with childhood malignant disease in general. We found that in children of mothers with epilepsy six of the 39 tumours were lymphomas (ICD, ninth revision, categories 200-202); of these six children, one was classified as having Letterer-Siwe disease and two were brothers whose tumours were classified as familial histiocytosis. If the proportion of lymphomas had been the same as that in the study as a whole, four cases would have been expected; similarly, in the children of mothers reporting tuberculosis five of the 27 tumours were lymphomas, whereas two would have been expected.

Li *et al*[6] suggested that there is an association between phenytoin and lymphomas; in this study, however, five of the mothers whose children developed lymphomas had been treated with phenobarbitone during pregnancy and none had received phenytoin.

While the slight excess of lymphomas found in the present study is of some anecdotal interest, the results reported here do not really provide any evidence of a transplacental drug effect in the aetiology of childhood cancer. Other illnesses during pregnancy may possibly have been treated by drugs that are carcinogenic to the fetus. Some degree of reassurance, however, may be derived from the present study, since we considered two of the illnesses most likely to yield positive results yet found no association between drugs used to treat them and cancer in children.

We thank Dr Alice Stewart, who collected the original data in the Oxford Survey of Childhood Cancers, and Dr L M Kinnier Wilson for her help in abstracting the data for this report.

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References

[1] Herbst, A L, Ulfelder, H, and Poskanzer, D C, *New England Journal of Medicine*, 1971, **284**, 878.
[2] Gold, E, *et al*, *Journal of the National Cancer Institute*, 1978, **61**, 1031.
[3] Pendergrass, T W, and Hanson, J W, *Lancet*, 1976, **2**, 150.
[4] Sherman, S, and Roizen, N, *Lancet*, 1976, **2**, 517.
[5] Blattner, W A, *et al*, *Journal of the American Medical Association*, 1977, **238**, 334.
[6] Li, F P, *et al*, *Cancer*, 1975, **36**, 1359.

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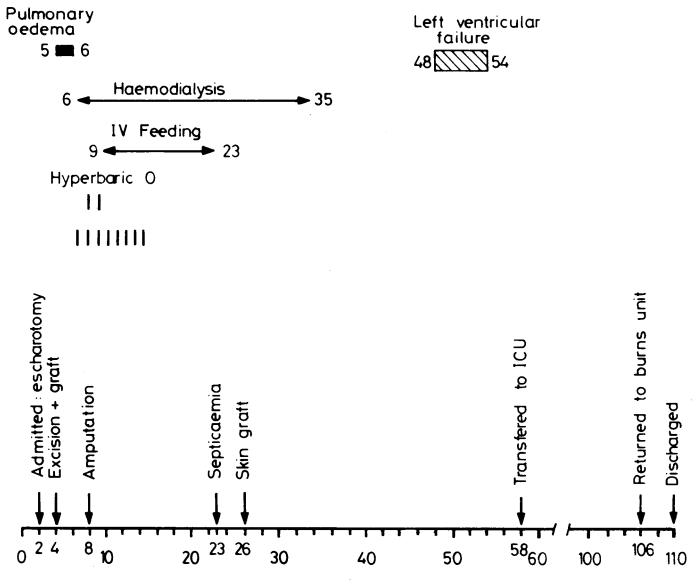
SHORT REPORTS

Survival after major burn complicated by gas gangrene, acute renal failure, and toxic myocarditis

Patients with burns who develop acute renal failure or gas gangrene rarely survive. We describe a patient who survived both these complications and believe that with early and aggressive treatment the outlook in such cases may be improved.

Case report

A 36-year-old man sustained a 53% burn (30% full-thickness) of trunk, thighs, and left arm from burning petrol. After resuscitation he was transferred to the McIndoe Burns Unit. Relieving incisions through the deep circumferential burn of the arm were performed immediately, and on the fourth day this burn was excised and grafted (see figure). Over the next two days urinary osmolality became fixed at 320 mmol(mosmol)/kg, although urine output remained at about 2 l/24 h. Plasma urea rose to 23 mmol/l (139 mg/100 ml) and pulmonary oedema developed. Non-oliguric acute renal failure was diagnosed, and on the sixth day haemodialysis was started by the mobile dialysis unit.



Time after burn (in days) of each major event.

