analysis does not take this into account. Nevertheless, with the precautions taken, in the experience of the assay laboratory, such variation alone would be unlikely to account for the results obtained.

Transplant function was arbitrarily defined as good, moderate, and poor, and the patients in these subgroups were fairly evenly distributed in respect of antibody titre groups. Though the numbers were small it is reasonable to claim that there was no correlation between the degrees of renal function and the response to vaccination. Moreover, the response to vaccination in the transplant patients seemed to be unrelated to the length of time since transplantation or to the total administered doses of prednisone used for immunosuppression. None of the patients whose transplant function was classified as good or moderate showed any evidence of rejection episodes after vaccination, but the four patients whose renal function was classified as poor, and who had clinical and biochemical evidence of rejection before vaccination, continued to reject their kidneys after vaccination and three had to be returned to the haemodialysis programme before the end of the 12-month period. None of the controls or the transplant patients reported or was considered to have had a clinical illness suggestive of influenza in the three months after vaccination.

When compared with the controls, who were not receiving immunosuppressive therapy, the IgG levels were significantly lower in the transplant patients who were receiving immunosuppressive therapy. The difference was apparent both before and after vaccination (Ross 1972).

The results suggest that it is safe to vaccinate kidney transplant patients with inactivated influenza vaccine and that a measure of protection can be achieved despite immunosuppressive therapy without increasing the risk of graft rejection. In view of the reported association between viral infections and transplant rejection (Simmons *et al.*, 1970; David *et al.*, 1972; Briggs *et al.*, 1972) this protection may have special significance.

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MEDICAL MEMORANDA

Acute Upper Respiratory Tract Obstruction Complicating Childhood Leukaemia

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Though acute leukaemia in children is still a fatal disease an aggressive approach to treatment has much increased the duration of survival (*British Medical Journal*, 1973). Some 50% of children can be expected to live for five years (Pinkel, 1972) and in 50% of all cases neurological complications will develop during treatment (Sinks, 1972). With longer survival potentially fatal crises may be expected to occur in other systems (Sherman *et al.*, 1973). The two cases reported here show that these crises should not be regarded as preterminal and that appropriate treatment should be given.

Case 1

The patient was a 3½-year-old girl in whom acute lymphoblastic leukaemia had been diagnosed 18 months previously. Remission had been induced with vincristine and prednisolone. In a relapse 13 months later remission was obtained with cytarabine and daunorubicin. A further relapse three months before admission did not respond to cytotoxic agents but prednisolone was continued.

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On admission she had a dry cough, vomiting, pyrexia (38·6°C), tachycardia, and a monilial infection of the mouth and posterior pharyngeal wall. She was treated with intravenous gentamicin and oral nystatin. The next day her condition deteriorated and there were signs of circulatory failure. Treatment with hydrocortisone, fusidic acid, and intravenous fluids was started. Investigations showed Hb 15·8 g/100 ml; white blood cells 800/mm³ (neutrophils 26%, lymphocytes 68%, monocytes 4%); and platelets 21,000/mm³. Blood culture grew *Streptococcus pneumoniae* sensitive to fusidic acid. Serum electrolyte values were Na 130 mEq/l., K 3·5 mEq/l., Cl 92 mEq/l., HCO_3 17 mEq/l., urea 39 mg/100 ml.

Her condition improved, but after two days she suddenly developed upper respiratory obstruction with a pool of mucus in the posterior oropharynx and a blue swelling visible on the posterior pharyngeal wall when she retched. A retropharyngeal haematoma was diagnosed. Within three hours increasing obstruction required the insertion of an airway. Pharyngolaryngoscopy showed a large, blue haemorrhagic swelling involving the right posterior pharyngeal wall, valecullae, both aryepiglottic folds, and spreading into the right pyriform fossa. The laryngeal vestibule was reduced to a small slit and the vocal cords were obscured. There were large white patches of monilia in the pharynx and larynx. A plastic nasotracheal tube, internal diameter 5·5 mm, was passed with some difficulty. After recovering consciousness she was nursed in a mist tent containing 30% oxygen. The nasotracheal tube was well tolerated without sedation and respiratory obstruction was relieved. During the next 48 hours her condition improved, but large bruises developed over the legs, the right side of the neck, and the trunk. Melaena stools were passed. A blood count showed Hb 8·1 g/100 ml; W.B.C. 600/mm³ (neutrophils 54%, lymphocytes 44%, blast cells 2%); and platelets 8,000/mm³. Four units of platelets and two of blood were given.

Within 72 hours of intubation she had improved. Pharyngolaryngoscopy showed that the haemorrhagic swelling had resolved apart from thickening of the aryepiglottic folds. Patches of monilia were still visible. On removing the endotracheal tube the vocal cords and subglottic region were easily seen and appeared normal. Her immediate postoperative recovery was uneventful. After 56 hours, however, generalized convulsions occurred and lumbar puncture produced heavily blood-stained cerebrospinal fluid. She died 36 hours later. Necropsy showed evidence of leukaemia with a left retroperitoneal haemorrhage and a subarachnoid haemorrhage over the left parietal lobe. Haemorrhagic areas were seen beneath

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the endocardium of the right atrium and left ventricle. The mucosa of the larynx and upper trachea was rough and haemorrhagic. Histology of the larynx showed oedema, haemorrhage, and inflammatory changes with abundant monilial hyphae and bacteria in the slough (fig. 1). Low-grade leukaemic infiltration was present, particularly in the glandular and periglandular areas of the supraglottic region (fig. 2).

