"CLINICAL TOXICOLOGY" VIEWED FROM AN INDUSTRIAL SETTING

by

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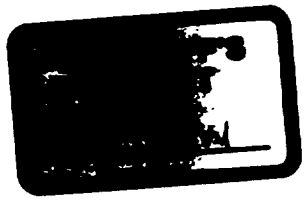

When requested to present my views on "Clinical Toxicology" in an industrial setting, my response progressed from a hearty laugh, to a query of what is it, to "what the hell" I will give it a try, no one else knows what it is either, to the anxiety of trying to fill-up 15 minutes with something other than somnolence. I have no illusions of negating somnolence; nonetheless, I am hopeful of providing a less than expert opinion of what needs there are in industry for worker and consumer health programs and how these needs may be circumscribed and called "Clinical Toxicology". Throughout this presentation, I equate industry to chemical industry.

In the 1929 Smithsonion Institute Annual Report, Boycott said "the difficulty in most scientific work lies in framing the question rather than in finding the answers, and by the time we are in a position to know what the crucial question is we have generally pretty well got the answers". Since training "Clinical Toxicologists" is an initiation of scientific work, Boycott's wisdom is prophetic. Therefore, I will attempt first to frame the questions before crystal-balling a prescription for training.

The first question is how are worker and consumer health programs handled currently? The most advanced programs consist of the following:

Toxicology Research - to elucidate the potential of chemicals to cause injury, inclusive is determination of the site and type of injury as well as the mechanism leading to its development when feasible.

Industrial Hygiene - to implement design of facilities to provide for the safe handling of chemicals and to monitor work environments to assure that proper control is a reality and to provide exposure data for analyses of associations with worker health status.

Occupational Medicine - to diagnose and institute treatment of "disease" incurred by workers or users of products and equally important, or more important, to collect data which may be analyzed to reveal subtle changes in the health of a worker population or absence thereof.

Epidemiology - to elucidate causal correlations between worker or user "disease" and exposure to chemicals.

Obviously, these disciplines must be associated inextricably. A well functioning program requires strong links since ~~adequate~~ optimum performance of each discipline depends on the adequate performance of all others. Consistently good decisions and relevant research require an integrated input.

Of course, it is also important to have strong links of communication and support from those disciplines addressing other areas of environmental research, business, manufacturing, and users. However, I will not address these aspects here. This perspective has led me to say on many occasions that the efficiency and proficiency of the industrial health program in toto is as good as the slowest ship in the convoy.

Slowness may be caused by the inadequacies of one ship or isolation of its communication system from the rest of the convoy. With respect to the latter, individuals trained for any of the areas indicated must be able to communicate not only with those in his or her specific area but with those in others, business, manufacturing, and perhaps most importantly with workers.

The second question to frame is where does a new ship called "Clinical Toxicology" fit in the convoy? I suspect most, as myself, perceive clinical toxicology to be diagnosis and treatment of chemically induced disease. However, I perceived this to be what occupational physicians are doing now, albeit they also conduct general physicals to detect spontaneous disease, treat disease not induced by chemicals, and attend to the host of administrative red tape such as insurance and disability claims. Thus, it appears that the "Clinical Toxicologist" may be an occupational physician who ignores traumatic injuries and spontaneous disease and concentrates on chemically induced disease.

If this is true, then the only reason I perceive for instituting a "Clinical Toxicology" speciality is to at least in name dignify the occupational physician. This may, in itself, be a worthy reason because the occupational physician has, for too long and unrightfully, been viewed by his colleagues as being rather low on the professional totem pole. This has, of course, deterred bright, dedicated physicians from careers in occupational medicine and resulted in utilizing doctors of

lesser qualities albeit there exist many exceptionally qualified occupational physicians. Nonetheless, I must conclude that what I perceive the "Clinical Toxicologist" to be in industry is a renamed "Occupational Physician".