On the seventh day gas gangrene of the left arm was diagnosed clinically and confirmed by culture of *Clostridium welchii*. The patient's condition precluded immediate operation, and treatment with hyperbaric oxygen was instituted by the mobile hyperbaric unit. Intravenous benzylpenicillin and metronidazole were started. One hour's treatment in the hyperbaric chamber, at three atmospheres absolute pressure, was given on 10 occasions over seven days until three consecutive bacteriological cultures were negative. On the eighth day the left arm was amputated by disarticulation at the shoulder. Daily haemodialysis was continued for 30 days. Total parenteral nutrition was given for the first two weeks until oral and nasogastric intakes were adequate. Plasma urea was kept below 30 mmol/l (181 mg/100 ml) and catabolism was controlled, there being an average rise in urea of 10 mmol/l (60 mg/100 ml) between dialyses.

On the 23rd day the patient developed *Escherichia coli* septicaemia, which was treated successfully with intravenous amikacin. On the 28th day skin grafts were taken from the legs and the back was grafted. Two weeks after dialysis had been discontinued he developed left ventricular failure with rapid atrial flutter, thought to be caused by a toxic myocarditis. Digoxin and frusemide were given and he was transferred to an intensive care unit (ICU). His anaemia (haemoglobin 6 g/dl) was thought to be aggravating the cardiac failure, and fresh packed red cells were given. Transfusion had been withheld till then because of its adverse effect on recovering renal function.

He was discharged home on the 110th day with a creatinine clearance of 66 ml/min. Three months later he had made an excellent physical and psychological recovery.

Comment

We can find only 11 reported cases of burned patients surviving acute renal failure and have recently described a further four.[1] Seven of these 15 patients had limb amputations. We can find only five reported cases of burned patients surviving gas gangrene.[2]

Several factors probably contributed to the successful outcome in the present case. Early recognition of non-oliguric renal failure permitted prompt and adequate dialysis. This improved the prognosis by keeping the blood urea below 33 mmol/l (199 mg/100 ml)[3] and removing enough fluid to allow adequate feeding.[4] Hyperbaric oxygen treatment of a patient moribund with gas gangrene improved his condition enough to permit operation, which removed a source of infection and possibly burn "toxin." Despite the large burn, a major operation, septicaemia, myocarditis, and anaemia the patient healed satisfactorily and did not develop progressive pulmonary insufficiency. This was almost certainly due to the control of catabolism by adequate

nutrition, by removing the arm, and by appropriate antibiotic treatment of septicaemia. Cellular and humoral immunity is improved by daily dialysis and feeding, and possibly humoral toxic factors due to a burn are removed across the artificial kidney membrane.[5]

The close co-operation of all the units concerned and the mobile capability of the two RAF teams made the most comprehensive management possible. Despite the appalling prognosis in such cases, we believe that treatment should not be denied.

[1] Davies, D M, *et al*, *Scandinavian Journal of Plastic and Reconstructive Surgery*. In press.
[2] Davies, D M, *Scandinavian Journal of Plastic and Reconstructive Surgery*. In press.
[3] Parsons, F M, *et al*, *Lancet*, 1961, **1**, 129.
[4] Rainford, D J, *Anaesthesia*, 1977, **32**, 277.
[5] Bartlett, R H, *et al*, *Transactions. American Society for Artificial Internal Organs*, 1973, **19**, 269.

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Carbimazole in respiratory failure

The induction of hypothyroidism with radioactive iodine has been used to manage severe respiratory insufficiency.[1 2] This was advocated as a means of lowering basal metabolic oxygen requirements, thereby releasing a relatively larger amount of tissue oxygen for other purposes. Occasional patients have benefited from the procedure. We describe a case in which a patient with unresponsive respiratory failure improved during treatment with carbimazole without the induction of hypothyroidism.

Case report

A 38-year-old housewife had suffered from bronchiectasis since childhood. She had undergone left lower lobectomy and lingulectomy in 1946 and left upper lobectomy in 1952. She had become progressively short of breath on exertion but was not admitted to hospital until January 1977, when she suffered an acute chest infection. Her response to antibiotics was poor. The table shows the results of ventilatory tests at the time of discharge. In March 1977 she was readmitted with severe dyspnoea and copious purulent sputum. Her respiratory rate was 24/min, temperature 38·5°C, and pulse rate 120/min. She had a pronounced flapping tremor. Respiratory failure was confirmed and the deterioration attributed to acute infection. Conventional treatment was begun with oxygen, intense physiotherapy, and antibiotics, and after 10 days the sputum was mucoid and less copious. Despite some clinical improvement, however, dyspnoea rendered her incapable of walking more than a few steps.

