Letters to the Editor

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Vinyl Chloride and Acroosteolysis

The excellent review of the article "Occupational Acroosteolysis" in the August issue (p 670) contains an error in the nonmedical field. The statement is made that cleaning of the polymerization reactors for vinyl chloride resins must be done by hand. This is in error, as solvent cleaning and steam cleaning, which obviate the necessity of the workers entering the kettle to carry out the cleaning is a technology that has existed for some time, and, of course, has been expanding since the advent of occupational acroosteolysis. It is of interest that in those installations where this method of cleaning has been carried out there is no acroosteolysis in their PVC workers.

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Hypersusceptibility and Genetic Problems

The recent article entitled, "Hypersusceptibility and Genetic Problems in Occupational Medicine—A Consensus Report," by Stokinger and Scheel[1] makes a number of assertions with regard to work published from our laboratory and which require clarification. While the authors state that they ". . . . have tried to present a cross section . . . . without author bias," it is evident that their paper represents their personal opinion.

The authors make reference to our paper[2] and note that it is unique in that it is the only paper that examines serum alpha-1 antitrypsin levels in an industrial situation. They proceed to discredit the paper by quoting a letter to the editor of JAMA[3] but omit to refer to our reply which followed on the same page.[4] Furthermore, we should also like to point out that the very comments we made about methodology in our reply were recently raised by others in a recent symposium.[5]

Of further interest, is that about the time our study was completed, Fagerhol and Laurell[6] reported on their crossed-immunoelectrophoresis phenotyping to detect genetic variants relative to alpha-1 antitrypsin deficiency. Subsequently, in a paper by Talamo et al[7] it was shown that with the exception of the homozygote deficient (PiZZ), no correlation between serum trypsin inhibitory capacity (TIC), or concentration, and the heterozygous phenotype was obtained whether or not obstructive pulmonary disease was present. Overlapping quantitative values were reported including those with variants PiMM, PiMS and PiMZ. In our study we also found it impossible to separate heterozygotes from normal by means of TIC determinations. Talamo et al[7] go on to state that, "the clinical importance of intermediate serum alpha-1 antitrypsin deficiency remains uncertain." The recent studies by Galdston et al[8] implicating leukocyte lysosomal proteases, as well as, the studies of Starkey[9] and Werb[10] on the inhibition of cathepsins and collagenase by the alpha-2 macroglobulin fraction may prove to be relevant; it is certainly too early to tell.

There is another matter raised by Stokinger and Scheel to which we should like to address ourselves. The authors make comment on the poor reception by industry of "genetic" testing. The reason for this may be that a "cause and effect" relationship between genetic predisposition and industrial disease has not been demonstrated. Indeed there is no biological phenomenon which is not in part a result of heredity; man is a "colossal variant." What is required in this important area of research is more quantitative studies and more facts rather than glib and facile explanations. An examination of the five (5) genetic tests and criteria suggested by Stokinger and Scheel suggests that their opinions are based on hypothesis rather than fact.

Serum alpha-1 antitrypsin deficiency. — With respect to the heterozygote state, no definite association between predisposition and occurrence of bronchopulmonary disorders has been established - especially in an industrially-oriented environment. The comments by Robin[11] are particularly relevant in this connection. Furthermore, with respect to prevalence, we should like to remind the authors that Eriksson[12] found only four (4) homozygote deficients after screening a random population of 6995; and only two (2) of the four had any history of emphysema. Would this be considered by the authors a relatively high prevalence in a working population? We hardly think so, although we still feel that the test should be performed. Furthermore, it should be stated that we know of no study indicating "respiratory irritants" in conjunction with alpha-1 antitrypsin deficiency may predispose to chronic obstructive pulmonary disease.

Glucose-6-Phosphate Dehydrogenase Deficiency. — The relatively high prevalence of heterozygotes for glucose-6-phosphate dehydrogenase deficiency appears to be the primary reason that this test should be performed rather than the "promise" of detecting chronic "pill-takers;" the individuals in the latter category are more in need of psychiatric counseling than genetic testing. Furthermore, the effects due to chemical exposure and those due to genetic variations should be delineated. While the drug induced anemias can compound the situation when a genetic deficiency is present, the nature of the effects of these compounds on the erythrocyte is varied and complex. This is especially true in a redox system where the integrity of the cell membrane is clearly dependent on the integrity of the thiol (-SH) groups. Thus urea, a common nitrogen-containing metabolite, which is freely diffusable through the erythrocyte cell membrane and a strong proton binder (pK in the neighborhood of 10^{-14}) does not, to the best of our knowledge, have any potentiating effect on those with glucose-6-phosphate dehydrogenase deficiency disease.

