Down's Syndrome, Hypothyroidism, and Diabetes Mellitus

Sir,—The observation that some diseases are associated with chromosomal disorders—for example, congenital heart disease and Hirschsprung's disease in Down's syndrome—has raised the question of whether this association therefore seems right to draw attention to other, similar associations. There have been two previous reports of patients with Down's syndrome who have developed both hypothyroidism and diabetes mellitus1 and I now report a third.

The patient, a girl, was the sixth child of a 35-year-old mother. She was diagnosed at birth as having Down's syndrome and this was later confirmed by chromosome analysis (trisomy-21). Her growth and development were slow but she was cherished by her family and during her fifth year she began to attend a junior training centre. However, at the age of 5 years it was noticed that she appeared to be hypothyroid. Her height and weight were well below the third centile and she had thin, dry hair, a pale puffy face, and cold hands. Her bone age then was 1 year 3 months (Greulich and Pyle's method), her Thyroac-3 ratio was 1.24, her hypothyroid range, and her serum thyroid-stimulating hormone (TSH) level 480 u/m1. She was therefore started on treatment with thyroxine and this resulted in a definite growth spurt. When she was 61 years old her raised serum TSH, which had been in diabete comata, her blood sugar being 1,800 mg/100 ml, she was treated with 125 mg/100 ml. She died the day after and necropsy was not performed.

This patient's history suggests two things. The first is that it now seems unlikely that the association of hypothyroidism, diabetes mellitus, and Down's syndrome should have occurred by chance. The second, confirmed by her raised serum TSH level, is that hypothyroidism in Down's syndrome, an association that has been reported on several occasions,2 is of thyroid rather than pituitary origin.—I am, etc.,

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Threshold for Oxygen Pneumonitis

Sir,—In a recent paper by Sewitt it is suggested that it may be dangerous to expose patients to higher concentrations of oxygen than 40% on the grounds that this may give rise to focal or diffuse pneumonitis. It has been appreciated for many years that oxygen therapy carries certain hazards but it is generally considered that to cause pulmonary damage the concentration must be appreciably greater than 40%. Because of the extensive use of oxygen therapy in wards and special units we believe it is important to review the evidence presented in the paper before accepting the opinions expressed, with all their implications.

Out of 21 patients surveyed, 18 had sustained pulmonary trauma either directly or indirectly. These included: inhalation, 3; carbon monoxide inhalation, 3; possible fat embolism, 2; smoke inhalation, 2). Three patients did not have primary pulmonary damage but had sustained head injuries, and no mention is made of the possibility of consciousness of these (or other) patients.

The values quoted for the concentrations of oxygen breathed by the patients were spread over a very wide range and were measured in only six cases, and no blood gases tensions are given. One adult patient is stated to have been maintained inside an oxygen tent at 40% (measured) for eight days. This is almost impossible to achieve unless the tent was never opened for feeding or other nursing or therapeutic procedures, because each time it is opened the atmosphere returns to that of ambient air and, because of its large capacity, there is a considerable delay before the desired oxygen concentration can be achieved after each manoeuvre.

Finally, the paper is reference made to other methods of treatment or to coincidental clinical disturbances such as sepsis, cardiac failure, or renal failure. There are several reasons why these omissions may be significant in this context. It has been known for many years that respiratory failure is an important cause of the morbidity and mortality of patients suffering from trauma, haemorrhage, or poisoning and the syndrome of post-traumatic respiratory insufficiency ("shock lung") is of great interest. There are many possible causes for this condition which include hypoxaemia, fat embolism, pulmonary oedema, pulmonary congestion, endotoxaemia, disseminated intravascular coagulation, and pulmonary micro-emboli originating in transfused blood or pulmonary injury and the syndrome of oxygen toxicity may also be incriminated, but it is essential to exclude these other conditions before attributing this clinical syndrome exclusively to oxygen toxicity.

Finally, it must be recognized that the lungs can respond in only a limited way to a variety of physical, infective, or metabolic insults and that the histological changes described in the paper may be seen in conditions as varied as infection, pulmonary burns, renal failure, and paraquat poisoning.

We believe that this paper draws attention to the potential hazards of oxygen therapy but that the findings may be interpreted in another way.—We are, etc.,

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4 Stoddart, J. C., and Wardle, E. N., British Journal of Anaesthesia, 1974, in press.

* Drs. Ferris and Stoddart sent a copy of their letter to Dr. Sewitt, whose reply we print below.—Ed., B.M.J.

Sir,—My paper is criticized by Drs. Ferris and Stoddart on a number of grounds, though it admit that high concentrations of inspired oxygen for a sufficient time can cause serious hypoxaemia from pulmonary damage. My purpose was to try to ascertain the threshold oxygen concentrations and periods of exposure which can produce lung damage in man. This important aspect is very difficult to establish in man from clinical observations alone as so many factors are involved, and it has not apparently been investigated in animals. A combined clinical-pathological approach was required.

A group of patients who reached necropsy after various exposures to oxygen therapy were studied, some of whom died with and others without hypoxaemia. Essential details of the arterial Po2 values are given in the paper if Drs. Ferris and Stoddart will read it again. For histological assessment the definitive criteria of pulmonary hyaline membrane and proliferative pneumonitis were used and the findings divided into diffuse and focal pneumonitis. These were correlated with the presence or absence of hypoxaemia, radiological changes, and other matters, and from the overall findings it was concluded that breathing 40% oxygen for a sufficient time seems to be the threshold for dangerous lung effects. Higher 'shock lung' was observed, investigated, and not confirmed. Pneumonitis appeared only when oxygen had been given.

My critics state that "it is generally considered that to cause pulmonary damage the exposure of oxygen must be appreciably greater than 40%". What evidence have they for this statement? By comparing the pulmonary effects of concentrations ranging from 30% to 100% oxygen given for various periods, they found that the pulmonary lung changes, and threshold. This approximation has been confirmed in two more recent patients given 40% oxygen for days. One died with severe hypoxaemia and diffuse bilateral pulmonary necrosis, while the other recovered.

With great respect to Drs. Ferris and Stoddart, may I add that their letter reflects a kind of rearguard action of the curious opposition in certain circles during recent years to the concept that too much oxygen can damage the lungs?—I am, etc.,

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Other Systemic Effects of Eye Drops

Sir,—The interesting report by Mr. M. K. Wang and Dr. J. R. Tatane (9 March, p. 453) of hallucinations in their 6-year-old patient which followed the installation of one drop to each eye of 1% cyclopentolate followed by one drop of 0.25% hyoscine