

Models of Unexplained Symptoms Associated with Occupational and Environmental Exposures

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Unexplained illnesses characterized by nonspecific, multisystem complaints are often attributed to occupational or environmental chemical exposures. This raises difficulties for the regulatory authorities, who are frequently unable to agree on the existence, nature, or source of such illnesses. It is proposed that many of these difficulties derive from an adherence to a traditional medical model of disease and that the application of a biopsychosocial approach would be more effective for both research and individual case management. A number of models derived from the field of health psychology are discussed in terms of their application to occupational and environmental syndromes. A specific example is described that relates to the health problems experienced by sheep farmers in the United Kingdom who are exposed to organophosphate-based pesticides. The source of their complaints and the responses of the health professionals and the regulatory authorities are discussed within the context of a biopsychosocial approach that focuses on illness rather than on organic disease as the unit of study and explores the interaction between the various physical and psychosocial variables involved. It is proposed that this approach, which is already well established in the fields of human and social sciences, should be adopted more readily by those concerned with occupational and environmental epidemiology. **Key words:** biopsychosocial, determinants, farmers, models, organophosphates, symptoms. *Environ Health Perspect* 110(suppl 4):601–605 (2002).

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Throughout much of the 20th century the related fields of occupational and environmental health have been heavily influenced by what is generally termed the medical model, a framework that makes a distinction between disease and nondisease and often between physically and psychologically based complaints. The essential concern has been to examine the relationship between exposure to suspected hazards and the subsequent development of particular forms of ill health. This approach has been driven both by scientific methodology and by the political constraints of risk management and compensation. It has served occupational and environment medicine extremely well in the past, as evidenced by the huge reduction in most major industrial diseases during the last 100 years, accompanied by a corresponding improvement in public health. Recently, however, a number of baffling occupational and environment illnesses have come to the fore that appear to challenge the traditional model. These illnesses are characterized by a range of chronic physical, frequently multisystem complaints that cannot readily be linked physiologically or toxicologically to a specific hazard exposure, although they are often attributed to such by the sufferer. For want of a better descriptor, these conditions tend to be grouped under such general headings as “unexplained symptom syndromes,” “functional disorders” (i.e., no pathology), or simply “symptom-based conditions.” Common current examples are chronic fatigue syndrome (CFS)—sometimes referred to as myalgic encephalitis—as well as fibromyalgia,

multiple chemical sensitivity, sick building syndrome, and most recently Gulf War syndrome. One might also include some nonspecific, nontraumatic conditions such as chronic brucellosis and atypical polio. Finally, a number of conditions involving musculoskeletal pain have major unexplained components in addition to well-defined ergonomic risk factors.

However, inspection of medical history books shows that these syndromes are not new. Similar conditions have in fact been reported for many years (1). Only the names and the attributions appear to change. Note, for example, “railway spine,” a complaint said to result from traveling on the newly developed railway systems, or “telegraphist’s cramp,” both of which appeared during the second half of the 19th century. Perhaps not surprisingly, therefore, the heated debate generated by these conditions in recent years has largely failed to resolve questions such as definition, diagnostic criteria, etiology, and treatment, and the broader issues of risk assessment and management. This has led some researchers and clinicians to suggest that many of the problems associated with investigating these syndromes have arisen because of a natural but perhaps inappropriate attachment to the medical model (2) that in this context is proving unhelpful, if not positively obstructive.

A potentially more fruitful alternative is to approach the problem from a “biopsychosocial” standpoint. This position is perhaps more familiar to psychiatrists, psychologists, and social workers than to epidemiologists.

Indeed, it was well described and advocated almost exactly 25 years ago in a seminal paper by George Engel (3). The biopsychosocial approach essentially recognizes the complex interaction between physical and psychological processes and views health as a continuum rather than as a dichotomy between the presence or absence of disease. Further, illness may often reflect the personal interpretation of a condition (real, organic, or otherwise) by the patient, the doctor, or the therapist rather than constituting an objectively defined state. Where unexplained symptom syndromes are concerned, this approach appears to offer better prospects for understanding and managing ill health than the more traditional medical paradigm.

