This time of peak immunological activity is also likely to be the time when plasma concentrations of therapeutically administered immunosuppressive drugs are at a minimum.

Circadian variations in immune response have not been emphasised but have implications for the understanding, assessment, and treatment of many diseases. There is clearly a need to consider standardisation of tests for immune responses according to the time of day.

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Unusual submandibular swelling

Two cases of enlargement of the anterior belly of the digastric muscle are reported. Although several causes of lateral submental swelling were considered, the correct diagnosis was made in neither case because diseases of the submental muscles were not considered.

Case reports

Case 1—In 1968 a 28-year-old hairdresser had a tooth extracted. For two years a swelling had been present below her mandible, and her dentist had diagnosed "a tumour." A sialogram was normal. A surgeon thought that the lump was a dermoid cyst, but confined himself to taking a biopsy specimen. In November 1969 she complained that the lump had regrown and had become painful. A firm, mobile, lobulated mass was found and this was taken to be a salivary gland, but operation showed that the anterior belly of the digastric muscle was enlarged. This had a braided, "rope-like" appearance with prominent fascicles and a coarse granularity of the cut surface. Histologically there were foci of atrophy of muscle fibres in which fibres with eosinophilic, structureless sarcoplasm and centrally placed nuclei were considered to be degenerating, while basophil fibres with vesicular nuclei appeared to be regenerating fibres (figure). In a few areas degenerate fibres were undergoing removal by inflammatory cells. Areas of complete loss of muscle fibres were replaced by patches of fibrosis. There was variation in the size of fibres, many larger ones having central nuclei. These changes were interpreted as resembling an early form of localised muscular dystrophy.

Section of muscle showing degenerate eosinophilic fibre (closed arrow) and regenerating basophil fibre (open arrow). (Haematoxylin and eosin. $\times 228$)

Postoperatively the serum creatinine phosphokinase and lactate dehydrogenase concentrations were normal, and a neurologist found no evidence of systemic myopathy. In 1978 she had no symptoms.

Case 2—Six months after dental clearance in 1973 a man of 31 noticed a lump below his jaw. His family doctor diagnosed "chronic adenitis." At hospital a reniform swelling was found, each lobe being 1 cm in diameter. The lump was thought to be neoplastic, but operation disclosed only the coarse, braided fibres of the enlarged anterior belly of the digastric muscle. The muscle was removed and the patient has since been free of symptoms. The pathologist reported changes resembling widespread foci of non-specific myositis.

Comment

Idiopathic hypertrophy of the masseter muscle was described in 1880,¹ and Mancall *et al*² coined the term "hypertrophic branchial myopathy." Apparently the histology of this syndrome varies from case to case and from one part to another in an affected muscle. Mancall *et al*² described changes similar to those in our case 1. Nevertheless, Lambert and Young³ found only one area of myopathic change and a great preponderance of hypertrophic type I fibres with the ATPase reaction. The picture is confused by the variation in fibre size in the normal masseter muscle.⁴ Unfortunately, no histochemical studies were done in our cases since the operative findings were unexpected. Today the examination of specimens by frozen section with histochemical staining and by electron microscopy add precision to the diagnosis of diseases of muscle.

The clinical features of branchial myopathy have been well described.^{2,5} Usually this affects the masseters, but also occasionally the temporalis or muscles of the pterygoid group. All are innervated by the mandibular division of the trigeminal nerve, as is the anterior belly of the digastric muscle. In our cases the myohyoid muscles were not affected, nor were the posterior bellies of the digastric muscles, the latter being innervated by the facial nerve. Biopsy exacerbates the condition and hypertrophy progresses relentlessly, although spontaneous resolution has been recorded.² Patients with isolated disease of the anterior belly of the digastric muscle would seem to be fortunate because complete excision is seemingly curative and without ill effect.

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Sympathetic overactivity in tetanus: fatality associated with propranolol

Over the past decade there has been considerable interest in sympathetic overactivity in patients with tetanus.¹ Various pharmacological agents have been used to control these sympathetic crises, of which propranolol is considered the most acceptable.¹ We report the death of a child with tetanus, apparently due to the use of propranolol.

Case history

A 7-year-old black child with classical tetanus was referred to the intensive care unit from a neighbouring hospital. Intubation and full ventilation were instituted, relaxation being achieved with pancuronium bromide, 1 mg

hourly, and diazepam, 3 mg hourly, both intravenously. An indwelling radial artery line was inserted and connected to a Hewlett Packard trend recorder (Model 7825 A), which allowed for the continuous monitoring of heart rate, and diastolic, mean, and systolic blood pressure. Such recording permitted the recognition of three forms of sympathetic overactivity in this patient: (1) spontaneous—that is, apparently unprovoked by specific stimuli, such as handling or hypercarbia; (2) spasm-associated, occurring in association with a tetanic spasm; (3) iatrogenic, provoked by handling the patient, physiotherapy, or tracheobronchial toilet.

On the 6th and 7th hospital days (figure) 11 spasms occurred over 21 hours, but all were mild and occurred at times when sedatives were due. Nevertheless, sympathetic overactivity was almost continuous, and at one point (seen on the right-hand side of the recording) the patient had a systolic blood pressure of about 300 mm Hg and a diastolic blood pressure of 200–220 mm Hg. This was treated with 10 mg propranolol given by nasogastric tube. By following the recording from right to left, it may be seen that a progressive but mild reduction in the blood pressure resulted, with a shorter-lived reduction in the heart rate. A further 10 mg propranolol was given 12 hours later, as blood-pressure control was considered inadequate—after which there was a profound fall in blood pressure with compensatory tachycardia. The patient developed gross pulmonary oedema three hours after the second dose of propranolol and had a cardiac arrest. Resuscitation failed.