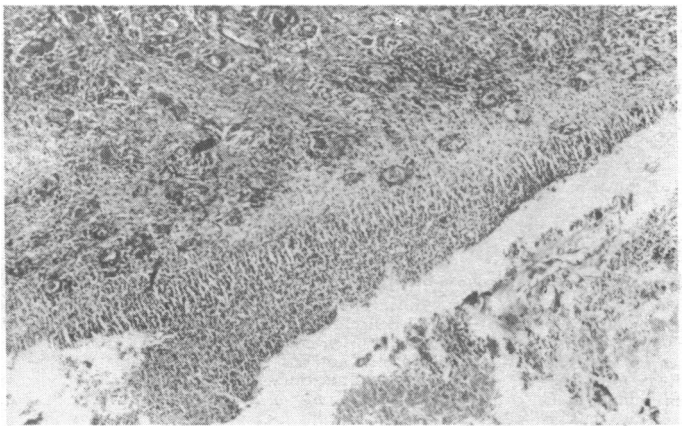

FIG. 1—Photomicrograph of supraglottic region showing submucosal hyperaemia, haemorrhage, and cell infiltration. (Haematoxylin and eosin. × 52.)

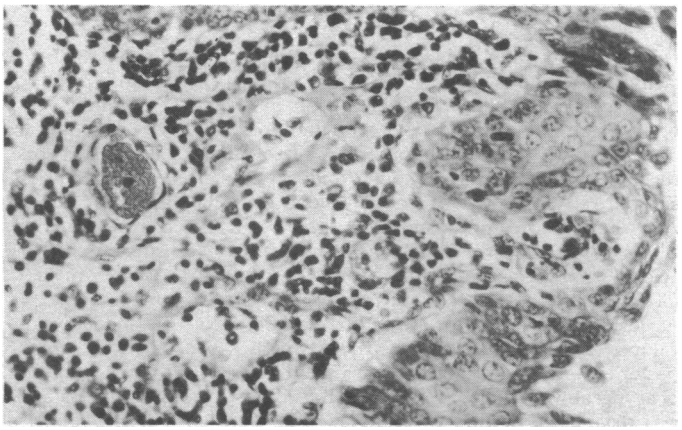

FIG. 2—Photomicrograph of mucosa and submucosa of supraglottic region showing leukaemic infiltration. (Haematoxylin and eosin. × 350.)

Case 2

A 15-year-old girl was admitted to hospital with a history and clinical findings suggestive of acute leukaemia. A blood count showed Hb 4 g/100 ml; W.B.C. 2,200/mm³ (neutrophils 4%, lymphocytes 93%, blast cells 3%); and platelets 28,000/mm³. Bone marrow investigation confirmed the diagnosis of acute lymphoblastic leukaemia. She was treated with blood transfusion and antileukaemic therapy according to the Medical Research Council UKALL II regimen. Two weeks after admission she complained of sore throat, cough with sputum, and dysphagia. A throat swab grew monilia and *Staphylococcus aureus* and a course of penicillin was started. Later that day she developed acute upper airway obstruction. Laryngoscopy showed a grossly oedematous and distorted larynx, the oedema particularly affecting the left arytenoid area, aryepiglottic fold, and left false cord. The obstruction was relieved by inserting a 5·0 mm internal diameter nasotracheal tube—the largest that would pass through the larynx. Eight hours later an elective tracheostomy was performed and an 8·0 mm internal diameter tracheostomy tube inserted. Laryngoscopy under general anaesthesia eight days later showed a decrease in the glottic oedema but an inflamed larynx and subglottic narrowing. The tracheostomy tube was removed without difficulty 15 days after its insertion. The sore throat had resolved and there were no respiratory problems. One month after admission she was discharged, and 17 months later she was still in remission.

Comment

There have been few reports of upper respiratory tract obstruction in acute leukaemia. Leukaemic infiltration, infection, or haemorrhage affecting the larynx or surrounding structures may be the cause. Hersh *et al.* (1965) make no mention of respiratory obstruction in a 10-year study of 414 patients dying of acute leukaemia, though two cases of massive nasopharyngeal haemorrhage were recorded. Leukaemic infiltration of the larynx in adults probably occurs more often than reported (Vaughan Jones and Shalom, 1967). This may be so in children also, though laryngeal symptoms are uncommon (Morris Jones, 1973). The infiltration in the supraglottic region in our case 1 was not considered to be the cause of the respiratory obstruction. There was no definite evidence of infiltration in case 2, but this could have caused the subglottic narrowing seen after the acute episode. Immunosuppression by antileukaemic agents increases the tendency to infection, particularly with fungi (Simone *et al.*, 1972), and we think that the obstruction was caused by laryngeal infection in our case 2 but not precipitated by moniliasis in case 1.

Bone marrow depression during antileukaemic therapy is common and episodes of haemorrhage are a real danger. The situation is similar to that in children with classical bleeding disorders. Haemorrhage into the retropharyngeal and laryngeal tissues produces a definite risk of respiratory difficulty and possible asphyxia. Haemorrhage was thought to be the cause of obstruction in case 1. Though there was no history of trauma haemorrhage may have been started by coughing or crying, as in cases of haemophilia (Pochedly and Rosales, 1968). There was no evidence of haemorrhage in case 2.

Respiratory obstruction can be successfully managed if energetically treated. A nasotracheal tube is preferable in infants and young children because it can be more easily managed and the hazards of tracheostomy, particularly when there is a bleeding tendency, can be avoided. In older children a tracheostomy may be necessary and should not be withheld.

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