obstructive embolism of the main pulmonary artery; a defective artificial valve; tamponade; a gross tension pneumothorax; and severe subvalvular obstruction as in pulmonary infundibular shutdown.

If one of the abovementioned conditions is present, permanent brain damage may ensue despite correctly executed cardiac massage and artificial ventilation. Failure of resuscitation will only become apparent when no signs of brain activity can be elicited and then it could be too late. The capnograph may give proof of ineffective cardiac massage at a stage when signs of brain activity are still present and other measures can be instituted at a much earlier stage, as was demonstrated in case 1. Here the surgeon was informed that the massage was ineffective at a stage where the pupils of the patient were still small. In case 2, signs of cardiovascular failure occurred only after CO_2 content of alveolar gases dropped to zero. The reason why it occurred at that late stage might be ascribed to the fact that the patient was cooled down to 30°C by surface cooling. In case 3, the surgeon could also have been warned at an early stage of impending cardiovascular failure.

It is felt that much can be gained and lives can be saved if capnography is used routinely in the care of the critically ill patient.

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Familial Waldenström's Macroglobulinaemia

A Case Report

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SUMMARY

A patient with Waldenström's macroglobulinaemia, whose father died of the same condition, is presented. The literature on familial occurrence of paraproteinaemia is briefly reviewed.

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The finding of a familial incidence of paraproteinaemia is most unusual, but it is known to occur both in Waldenström's macroglobulinaemia and in multiple myeloma. A patient with Waldenström's macroglobulinaemia, whose father died of the same illness, is presented.

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CASE REPORT

The father of our patient was born in 1892 and was first seen in December 1961 because of general malaise, irritability, loss of appetite and loss of weight. He had a previous history of pulmonary tuberculosis, malaria, Malta fever and a tendency to bony fractures, of which he had had several. He was found to be anaemic and his liver and spleen were palpable 3 cm and 2 cm below the costal margin, respectively. His ESR was constantly in the region of 130 mm/h (Westergren). He was found to have a total protein of 10,2 g/100 ml, with 7,6 g/100 ml globulin. There was no Bence Jones protein, and radiological examination and study of bone marrow aspirate were negative. He was referred to Germany where he was seen by Professor L. Heilmeyer in July 1962. Investi-

gations confirmed monoclonal gammopathy, and ultracentrifugal analysis showed a marked increase in macroglobulins. Biopsy specimens of marrow, liver, and spleen revealed infiltration by the plasmacytoid lymphocytes which are seen in Waldenström's macroglobulinaemia. He was treated with steroids and received transfusion as required. In 1966 a splenectomy was performed, which showed infiltration characteristic of Waldenström's macroglobulinaemia. The patient died shortly thereafter, but the cause of death is unknown.

His son, born in 1929, was first seen in November 1975 because of complaints of generalized muscle aching, malaise and lack of energy. He had had a thyroidectomy in 1960 and was on replacement therapy. Examination was entirely negative. Laboratory studies revealed normal thyroid function and a normal peripheral blood count. The ESR, however, was elevated at 40 mm/h (Westergren). Chemical investigation of serum showed normal renal and liver function, normal calcium levels, and an elevated total protein of 9,4 g/100 ml of which 4,9 g/100 ml was globulin. The monoclonal gammopathy was due to IgM, which had a concentration of 2,73 g/100 ml. IgG and IgA levels were within normal limits. Bone marrow aspirate and trephine biopsy specimens appeared normal. It was decided to observe him at monthly intervals. Some 3 months later he was overtly depressed; treatment with a tricyclic antidepressant cleared all his symptoms, including those present at first. Eight months later, while still on antidepressant therapy, he again complained of stiffness of muscles and general lack of energy. Physical examination was entirely negative, but bone marrow biopsy demonstrated areas of infiltration by plasmacytoid lymphocytes. Repeat bilateral bone marrow aspirates and trephine biopsies confirmed the abnormal cellular infiltrate and, in view of this, therapy with chlorambucil and prednisone was commenced.

DISCUSSION

The first well-documented case of multiple myeloma which occurred in a family appears to be that reported by Mandema and Wildervanck,[1] followed by reports from Nadeau *et al.*[2] and Herrell *et al.*[3] Waldenström's macroglobulinaemia in 2 brothers was documented by Massari *et al.*[4] in 1962.

Seligmann *et al.*[5,6] studied the sera of 216 close relatives (192 first-degree) of 65 patients with Waldenström's macroglobulinaemia. An IgM-type 'M-component' was found in 8 of the 216 relatives, 6 of whom were apparently healthy. Typical Waldenström's macroglobulinaemia occurred in 2 siblings in each of 2 families.

Spengler *et al.*[7] reviewed the available literature and could find only 21 families with a familial incidence of paraproteinaemia and added 4 patients of their own. Of these 4, 1 patient's maternal aunt had died of myeloma, and 2 patients each had an affected sister — 1 with an asymptomatic IgG and 1 with an asymptomatic IgM paraprotein. The 4th patient had Waldenström's macroglobulinaemia and his daughter showed an IgM paraprotein.

The familial association demonstrated is clearly significant, and the incidence of elevated IgM levels, as reflected in electrophoretic 'spikes' in relatives of patients with Waldenström's macroglobulinaemia, is much higher than in the population at large. The incidence of elevated immunoglobulin levels in a random sample of the adult population of Sweden was less than 1%,[8] and only 8% of the spikes on electrophoretograms were of the IgM class. Seligmann *et al.*[6] found no IgG or IgA spikes in the relatives of their patients with Waldenström's macroglobulinaemia.

The brother reported by Massari *et al.*[4] appeared to have macroglobulins of a very similar, if not identical, structure. Their mother had no clinical symptoms, but her serum contained elevated levels of γ-I-macroglobulin. The authors felt that the disease might be inherited, becoming manifest only in the homozygous state.

Seligmann *et al.*,[6] on the other hand, found that in different affected family members, the biochemical and antigenic structures of the paraprotein were never identical. Of great interest is one family in which the asymptomatic mother's serum contained a single electrophoretic IgM spike with two distinct types of macroglobulin. One possessed individual antigenic specificity similar, if not identical, to the macroglobulin of the son, while the other shared the individual specific antigens of the macroglobulin of the other son.

It has been postulated that environmental factors may be of importance, but the evidence for this is unconvincing. Transmission by sex-linked inheritance and by autosomal inheritance has been suggested. Although no definite mode of inheritance has been formulated, it seems highly probable that a genetically determined immunological abnormality exists, perhaps requiring the influence of non-hereditary factors.

At present it is uncertain as to what proportion of asymptomatic patients with monoclonal spikes will develop the malignant process. There is no good correlation between the level of the paraprotein spike and the plasmacytoid-lymphocyte infiltration of the marrow. It is difficult to define the early stages of Waldenström's disease, hence our policy in this case has been to do marrow aspirates and trephine biopsies approximately every 6 months and to examine the patient clinically every month. In view of the fact that 'benign monoclonal gammopathies' of the IgM type do exist, a paraprotein spike in an asymptomatic patient is insufficient reason to commence therapy, even when there is a family history of Waldenström's macroglobulinaemia.

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