However, this said, a number of questions immediately arise. What exactly do we mean by a biopsychosocial model in this context? Are there models and methods that have been developed in other fields, notably health psychology, that may have useful application in occupational and environmental health? The purpose of this article is to describe such approaches in the context of a real example of an occupational health problem that involved the author’s own research.

What Do We Mean by a Biopsychosocial Model?

Workers in the field of health psychology are usually careful to make a distinction between *disease* and *illness*, the former being a biological event characterized by pathology in the structure and function of body organs and systems, and the latter the subjective experience of negative changes in well-being. This distinction provides the basis for much research that is concerned with the nature of symptom reporting and the response to disease onset and its treatment. It would appear to be central to the understanding of unexplained symptom syndromes because, implicitly or explicitly, when we adopt a biopsychosocial position we are concerned

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primarily with the understanding of illness rather than the explanation of disease. In this context, disease (or biological factors) represents just one possible contributor among many other (largely psychosocial) factors that help to determine illness or negative changes in well-being (Figure 1). When we view illness as the focus of our investigation, there is much less of a requirement to make potentially unhelpful decisions about whether something is a “real” disease (hence worthy of professional attention), or whether it should be dismissed as “all in the mind.”

It is of course well recognized that diseases may have multiple contributory causes. In the past, occupational and environmental epidemiology moved rapidly from a straightforward linear cause–effect model to one that took account of various factors with the potential to influence the outcome of interest. Such factors, often termed “effect modifiers,” might include aspects of lifestyle and behavior such as smoking, alcohol consumption, diet, and exercise and also some forms of genetic susceptibility. However, the biopsychosocial approach can be said to move this approach one stage further by ascribing a central rather than a subsidiary role to effect modifiers and also by extending them to include frankly psychosocial issues such as attitudes and belief systems.

The reporting of symptoms therefore represents an outcome of a complex set of interactions between aspects of personality, attitudes, culture, and social climate as well as any pathological changes. Biopsychosocial models are essentially transactional in nature in the sense that the various biological, psychological, and social factors serve to continuously reinforce and amplify one another. This creates considerable difficulties for the traditional concerns of occupational and environmental health, namely, quantifying the risk associated with exposure to certain physical or chemical hazards, not to mention its clinical concerns of diagnosis and treatment. However, if it offers a better explanation of some current phenomena, it cannot be ignored.

Current Models

Work in the field of health psychology has produced a number of transactional models that help to explain and predict various aspects of health-related behavior. Primarily, these are concerned with the individual’s response to diagnosis, compliance with treatment regimes, and the maintenance of health-promoting activities (4,5). As such, they appear to have direct relevance to the clinical aspects of occupational and environmental health in terms of management of problems at the individual case level. For example, one of the more influential models in recent years has been Leventhal’s self-regulatory model of illness behavior (6), which describes such behavior as consisting of three stages of problem solving:

- a) interpretation: the individual’s cognitive representation of the illness in terms of identity, cause, consequences, time line, and availability
- b) coping: the development of coping strategies, which may constitute either approach, in terms of seeking help, or avoidance, in terms of denial
- c) appraisal: the evaluation of coping strategies and possible adoption of alternatives

Models such as this have been applied to predict functioning in complaints such as CFS with a moderate degree of success (7).