CS_2 Genetic Testing. — The genetic risks in predisposition to CS_2 have never been clearly delineated; no genetic criteria relevent to CS_2 susceptibility have been determined. Furthermore, as the authors themselves noted, the available data (large spread in values) make the use of TETD for genetic testing highly questionable. The rate of formation of metabolic products from TETD may not be a consequence of a genetic "defect" *per se*.

Isocyanate Genetic Testing. — The immunologic testing for isocyanate allergic

reaction (delayed hypersensitivity) should be taken in context of individuals susceptible to various allergies; there is no definitive information on individuals being hypersusceptible to isocyanates which would indicate a specific genetic trait. Furthermore, the test is performed after the fact, i.e., after exposure; this could hardly be of any value in the preemployment medical examination. Moreover many doubt that the bronchoconstriction that occurs with exposure to isocyanates has anything whatsoever to do with delayed hypersensitivity. Stokinger and Scheel state that in two plants utilizing the tests — screening procedure — that "clinical reactors" have been eliminated. The statement can hardly be construed as the final answer - certainly the authors give no data.

Sickle cell-trait; Hemoglobinopathies. — The screening for the sickle-trait or for other hemoglobinopathies in the preemployment medical examination in relation to occupational hazards has become highly controversial - no doubt due to sociological implications. With the exception of airline pilots and stewardesses, there seems no justification for denying employment because the potential employee has HbAS or any of the other variants. Of course, in the case of sickle-cell anemia (HbS), this is hardly a factor to be considered in employment since the overt symptoms have long been manifested prior to employment age.

In summary, we would hope that in the not too distant future a "genetic profile" can be performed in the preemployment medical examination for workers in various industries relevant to a particular occupational hazard that may exist. However, in view of the fragmentary information presently available in this area, prudence is certainly required not only in the selection of the genetic tests, but more importantly in the interpretation of results in terms of the worker's ability to handle a particular job requirement. In this regard, we are in complete agreement with the concise and rational opinion of Cooper.[13] We whole heartedly agree with the opinions expressed by this author whose insight into the problems related to genetic testing is well taken, and whose caution in prescribing various tests are well founded on facts as they are presently known. In the meantime, it would be helpful if those who spend their time writing "consensus reports" (sic!) would not cast aspersions on other investigators' works until *all* the facts are available.

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Are Medical Ethical Practices Sufficient in Industrial Medicine?

How frequently have you heard an industrial physician remark, after describing an occupational hazard with which he has had personal experience, "Of course, we couldn't publish that" or "Management refused permission to publish that study" or "We don't dare report the frequency of that reaction in our plant." We all know this situation exists now in the U.S. Many corporations maintain censorship of publications from their medical departments to protect themselves against lawsuits and raised insurance premiums and discontent among workers. Company physicians generally comply because to do otherwise would mean termination of their employment by that company and possible interference with future similar employment by other companies. The result has been that an uncertain volume of medical documentation of human occupational health impairment has been classified as secret by U.S. private industry with no assurance that the rest of the medical profession will ever benefit from this knowledge. It is probably a principal reason why occupational medicine is so little recognized and appreciated by the majority of physicians. This common practice of withholding industrial medical study results runs counter to the prevailing trend in other medical specialties to publish findings as soon as possible, so that the entire profession and the public it serves may benefit as quickly as possible from new concepts and documentation.

One of Hippocrates' fundamental precepts was that medicine is an ethical profession and should publish its failures as well as its successes, so that all should know what to expect. It follows that physicians who can document health hazards not generally known to the rest of the profession should, ethically, convey this knowledge in a scientific manner at least to the rest of the medical profession so that their colleagues could provide more effective services based on more complete knowledge. It also follows that failure to do this would be a breach of medical ethics by an act of omission. Note that we do not claim compromise of business ethics by management but rather compromise of medical ethics by physicians who must maintain a professional identity separate from management. Most industrial physicians identify strongly with management for sociologic and financial reasons, and some may forget that the ethical guidelines for the medical profession are more restrictive than for businessmen. Failure to recognize and adhere to medical ethical standards can only downgrade those who so stray, and that may be part of the nonrecognition problem that the occupational medicine specialty experiences today.

The question of professional publication of human toxicologic experience from industry is particularly pertinent now for two reasons. First, other physicians are generally eager to learn about health hazards of the environment now that public interest is