

CORRESPONDENCE

Haemolytic anaemia in a case of occupational asthma due to maleic anhydride

Sir.—The short report by Gannon *et al* (1992;49:142-3) is misleading in two important respects. In our view the patient did not have occupational asthma and there is insufficient evidence of a relation between his exposure to maleic anhydride and the development of haemolytic anaemia to suggest a hitherto unrecognised toxic effect of maleic anhydride.

The patient is atopic and there is some documentary evidence of childhood asthma although he does not recall this. During the first few days of his work on the maleic anhydride plant in 1961 he had an episode of bronchospasm almost certainly as a reaction to heavy exposure to fume including maleic anhydride among other irritants. This must be presumed to have been an irritant response as he had not had sufficient exposure to have acquired immunological hypersensitivity. He was removed from heavy exposure on the manufacturing plant but then worked in laboratory environments where he continued to have substantial exposure to maleic anhydride for a further 15 years. There was also some exposure to phthalic anhydride during this period. Nevertheless, at no time did he report to his family doctor or to the works medical department with symptoms of asthma. In fact there is no record of his attendance at the medical department for any reason during this period. IgE concentra-

tions were not measured until after his two haemolytic episodes when they were found to be raised. This probably only reflects exposure; a study now in progress indicates that about 15% of those exposed to maleic anhydride show, by RAST, IgE binding to human serum albumin-maleic anhydride conjugates without any respiratory symptoms.

Clinical asthma first developed in this patient soon after his return to work after his first haemolytic episode. This was before he resumed a work pattern that would have increased his exposure to maleic anhydride (see figure). When, in fact, his exposure did increase his asthmatic symptoms did not get worse. On the other hand they persisted after his second haemolytic episode despite his having ceased work at the factory. He lives about 8 km from the works and significant exposures from gaseous emissions are hardly credible.

Autoimmune haemolytic anaemia is normally cryptogenic. No external causative agent is detectable in most cases although a few medicaments have been associated with it. In this case the first episode had been preceded by an illness presenting with malaise, tiredness, weakness, headache, and shivering. Any presumptions about a cause for his haemolysis, if it existed, must be speculative. Logically, however, a preceding viral illness would seem to be at least as likely a precipitating factor as a chemical substance.

It is, of course, impossible to exclude maleic anhydride as the causative agent. We believe the connection is unlikely because:

(1) there were many years of expo-

sure to maleic anhydride before his first episode of anaemia; (2) there were no haemolytic antibodies to red cell-maleic anhydride complexes; (3) there is no similarity whatsoever between the pulmonary haemorrhagic and haemolytic condition associated with trimellitic anhydride and the pathology in this case.

In the unlikely event of his haemolytic anaemia being caused by maleic anhydride in our view there was no demonstrable additional association with occupational asthma. Although his second episode of anaemia occurred after his return to shift work with its attendant increased exposure to maleic anhydride his asthma preceded this by several weeks. The time relations are shown in the figure.

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The Authors' reply

The one clinical fact about which we agree with Jackson and Jones is that this man is highly sensitised to maleic anhydride with extremely positive IgE antibodies to maleic anhydride: human serum albumin conjugate.

The basis of diagnosis of occupational asthma in this case was from the history of asthmatic symptoms deteriorating at work and improving away from work, which is the usual method of making this diagnosis. It is correct to suggest that in general allergic reactions do not occur with the first exposure and a period of exposure without symptoms would usually be expected; however, sensitisation may be induced by a single large exposure. Once sensitised, very small exposures can elicit symptoms. It is quite likely that exposures could be sufficient to cause asthma in a sensitised subject without haemolysis or that the immunological mechanisms responsible for the haemolysis took longer to develop. A similar situation occurs in patients with asthma and alveolitis, where much larger exposures are required to elicit the alveolitis. The persistence of asthmatic symptoms after removal from exposure is in keeping with the natural history of asthma induced by other chemicals including isocyanates.

The maleic anhydride exposure