Application of health psychology and its concepts to the field of risk assessment and management, which is more usually the domain of epidemiology and toxicology, is perhaps less obvious. However, its relevance becomes apparent when we consider approaches to the investigation of symptom reporting, one of the “softer” but nevertheless important outcome measures in health research. Pennebaker (8) has argued convincingly that the human perceptual processes of selectivity and interpretation that are operative regarding external stimuli also affect the individual’s response to internal bodily activity. Thus, a range of factors may be important in determining whether or not internal body stimuli are attended to, how they are interpreted, whether or not they are reported, and whether they elicit a response,

medical or otherwise. These factors have been summarized as follows (8):

- A selective attention to body state that is likely to be accentuated, a) where the external environment is tedious and unstimulating, b) where communication with others (which facilitates normalizing comparisons) is limited or absent, c) where the environment is highly stressful but direct expression of anxiety or depression and its source is unacceptable, d) where individuals experience a sense of powerlessness, or e) where there is a culture of illness expression.
- An attributional style that tends to be determined by the individual’s “mental models” or schema, which are internal cognitive representations of the world comprising our attitudes and beliefs, by which we organize and interpret our experiences.
- The mood-related disposition of negative affectivity that appears to underpin the more familiar personality factor of neuroticism, characterized by an introspective tendency to experience more distress and dissatisfaction with both self and others and to dwell on failures and shortcomings.

Models of symptom reporting that incorporate these factors tend to focus on individually based determinants of subjective well-being (9). From the point of view of occupational and environmental epidemiology, however, such models contain an important omission.

Information from external sources is regarded as influential only in terms of whether its absence or poor quality encourages the individual to focus more narrowly on internal states. Where the response to hazard exposure is concerned, however, the form and source of external information and its social and cultural context are crucial elements in determining the interaction with the individual’s particular mental models. For example, communication with others may in some circumstances act to focus an individual’s attention on his or her internal state and increase rather than reduce anxiety. This aspect has been better addressed in the field of risk perception, where attention is drawn to the following factors (10):

- heightened concern about risk determined by factors such as their involuntary, uncontrolled nature; lack of scientific information; or particularly dreaded consequences
- prevailing levels of trust (or mistrust) relating to government, industry, and professional bodies
- prevailing attitudes and beliefs about medicine and other health-related professions
- the current political agenda
- the current legal agenda
- the current social and political climate
- current media and pressure group activity

The complex process of symptom reporting therefore requires simultaneous consideration

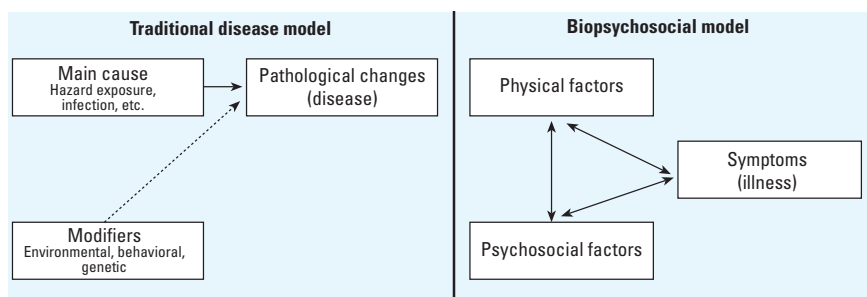


Figure 1. Two models of symptom reporting.

of all these factors, which may be both individually and socially determined.

The U.K. Sheep Dip Story

The Problem

Since 1976, sheep farmers in the United Kingdom have been legally required to treat their animals with a pesticide at least once a year to control the widespread problem of sheep scab, a serious and often fatal parasite-borne disease that attacks the skin of the animals. Farmers were required to make up a solution of pesticide concentrate and water in a dip bath and immerse each animal in the bath, thus soaking the fleece and skin. During this procedure, despite the specification of various precautions, the farmers themselves often become soaked in the solution, thus experiencing pesticide exposure via both skin absorption and inhalation. In 1984, because of continuing problems with sheep scab, the dipping requirement was increased to twice yearly. That same year organochlorine-based pesticides were banned in the United Kingdom, leaving organophosphates as the only realistic alternative. Soon after 1984 some farmers began to complain of symptoms of ill health that they associated with the dipping process. Most frequently they reported excessive fatigue, gastrointestinal pain, headache, memory problems and other cognitive confusion, depressed mood, and feelings of anxiety. However, a comprehensive list of all symptoms reported at least once contained no fewer than 67 items (11). A proportion of the farmers claimed that the symptoms did not disappear after exposure had ceased and that they were developing chronic ill health. From the clinical and toxicologic point of view, this raised some difficult issues:

