by Howard M. Sandler, M.D.

Occupational Causation: Did My Job Make Me Sick?

Determining the link between work and illness can be a real...well, pickle.

EARLY IN MY CAREER as a medical officer with NIOSH, I became acutely aware that the occupational link for illnesses was frequently missed. I commented in a letter published in the *New England Journal of Medicine* in 1980 that a high percentage of pathologists missed a straightforward case of asbestosis on an autopsy. Since then, occupational safety and health professionals have made great strides in identifying work-related health effects. But the question remains: Are we doing a good job of determining when illnesses are caused by work?

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I am sure we are all frustrated by some clinicians' matter-of-fact opinion, "Well, he works with chemicals; therefore, his asthma (or you fill in the condition) must be the result of his job." Another good standby is, "I can't find any other reason; therefore, it must be work!"

Let's discount the obvious motivators for making an arbitrary work-relationship determination:

- Higher medical fee schedule;
- Workers' compensation indemnity payments;
- "Keeping the patient happy."

What unfortunately remains is that few clinicians employ a formal scientifically based methodology to make a determination of causation. A true "weight of the evidence" decision based on sound science requires criteria weighting on either a broad substance exposure effect/causal association or an individual worker basis. For example, did exposure to triethyl doorknob cause my permanent hair loss (a concern near and dear to my head!)? In order to begin to address a causal relationship in this instance, one must answer the following questions:

- What is permanent hair loss?
- Did the exposure occur before or after the primary hair loss?
- How much exposure must occur over what timeframe for the effect to occur?
- Did the exposure simply aggravate an underlying condition?
- Has the effect been documented in humans?

Association vs. Causation

Armchair scientists will use deductive reasoning like Sherlock Holmes in causal determination: "If you rule out all probabilities, the remaining possibility, no matter how unlikely, is the culprit!" The fatal flaw in this approach is that, in medicine, we simply don't know the cause of the disease in many instances. For example, most causes of interstitial fibrosis are unknown or idiopathic. Simply because a worker happened to work in a building containing asbestos doesn't mean his interstitial fibrosis is asbestosis, the interstitial fibrotic disease produced by high-level, long-term asbestos exposure.

On a global basis, inappropriate deductive reasoning can also lead one astray. Consider this statement: "Everyone who ate a pickle in 1869 is dead today. Therefore, pickles cause death."

Statistically speaking, there is a 100 percent association in the pickle example, but, epidemiologically, it is clearly without scientific foundation. It is simply not biologically plausible. But, as some might point out, "Somebody could choke to death on a pickle!" Possibility does not equate with probability, much less certainty.

Defining the Disorder

Showing a work association for a worker's complaints is often difficult because, frequently, all you have to go on are symptoms such as pain, cough or headaches. Symptoms such as these and others frequently occur in the general population at rates of 30, 40 or 50 percent or higher. They can result from allergies, stress and a whole host of different causes. Frequently, they simply occur without a clearly identified disease.

It is important to have specific disease-identifying criteria in order to make a diagnosis. This is frequently a problem when you evaluate scientific studies. For example, most studies of carpal tunnel syndrome and work fail to use nerve conduction studies, commonly accepted as the gold standard to determine the presence or incidence of CTS. Recent studies have shown proper diagnostic identification can greatly affect the number of workers who are considered to have CTS. The impact of diagnostic criteria can seriously affect the results of studies especially for relatively ill-defined disorders, such as tendinitis, respiratory symptoms or pain.

Defining Exposure

Another area of critical importance in determining whether a study can be used to establish causation is how the exposure was derived. Unfortunately,

few studies exact measurements of specific exposures to employ. For example, many chemicals are used in the same job. The amount of chemicals changes over time and the ability to ascertain the level even simply, (low, medium or high), is often a guess. Researchers may say that all workers within a production area are similarly exposed. While this makes the study possible, any safety and health professional knows how inappropriate such a designation is.To think that the results of studies employing these and other less-than-exact methods are used by regulators, juries and workers' compensation judges and in the media illustrates the role of scientific uncertainty in everyday occupational safety and health events.

What Does Work-Related Mean?

Before we can create a study to understand the relationship between an exposure and an effect, we must carefully define how the effect is considered work-related. Ideally, we would want to follow a group of workers who do not have the disease from the time they are first exposed over a sufficient time to allow the expression of the effect. This prospective study should also include a control group of workers similarly selected and see if there is a significantly higher amount of the disorder (dependent variable) in the exposed group versus the unexposed (control) group.

Without this type of study, we may be simply looking at aggravation of an underlying disorder or the inability to select the study group (cohort) or causal factors without bias. Bias can critically flaw cause-effect investigations.

