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Letters to the Editor

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.

R. Emmet Kelly, M.D.
Box 526
St. Louis, Mo. 63166

Hypersusceptibility and Genetic Problems

The recent article entitled, "Hypersusceptibility and Genetic Problems in Occupational Medicine—A Consensus Report," by Stokinger and Scheel¹ 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 paper² 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 JAMA³ 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 Laurell⁶ reported on their crossed-immuneoelectrophoresis phenotyping to detect genetic variants relative to alpha-1 antitrypsin deficiency. Subsequently, in a

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paper by Talamo et al⁷ 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 al⁷ go on to state that, "the clinical importance of intermediate serum alpha-1 antitrypsin deficiency remains uncertain." The recent studies by Galdston et al⁸ implicating leukocyte lysosomal proteases, as well as, the studies of Starkey⁹ and Werb¹⁰ 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 Robin¹¹ are particularly relevant in this connection. Furthermore, with respect to prevalence, we should like to remind the authors that Eriksson¹² found only four (4) homozygote deficient after screening a random

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population of 695; and only two (2) of the four had a 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 the 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 readily diffusible through the erythrocyte cell membrane and a strong proton donor (pK in the neighborhood of 10⁻⁴) does not, to the best of our knowledge, have any potentiating effect on those with glucose-6-phosphate dehydrogenase deficiency disease.

CS₂ Genetic Testing. — The genetic risks in predisposition to CS₂ have never been clearly delineated; no genetic criteria relevant to CS₂ 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