- Symptoms reported immediately after dipping were consistent with a well-understood acute cholinergic response to organophosphate exposure: mild flulike symptoms. These symptoms are well accepted clinically but would normally be regarded as totally reversible. Persistent chronic effects should not therefore occur.
- Biological monitoring (i.e., investigation of changes in the farmers' blood and plasma cholinesterase levels during dipping) did not suggest exposures occurring at levels likely to result in these cholinergic responses.
- There was no documented clinical evidence of people experiencing long-term health problems as a result of either one or several episodes of high exposure, except perhaps in a few patients who had experienced severe life-threatening intoxication, and no such cases had occurred as a result of sheep dipping.
- The persisting symptoms experienced by the sufferers were diverse, lacking any

coherent pattern, and no pathological changes could be identified.

These farmers therefore had developed an "unexplained symptom syndrome." They proceeded to voice their complaints through the media and via increasingly sophisticated pressure group activity and persistent lobbying of sympathetic members of Parliament. Some individual farmers embarked on a series of largely unsatisfactory encounters with members of the medical profession in an attempt to secure a diagnosis and/or treatment, and a much smaller group achieved some satisfaction in the law courts.

The government departments involved were initially inclined to dismiss the problem, basing their view on the available scientific evidence. Subsequently, in response to public pressure, they commissioned two large-scale research projects (12,13), the first of which was carried out by the author. Unfortunately, the results appear only to have added to the indecision and confusion surrounding this issue. Essentially, because organophosphates are established neurotoxins, and because of the nature of most of the complaints, the commissioned research focused on psychological outcomes, notably, effects on cognitive functioning and mental health. The assessment of cognitive functioning, in particular, created difficulties of interpretation for those used to dealing with defined disease end points. Functions such as attentional control and information processing are measured on a continuum, and any cutoff point denoting impairment is likely to be, if not arbitrary, at least dependent on the characteristics of the population under study (age, educational level, attitudes, motivation, etc.). Like symptom reporting, performance on cognitive tests represents the result of a complex interaction of physical and psychological variables. Hence, it was always going to be difficult to determine whether organophosphate exposure "caused" significant changes in cognitive function by producing structural and functional changes to the nervous system.

In a sense, the use of neurobehavioral testing in this context represented an attempt to harness psychological methods to the medical model. In the absence of any identifiable pathological changes that could be measured more objectively, the disease end point was to be defined in terms of scores on psychological tests. Operating within this framework, the author's study (12) did manage to isolate some subtle differences in cognitive functioning between sheep farmers and controls that remained after numerous other potential influences on performance had been adjusted or controlled for. Some of these changes also appeared to be related to the duration and intensity of exposure, suggesting a dose-effect relationship.

However, because lowered psychological test scores could not be said to constitute an identifiable disease, the regulatory authorities were uneasy and skeptical. Moreover, they pointed to the myriad psychosocial factors that might influence the results as a reason for rejecting the findings.

This response can perhaps be readily understood when one considers the regulatory framework within which the government department concerned (the then Ministry of Agriculture) was required to operate. One of its primary responsibilities was to act as a licensing authority for veterinary medicines, which included sheep dip. Hence, there was a requirement to decide unequivocally whether the substance in question was "safe" or "unsafe" for use. Decisions of this nature are more easily arrived at in the context of a disease/nondisease framework (i.e., a medical model) than in situations where illness is ill-defined and of multifactorial origin. The impetus therefore is toward a rejection of complex interpretations of the data and a maintenance of the requirement for proof of objectively verifiable organic disease.