Tremor and sinus tachycardia persisted. These signs were initially attributed to hypercapnia but hyperthyroidism was later suspected and the free thyroxine (T4) index found to be slightly raised (see table). Treatment with carbimazole was started on day 18. The free T4 index was again marginally raised but a thyrotrophin-releasing hormone (TRH) stimulation test failed to confirm thyrotoxicosis (concentrations of thyroid-stimulating hormone: basal 6·6 mU/l; at 20 min 17 mU/l; at 60 min 11·5 mU/l). Her clinical improvement was so noticeable after carbimazole treatment was begun, however, that the drug was continued. Six weeks after starting antithyroid treatment the free T4 index had fallen to normal and she was able to walk 500 m at a steady pace. She was discharged from hospital. After a further two months carbimazole was discontinued, but within four weeks she was incapable of walking 20 m without severe dyspnoea. The free T4 index was again slightly raised but a TRH stimulation test was normal. Carbimazole was restarted, and two months later her condition had improved dramatically, exercise tolerance being increased to 400 m. The improvement has been sustained with small doses of carbimazole, and results of thyroid function tests have remained within the normal range during 14 months' observation.

Comment

After antithyroid treatment was begun a rapid and dramatic improvement in general wellbeing and exercise tolerance occurred. We initially considered the patient to be hyperthyroid and attributed the beneficial effect of carbimazole to reversal of a possible thyrotoxic respiratory myopathy. The TRH stimulation test, however, is a reliable method of detecting thyrotoxicosis,[3] and a minor increase in the free T4 index cannot be considered to indicate hyperthyroidism when the results of this test are normal. Moreover, when the Wayne index[4] was applied to assess clinically her thyroid state a score of 10 was obtained, indicating non-toxicity. The table shows that no appreciable change in ventilatory function followed antithyroid treatment.

A fall in the free T4 index and thus, by inference, in the basal metabolic rate occurred. This is presumably the basis of the clinical improvement that occurred while thyroid function tests were within the normal range. Patients with chronic lung disease treated with radioactive iodine in the past have been rendered permanently hypothyroid. Myxoedema produces changes in pulmonary function with values below the predicted normal for vital capacity, residual

Clinical details and measurements of respiratory and thyroid functions (blood gas measurements taken breathing air). Normal range or values given in parentheses

Date	Clinical details	FEV_1 (l)	FVC (l)	Oxygen pressure (kPa)	Carbon dioxide pressure (kPa)	T4 (nmol/l)	Free T4 index	T3 (nmol/l)	Free T3 index	Antithyroid treatment	Exercise tolerance
Dec 1946	Aged 8 years; before left lower lobectomy		0·53								
Feb 1947			0·7								
Oct 1951	Before left upper lobectomy		1·1								
Feb 1953			1·0								
Jan 1977	Chest infection treated	0·45	0·55								
Mar 1977	Day 1 of admission	0·2	0·3	4·9	9·8						Severe dyspnoea at rest
„ „	Day 3	0·25	0·4	4·6	9·65						„
„ „	Day 10	0·4	0·6	5·2	7·4	157 (50–140)	148 (48–134)				Few steps with oxygen
„ „	Day 15	0·5	0·7			143	136	2·45 (2·75)		Carbimazole started on day 18	„
May 1977	8 weeks after admission	0·6	0·85	6·6	6·35	128	128			Carbimazole 30 mg/day for 5 weeks	500 m at steady pace + 1 flight stairs
July 1977	4 months after admission	0·55	0·75							Had received carbimazole for 13 weeks.	„
Aug 1977	5 months after admission	0·5	0·65				132* (70–125)		3·0* (1·7–2·7)	Had received no carbimazole for 4 weeks	20 m + ½ flight stairs
Jan 1978	10 months after admission	0·5	0·63	6·5	6·3					Had received carbimazole for 2 months	400 m + 1 flight stairs

FEV_1 = Forced expiratory volume in one second. FVC = Forced vital capacity. T4 = Thyroxine. T3 = Triiodothyronine.
*Assay changed.
Conversion: SI to traditional units—T4: 1 nmol/l ≈ 78 ng/100 ml. T3: 1 nmol/l ≈ 65 ng/100 ml.