If the effect is not easily diagnosable, then the definition of work-related becomes even more muddled. For example, various researchers have proposed that keyboard users develop musculoskeletal disorders more frequently than nonusers. Similar to how OSHA includes work-related aggravation of an underlying disorder as a recordable occupational disease (for example, age or weight-related carpal tunnel syndrome), studies have often merely examined workers without addressing whether they have musculoskeletal problems which existed prior to their office work or they have not adequately ruled out the many causes (confounding variables) or potential causes of carpal tunnel syndrome. These cross-sectional studies, the bulk of the science in so-called cumulative trauma disorders, lack the capability to determine a causal effect.

Other studies have looked at workers exposed to certain dusts and whether there is a small but significant decrease in pulmonary function. These studies may show a drop, but they do not tell us whether this is a permanent effect. Moreover, the effect is rarely of clinical significance. For instance, the drop in the respiratory test does not affect health. Temporary, minimal changes in function should not be considered to be work-related health effects.

Causation and Bias

As mentioned previously, bias can severely affect the findings of any cause-effect study. Sources of bias include how study participants are selected, as well as how effects are defined or events are recalled. However, more recently, the scientific community is coming to grips with a more insidious bias, journal publication. As Andy Rooney of *60 Minutes* fame used to say, "Did you ever notice" how the vast majority of published studies find a positive effect? Is this simply coincidence, or is there a bias for journals to publish those studies with a positive outcome or effect? Research into this area clearly documents this and other types of publication bias.

Another bias I feel is important to recognize is how results are interpreted. Frequently, studies will find no effect, an increased effect or a reduced effect: that is, a dearth of the expected amount of the disease/disorder.

For example, in studies of the neurobehavioral effects of chemicals such as lead and solvents, study participants frequently do better on some neuropsychological battery tests and worse on others. If we interpret the negative test scores as a deleterious effect of exposure, then why don't the same researchers also speculate that the higher test score areas represent enhancement of neurologic function? Although I can't find any benefits from lead exposure, the same type of critical weighing of evidence should be used on positive and negative data as noted

here to ensure the proper assessment and use of good science.

Global Causation Determination

Although Sir Bradford Hill has been frequently quoted and his 1963 causal criteria used by various scientists, few safety and health professionals are familiar with and use those criteria, outlined below, or a similarly constructed decision-making approach:

- Strength of association
- Consistency
- Temporality
- Biologic gradient
- Plausibility
- Coherence
- Experimental analogy
- Analogy

The trick is not simply to show that the critically important criteria are fulfilled, but– just as important– how they are satisfied. For example, NIOSH used four of the criteria listed above in its 1997 musculoskeletal study review of workplace factors. While NIOSH defined categories such as "evidence for an effect" and "strong evidence," they never revealed the method employed and results used for the workplace connection. Scientists must be able to review and reproduce studies like the NIOSH study. Without an understanding of the evaluation weighting scheme used, how do we know they were accurate in their classification? For example, did they weigh negative studies equally to positive studies? Did one poorly performed study with extremely positive findings have a disproportionate influence on the ultimate assessment of all studies? The same can be said for diesel exhaust cancer studies. With such small diesel exposure-cancer effects noted and poor exposure determination and confounder control, *i.e.*, smoking, do small positive effects really mean anything?

Individual Causation Determination

How does the local clinician know that your employee's carpal tunnel syndrome, cancer or apparent memory loss is due to work? Just as the global assessment of causation for a specific exposure effect requires solid methodology for evaluating individual studies and overall assessment of all scientific evidence (causal criteria), individual case causation assessment also requires a clear step-by-step approach. In its 1977 occupational disease recognition guide, NIOSH outlined a number of criteria to aid practicing clinicians. Others have outlined similar approaches. The following criteria represent a melding of the critical factors to ensure proper individual causal association:

- Does the person really have what is prospected/alleged?
- Has the clinician diagnosed the disorder according to accepted practice parameters and using appropriate ICD-9 designators?
- Has the extent of the disorder been assessed using a well-constructed, functional assessment, or is it simply a loose association of symptoms which reportedly affect social or work performance?
- Was there actual exposure (not risk of exposure)?
- Was the exposure sufficient in duration and extent compared with that assessed globally in the scientific literature?
- Did the exposure occur before the effect (not just the clinical detection, but the onset of the pathogenesis)?
- Did the exposure have the appropriate latency?
- Did the acute reversible effect stop once exposure ceased?
- Does the global cause/effect occur in humans, and is it based on appropriately assessed weight-of-the-evidence causal determination?
- Are there other causes (alternative etiologies) which more likely explain the effect? Was a weighting method used to determine the likely cause, *e.g.,* regression coefficients?

Summary

As occupational health is focused on prevention, it is critical that accurate causation assessments be used in regulation, clinical practice, claims and litigation, and in the press. It is just as important to warn and prevent as it is to avoid the harm done to jobs, industry and workers' peace of mind by making unfounded allegations of workplace hazards. In the end, that's all sound science is really about. **OH**

Contributing Editor Howard M. Sandler, M.D., is president of Sandler Occupational Medicine Associates, Inc., a Melville, N.Y., consulting firm.