This position tends to be reinforced by the attendant liability implications. A particular feature of licensing authorities that is not shared by other regulators in the United Kingdom, such as the Health and Safety Executive, is that the act of licensing effectively transfers the legal responsibility for safety from the consumer to the authority. Thus, the consumers are absolved from such responsibility provided they use only licensed products and in the approved manner. This factor is undoubtedly a strong determinant of the decision-making approach of the regulators and, perhaps more important in this context, the attributional style of the consumers when experiencing health problems. Further licensing decisions tend to have at least an outward appearance of risk removal (i.e., achievement of zero risk) rather than a more realistic one of reducing risk to a level deemed acceptable in societal terms. Again, risk removal tends to be incompatible with situations involving complex illnesses that are difficult to define or quantify. Paradoxically perhaps, the apparent adherence of both farmers and policy makers first to a medical model and then to a requirement for a zero-risk situation produces a conflict that is difficult to resolve.

The initial research on organophosphate sheep dip therefore served only to intensify the controversy and antagonism between campaigners and government, both of whom claimed that the results supported their position. Amidst continuing acrimonious debate, the government commissioned further research (13), this time requiring objectively measurable outcomes (neurophysiological

parameters) in addition to the more controversial psychological tests and symptom questionnaires. The problem was once more approached from the standpoint of the medical model, and the results were again unsatisfactory. Some similar subtle differences in performance were observed but few, if any, neurophysiological effects. The main outcome of note was the demonstration of a significant association between symptom reporting and handling of the organophosphate concentrate. Although this provided an opportunity for a minor policy decision (in this case improvements to the concentrate container), it provided nothing in terms of disease definition, diagnosis, or treatment and little more in terms of informing risk management.

Over the last few years, this ongoing research has been paralleled by the deliberations of a number of government committees and some officially commissioned evidence reviews (14–16). An interim decision was taken to withdraw the legal requirement to dip sheep in 1992 but without a formal admission that organophosphates represented a significant risk to health—when used appropriately. More recently, in 1999, organophosphate-based dips were withdrawn from sale on a temporary basis—in order to improve the aforementioned concentrate containers. A few months later sales were reinstated amidst rising concern that sheep flocks were once more being decimated by sheep scab.

At this point the problem is very far from being resolved. A large number of farmers feel they are suffering from a chronic and disabling health problem that lacks even official acknowledgment and for which they are unable to get either treatment or compensation. Both the government and the medical profession are experiencing indecision and division on the subject, and future policy on risk assessment and management of these substances appears to be in some disarray.

Why Did the Farmers Become Ill?

Hindsight shows that a number of factors were in place that together might predict the situation:

- exposure to a chemical that is known to be hazardous, associated with high dread consequences, and for which the symptoms are well documented
- modern farming practices that produce relative isolation of farmers in their working and social lives and thus increase their attention to internal states
- adverse economic circumstances that in recent years have created major work and life stressors for rural workers; risks of mental health problems and suicide are known to be significantly elevated in this group
- prevailing negative social attitudes toward chemicals in general and pesticides in

particular, as part of general environmental concern; farmers may be vilified by the public because of pesticide use and experience conflict between economic and social concern, compounded by individual anxiety about their own health

- the involuntary nature of the risk (legal requirement) that offers the opportunity to attribute blame externally; the problem received very little public attention before the introduction of mandatory dipping and appears not to have become an issue in other areas of agriculture where organophosphates are used (e.g., orchard spraying)
- prevailing attitudes of mistrust toward government and industry
- lack of definite scientific information or agreement among medical and other health professionals
- interest and stimulation offered by the media and social and emotional support offered by pressure groups in contrast to a prevailing attitude of skepticism among sections of mainstream medical opinion

Added to these factors, certain personality variables are likely to explain some of the individual differences in farmers' responses.