A trend tracing over 21 hours showing 11 spasms (—) with almost continuous sympathetic overactivity. Physiotherapy (..) and tracheal suction (- -) are also shown. Propranolol, 10 mg orally, was given initially at 1500 (↓) and then again 12 hours later (↓). The decline in blood pressure is clearly seen after the second dose. The terminal increase in blood pressure was related to resuscitative procedures.

Comment

The present case illustrates the potential hazards of using beta-blockers in patients with tetanus. It is well known that life-threatening complications such as acute congestive cardiac failure and pulmonary oedema may occur with propranolol.² Such reactions are not dose-related and occur most frequently after intravenous administration, but may occur with short-term oral treatment.³ It would appear that certain patients with underlying heart disease are in part dependent on adrenergic stimulation for compensated cardiac function and cannot tolerate even a small decrease in sympathetic drive. There is no evidence that our patient had underlying cardiac disease. Keilty *et al*⁴ have shown a rise in the circulating concentrations of adrenaline and noradrenaline in patients with tetanus, and suggested that this may cause the sympathetic crises seen in this disorder. Moreover, a 160–250% increase in cardiac output has been shown in patients with tetanus, while it has also been postulated that such patients may have a “toxic myocarditis.”⁵ Nevertheless, the evidence for the last is not convincing. Whether in some patients with tetanus the myocardium becomes dependent on such drive must remain conjectural, but if this were so then treatment with beta-blockers might be potentially dangerous.

In other patients our clinical experience has been that sympathetic overactivity can be damped down by increasing sedation. The decision when to start beta-blockade is difficult and no guidelines exist. Propranolol would appear to be the best drug to use for this clinical problem, but it must be given with extreme caution, preferably by recurrent small-dose intravenous boluses.

We are indebted to Dr P J Beukes, Superintendent of Baragwanath Hospital, for permission to publish these data, and Dr S Miller, of Coronation Hospital, who referred the patient to us.

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Copper intrauterine devices and the small intestine

Copper 7 and Copper T intrauterine contraceptive devices (IUCDs) have gained wide acceptance despite the disadvantage that their effectiveness declines rapidly after two years, necessitating frequent reinsertions. Less attention has been given to a more serious defect—namely, their tendency to enter the peritoneal cavity and once there to penetrate viscera and to provoke tissue reactions.

Case reports

Case 1—This patient's general practitioner fitted a Copper 7 six weeks after her second delivery. Eighteen months later she conceived and after an uneventful pregnancy she had a normal delivery with no sign of the IUCD. X-ray examination showed the device in the left iliac fossa and Eugynon 30 (norgestrel and ethinylloestradiol) was given until the infant was eight months old and could be left with a relative. One month before admission for laparotomy, the Eugynon 30 was stopped and the couple were advised to use a condom and Delfen (nonoxynol) Foam. At laparotomy under x-ray control the Copper 7 was found embedded in the wall of the small intestine and two small incisions were required to remove it. The mucosa was intact, but 40% of the device was within the intestinal wall and the entire device was covered by peritoneum. The patient made an uneventful recovery from the operation but was subsequently found to be pregnant having conceived in the preoperative cycle. Because of the exposure to irradiation the pregnancy was terminated.

Case 2—A Copper 7 was fitted in an advisory clinic at the time of menstruation in a single girl aged 21, and she was advised to use Delfen Foam as well. No further period occurred and pregnancy was confirmed. Because of psychiatric problems, a termination was carried out and the laparoscope was used to look for the Copper 7 without success. The patient was readmitted for laparotomy under x-ray control and the Copper 7 was found to be penetrating the wall of the small intestine. It had penetrated the muscle coat but not reached the lumen and was bound down by filmy adhesions. The device was dissected out and the track was oversewn with catgut; the patient made an uneventful recovery and now, three years later, has a wanted intrauterine pregnancy.

Case 3—This patient had a Copper T fitted by her general practitioner after the delivery of her second child. She conceived despite this and the Copper T was not found at delivery, which was by emergency caesarean section for a transverse lie with hand presentation. Subsequently the device was removed at laparotomy under x-ray control and was found to be bound down to, but not embedded in, the lower part of the posterior surface of the uterus. It was excised and the peritoneum was repaired. The patient made a satisfactory recovery.

Comment

None of these devices was inserted in the hospital clinic where plastic devices, mainly Lippe's loops, are used. During the same three year period two plastic IUCDs were removed from the peritoneal cavity: one was lying free and one was wrapped in omentum; both were removed easily. In contrast, the copper-carrying devices were all buried in adhesions and both the Copper 7s had penetrated into the bowel, necessitating excision from and repair of small intestine. In case 1 the history suggests that the device was properly placed in the uterus at the time of insertion as it was effective as a contraceptive for 18 months.

The cases described here give no indication of the incidence of perforations but the figure quoted by Cederqvist and Fuchs¹ for perforations by the Lippe's loop is 0.4/1000. Cederqvist and Fuchs¹ reported two perforations by the Copper T in 880 cases and Newton