not all of which are necessarily evident to the same degree in every patient:

- (1) It involves unpleasant, distressing feelings expressed in such terms as 'it's too much', 'it's no use', 'I can't take it any more', 'I give up', and the like. These feelings are sometimes ascribed by the patient more to failures or deficiencies in his environment (helplessness) and sometimes more to his own personal failures or inadequacies for which nothing can be done (hopelessness).
- (2) The patient perceives himself as less intact, less competent, less in control, less gratified, and less capable of functioning in his accustomed manner, though he may continue to attempt to do so.
- (3) Relationships with other persons or roles in life are felt to be less secure or gratifying. He may have suffered or be threatened with the disruption of a relationship or role, he may feel himself given up or rejected by persons important to him, or he may give up on himself.
- (4) He perceives the external environment or his own performance as differing significantly from expectations based on past successful experience which no longer seems as useful a guide for current or future behaviour.
- (5) He feels a loss of continuity, of the sense of sequence between past and future, and a lessened ability to project himself into the future with hope or confidence. Hence, the future sometimes may appear relatively bleak or unrewarding.
- (6) He is prone to revive feelings, memories, and behaviour connected with occasions in the past which had a similar feeling quality. Hence, there may be a cumulative quality to the experience,

the reawakened and unsuccessful or frustrating aspects of the past weighing heavily on the present.

The role of the 'giving up - given up' complex in the development of somatic disease remains to be clarified. A study of the setting in which acute psychiatric illness occurs also shows a high incidence, indicating that any kind of illness may occur with this complex (Adamson & Schmale 1965). Other studies have shown that the complex also occurs without being followed by any illness. When 59 non-sick volunteers were studied for the occurrence of 'giving up - given up' episodes and changes in health over a period of one year, it was found that incidents of 'giving up - given up' not followed by illness and of illness not preceded by 'giving up - given up' both occurred. But the sequence of 'giving up - given up' followed by illness occurred significantly more frequently than either of these (Schmale 1965). In a study of 14 previously healthy women between 20 and 50 years of age, exposed to the severe stress of the terminal illness and death from cancer of their husbands, it was found that of the 9 who responded with 'giving up - given up' feelings, all developed somatic or psychiatric illness sometime during the eighteen months of observation. Only one of the 5 without such feelings became sick. All 14 manifested various patterns of grief (Schmale 1965).

From these and other data we take the position, that *the 'giving up - given up' complex can be considered as neither necessary nor sufficient for, but only as contributing to the emergence of, somatic disease and then only if the necessary predisposing factors are also present.* Any notions as to how such psychological reactions are related to disease onset remain purely speculative. We have purposefully kept our theoretical construct in this area general since we have continued to focus our attention at the level of clinical observation. In our view man is constantly interacting with his many environments, and at many levels of organization, from the subcellular and biochemical to the most external or peripheral, that of family, work and now even his universe. We postulate that when he gives up psychologically he disrupts the continuity of his relatedness to himself and his many environments or the levels of organization. With this loss of continuity he may become more vulnerable to the pathogenic influences in his external environments and/or more predisposed to internal derangements with separation from the external environments. These in essence presumably would constitute failures or complications of the

'flight-fight' or 'conservation-withdrawal' systems as biological defences. Thus disease is more apt to appear at such time of disruption and increased vulnerability. But we think it important to emphasize again that periods of giving up are not always followed by disease and all episodes of disease do not occur in a setting of a giving-up reaction. Indeed, until mediating mechanisms and their interaction with processes involved in the pathogenesis of various diseases are worked out, it is prudent to assume that in some instances the interaction may have no influence on the course of the disease, in some instances it may modify the clinical picture without influencing the course, and in some instances it may even influence the course favourably. Elucidation of these inter-relationships is a task for the future.

REFERENCES

- Adamson J D & Schmale A H (1965) *Psychosom. Med.* 27, 557
 Black S (1816) *Med.-chir. Trans.* 7, 70
 Darwin C
 (1872) *The Expression of Emotions in Man and Animals*. London
 Engel G L
 (1955) *Amer. J. Med.* 19, 231
 (1962) *Psychological Development in Health and Disease*. Philadelphia
 Engel G L & Reichsman F (1956) *J. Amer. psychoanal. Ass.* 4, 428
 Engel G L, Reichsman F & Segal H
 (1956) *Psychosom. Med.* 18, 374
 Greene W A, Young L E & Swisher S N
 (1956) *Psychosom. Med.* 18, 284
 Kaufman C & Rosenblum L A (1967) *Psychosom. Med.* (in press)
 Schmale A H
 (1958) *Psychosom. Med.* 20, 259
 (1965) In: *Symposium on Medical Aspects of Stress in the Military Climate*. Walter Reed Army Institute of Research, Washington, DC; 1965-788-714, p 433
 Seay B & Harlow H F (1965) *J. nerv. ment. Dis.* 140, 434
 Spitz R A
 (1945) *Psychoanal. Stud. Child* 1, 53
 (1946) *Psychoanal. Stud. Child* 2, 313

Meeting December 13 1966

The Pink Spot

**Dr A Pauline Ridges and
 Dr R E Bourdillon**
*(Nuffield Unit of Medical Genetics,
 Department of Medicine, University of Liverpool)*

Schizophrenia, Transmethylation and Pink Spot

In 1962 Friedhoff & Van Winkle (1962a) reported the excretion of 3,4-dimethoxyphenylethylamine (DMPE) in the urine of schizophrenics. This finding together with other recent experimental work has provided evidence that schizophrenia may be associated with an abnormality of the trans-methylating mechanisms of the body (e.g. Pollin *et al.* 1961, Brune & Himwich 1962, Smythies 1963, Greiner & Nicolson 1965). Later reports concerning DMPE excretion have been contradictory and have resulted in considerable confusion.

The importance of transmethylation reactions in the metabolism of normal body constituents was not appreciated until the late 1950s when Axelrod & Tomchick (1958) and Axelrod (1961) described the isolation of both O-methyl transferase and N-methyl transferase. Since then, methylation reactions have been shown to be intimately connected with the biosynthesis and metabolism of a variety of compounds (Axelrod 1965), and it has become apparent that these

enzymes are of major importance in the metabolism of noradrenaline and adrenaline.

Before anything was known of the enzymes involved in transmethylation, Osmond & Smythies (1952) had proposed that in schizophrenia a compound might be formed which resembled in chemical structure both adrenaline and mescaline and which had the physiological properties of mescaline. Harley-Mason (1952) suggested that such a compound might arise during the methylation reaction which occurs in the final stage of the biogenesis of adrenaline. This hypothesis was extended in 1963 by Smythies, who postulated that a more generalized disturbance of the methylation reactions may occur in schizophrenia resulting in the formation of abnormally methylated metabolites of catechols and indoles related to known psychotomimetic compounds.

The interest in Osmond & Smythies' hypothesis had, by this time, been heightened following Friedhoff & Van Winkle's account of the isolation of DMPE from the urine of 15 out of 19 schizophrenics and its absence from the urine of 14 normal subjects (Friedhoff & Van Winkle 1962a). This substance was extracted from the urine using chloroform and was separated from other materials in the extract by two-way paper chromatography. The substance isolated