It is important to reiterate at this point that discussion of the determinants of symptom reporting does not constitute a dismissal of the farmer's illness but simply a recognition that it is likely to result from a complex interaction of physical, psychological, and social processes. A similar picture can be identified in relation to numerous other conditions, for example, sick building syndrome, CFS, and the development of low back pain.

Future Directions

The failure of government-funded research into the sheep dip problem to provide answers that can inform policy represents one example where conventional medical models appear to be inappropriate. The biopsychosocial approach has in fact gained some acceptance in the context of individually based treatments but has had much less influence on the conduct of larger-scale group investigations, and it is here where perhaps most change is needed. It seems that where we have unexplained symptom syndromes, we must be prepared *a*) to have no objectively measurable diagnostic criteria and to treat perceived illness rather than demonstrable organic disease as the focus of our investigation, *b*) to measure a wide range of factors that may contribute interactively and to varying degrees—psychosocial factors are likely to predominate here, and *c*) to accept the equal importance of all these factors rather than regarding most of them as “noise” in the data to be controlled or adjusted for.

This approach would appear to have application to a number of aspects of occupational

and environmental health practice, for example,

- individual clinical investigations to determine the course of illness and define treatment
- investigations of clusters or outbreaks of symptoms
- population-based studies of attribution, causation, and association
- the development of control strategies to prevent harm at both organizational and government levels
- the evaluation of the effectiveness of different interventions

In terms of methodology, many of these questions can be addressed by the adoption of a traditionally quantitative approach, using already existing questionnaire measures or purpose-developed psychometric tools to assess the various determinants of symptom reporting. A number of powerful statistical methods are available to address this type of data in ways that explore the relationships between different variables. For example, structural equation modeling combines the techniques of multiple regression and path analysis for this purpose. A useful addition in the future, however, might be greater use of qualitative approaches that are becoming increasingly popular in health-related research (17). These methods, comprising semistructured interviews and observational techniques, are ideally suited to the in-depth exploration of complex sets of interrelationships and provide rich sets of data to complement quantitative information.

The biopsychosocial approach may help to eliminate the need for sterile debates about whether an illness is “real” and whether it is “caused” by exposure to a particular agent and allow us instead to address the various needs of the sufferers as identified by the multiple contributory factors involved. The first neurobehavioral study of sheep farmers (12) found that in addition to lower scores on some psychological tests, the farmers reported significantly more symptoms of anxiety and depression than the controls. As a follow-up to this study, therefore, Jackson carried out a further investigation of the various possible determinants, including organophosphate exposure, of the farmers' poor mental health (18). Five contributors to symptom reporting were identified in this group, namely, personality type, perceived fatigue, adverse life events, dissatisfaction with the agricultural lifestyle—and handling sheep less than 48 hr after dipping. From a regulatory point of view, it is entirely reasonable to focus on the last factor (e.g., by advising avoidance of sheep handling immediately after dipping), and the occupational health regulators may be said to have fulfilled their particular obligations at that point. However, they would

perhaps be naïve to expect that farmers would no longer become ill as a result. Findings such as these simply provide pointers as to which aspects of the problem require intervention and assistance from different professional groups, agencies, and policy makers.

Essentially, therefore, the issue is as much one of attitude change among all those involved as it is a question of methodology. Most of us have an intuitive understanding that how we feel physically, and what we choose to say about our health is heavily influenced by our attitudes and beliefs, our mood, and our motives. We tend to accept this readily on a day-to-day basis while continuing to downgrade the importance or validity of psychological experiences when it comes to questions of disease. Witness the fierce desire of those with symptom-based conditions for recognition that they have a physical rather than a psychological complaint—even where the hazard in question is known to target the brain. Presumably, this derives from a collective consciousness that dismisses or, worse, attaches negative value judgments to psychological distress. Perhaps, therefore, the real

challenge is to change our own mental models. This achieved, it might not be too difficult to incorporate what we in fact already know into our scientific thinking and practice.

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