Now, let's get to what I perceive the critical issue to be, whether our renamed occupational physician needs training other than that needed to diagnose and treat chemically induced disease. The answer is, unequivocally yes! The most important endeavor of the occupational physician is to prevent chemically induced disease! Therefore, for some levity perhaps, but more importantly for concept, I propose consideration of the name "Clinical Nontoxicologist" rather than "Clinical Toxicologist".

Why is it that in the medical profession more prestige and glamour is given those who diagnose and/or treat disease rather than those who prevent it? In veterinary medicine, the most demanding and intellectually satisfying ~~aspect~~ of those veterinarians dealing with farm animals is herd health control, and that is the way it should be in occupational medicine.

We need most in industry physicians who will energetically pursue and establish worker health control programs or "clinical nontoxicology". Training of such individuals will demand some adjustment in emphasis or perhaps stated better, intensified emphasis on methods and concepts of disease prevention rather than diagnosis and treatment. To implement this training, a clinical nontoxicologist must have advanced training in the following:

Toxicology and Pharmacology with emphasis on mechanism of action, interactions of chemicals, and species and genetic differences.

Biochemistry with emphasis ~~of~~ how chemicals may influence normal biochemistry and the consequence thereof and how the chemical may be acted upon by the ~~bodies~~ biochemistry.

Pathology and Physiology with primary emphasis on the pathogenesis of chronic disease. In particular, I want to highlight the need to understand all aspects of chronic disease (mechanisms, progression, treatment) since these are the most important health problems of society currently. Essential is an intense understanding of spontaneous chronic disease associated with aging.

Immunology with emphasis on how chemicals may influence immunocompetence and how this may be manifested clinically.

Behavior and Neurotoxicology with respect to subtle subclinical effects of chemicals which may influence fine manipulative tasks, or reasoning, and mental activity or reactivity.

Pharmacokinetics with emphasis on effects of dose, chemical interactions, genetic differences, and influence of existing disease on pharmacokinetic parameters.

Quantitative Science not only statistical procedures utilized in epidemiology but mathematics through differential equations.

Chemistry sufficient to provide a good concept of chemical mechanisms and physical chemical properties.

In addition to the foregoing, the "Clinical Nontoxicologist" must have training in research to augment the individual's problem solving and conceptualization ability.

The primary responsiblity will be to anticipate chemically induced disease before it occurs. To do this, the "Clinical Non-Toxicologist" must integrate information from all of those areas now existing in the industrial setting and project its implication for the human organism.

The third question is how this new endeavor should be launched? At first a more definitive goal is needed which will augment attainment of the larger more esoteric goal. I suggest that the "Clinical Nontoxicologist" initiate development of a more individualized monitoring of chemicals being handled by workers. Clinical pharmacologists exist primarily because they have employed pharmacokinetics to maximize the beneficial effects of drugs while minimizing the adverse effects on an individual basis. Take a lesson from their success! Using pharmacokinetic procedures I foresee, in the reasonably near future, a determination whether a worker can detoxify normally the chemicals with which he will work. A person having poor ability for renal excretion of organic acids will be detected and not placed in a work environment where exposure to an organic acid may be sufficient to overwhelm the ability of the individual's kidneys to excrete the compound. An individual with a genetically

mediated low level of pseudocholinesterase will be detected and not assigned to production or use of organic phosphates if the work environment is found to cause further lowering of this enzyme. An individual taking a drug which lowers the availability of glutathione (i.e. acetominophen) will not be placed in a work environment if it is found that such a lowering may depress detoxification of chemicals found therein. Thus, I perceive as a reasonable short-term goal quantitation of, on an individual basis, the worker's ability to detoxify the chemicals with which he is to work. This may be done either experimentally or conceptually although I recommend emphasis of the former; this may be done by monitoring blood and/or urine levels of the chemical(s) determined during the first few days of work. I ~~am, however, not so naive as to~~ however, concede that both social and legal restrictions may inhibit such an endeavor in spite of its logic.

In summary, "Clinical Toxicology" in an industrial setting renames what I perceive as occupational medicine currently, perhaps advantageously, and training should be intensified to enable better anticipation of potential chemically induced disease rather than to diagnose and treat the disease.