xysmal tachycardia the presence of an artificial pacemaker makes it possible to give more effective doses of antiarrhythmic drugs without danger arising from further depression of the natural pacemaker. Large doses of a beta-adrenergic blocking drug are usually the most successful in these patients and may be combined with digoxin in patients with associated cardiac disease and heart failure. The high incidence of systemic embolism in patients with bradytachycardia makes it wise to employ long-term prophylactic anticoagulant treatment.

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New Laws for Doctors

Every doctor who prescribes medicines for patients should be aware of new regulations for the control of drugs that come into force on 1 July. Full details of the new regulations will be sent to all general practitioners by the Departments of Health before that date; information will also be available in hospitals and local authority health departments.

The regulations put into force the Misuse of Drugs Act 1971, which has replaced the old Dangerous Drugs legislation. Morphine, heroin, pethidine, and similar drugs are included in schedule 2 of the new regulations. Two important changes have been made in the way that doctors deal with these drugs. Firstly, every prescription for a schedule 2 drug must specify in words and figures the dosage and the total quantity of the drug to be supplied, and the form and strength of the preparation to be dispensed must be stated.

Secondly, the register kept by a doctor of his own use of schedule 2 drugs will in future have to include an entry on every occasion that he administers a dose of the drug or causes it to be administered under his own supervision. The full text of the relevant sections of the regulations should be studied by any doctor who may need to prescribe drugs in schedule 2. As with any new procedure, doctors will no doubt find following the regulations time-consuming and tedious at first. However, both pharmacists (who will have as many problems as doctors) and doctors themselves may take consolation in the thought that the purpose of the increased stringency is the prevention of misuse of drugs, and few of our current medicosocial problems deserve higher priority.

Lomotil Intoxication in Children

Tablets of Lomotil consist of 2·5 mg diphenoxylate hydrochloride and 0·025 mg atropine sulphate and are widely used for "traveller's diarrhoea." Indeed, the drug has accompanied man on his longest ever journey, to the moon. But recently there have been several reports of Lomotil poisoning in children from either accidental ingestion of large doses or wrongly prescribed medication. Of 18 children thus poisoned two have died.[1-8]

Diphenoxylate hydrochloride is structurally related to pethidine, is a powerful antitussive, and prolongs the transit time of the intestinal contents by its action on the smooth muscle of the gut. The onset of action is slow by all routes of administration and the duration of action longer than that of codeine or pethidine. The manufacturers recommend that the preparation should be avoided in the first year of life, by patients receiving barbiturates, and in cases of hepatic disease. Nearly all the children poisoned were under the age of 3 years. Ten had accidentally ingested toxic doses, and eight were receiving doses in excess of those recommended.

The toxic dose varies widely between children. For example, six tablets rendered a 2-year-old girl moribund before she responded to treatment,[1] and 12 tablets produced fatal respiratory depression in a 2-year-old boy.[2] Lomotil intoxication produced clinically recognizable atropinism in less than 50% of the children. Though in two cases described by M. E. Ament[3] there was an early phase of atropinism with high fever, generalized flushing, and tachypnoea for two or three hours. More commonly the first indications of poisoning were drowsiness, constriction of pupils, hypotonia, loss of tendon reflexes, nystagmus, and convulsions. Individual sensitivity to atropine may explain the variation in clinical patterns.

The cardinal sign, however, of Lomotil poisoning was respiratory depression with slowing of the respiratory rate followed by total apnoea. This was the presenting feature in several children in whom ingestion of Lomotil had not been suspected initially, but it also developed later in others known to have ingested toxic doses of the drug. In one case[4] apnoea developed 10 hours after ingestion and recurred, despite appropriate therapy, up to 16 hours after ingestion. Similar lapses in time between ingestion and symptoms were reported in other cases, confirming the slow absorption and long duration of action of diphenoxylate. Prolonged clinical observation over 48-72 hours is therefore obligatory in such cases.

Appropriate treatment depends on prompt recognition that Lomotil has been ingested. The child should be admitted to hospital and have his stomach emptied by gastric lavage. The late onset of respiratory depression must be anticipated and facilities for resuscitation made readily available. If respiratory depression occurs, general supportive measures (including the maintenance of an adequate airway and oxygenation) are mandatory, but nalorphine is the vital factor in treatment. The general paediatric dose is 5 to 10 mg/1·73 m^2, given intravenously or intramuscularly. In infants under 6 months the initial dose suggested is 0·25 mg. Nalorphine's duration of action is brief and the initial dose may need to be repeated several times at intervals of 15 to 30 minutes according to the clinical response. Some caution

is necessary because nalorphine can itself cause respiratory depression in normal patients. However, in several reported cases of Lomotil poisoning in children nalorphine undoubtedly saved lives, and there are few more dramatic drug responses in clinical pharmacology.

The dangers of poisoning with Lomotil in children are not sufficiently well recognized. Its use should be avoided completely for children under the age of 2 years. It is not an innocuous drug, especially when ingested accidentally by children or prescribed in excess of recommended dosage. Fortunately, there is an effective antidote if poisoning is promptly recognized, but prevention is very much better than cure.

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Ptosis

As judged by its frequency in passers-by in the street minor degrees of ptosis are common. The condition does rarely occur unilaterally or bilaterally as a hysterical symptom, but most are organically based pareses of neuropathic or myopathic origin.

Unilateral ptosis may be voluntary, suppressing diplopia, while so-called pseudoptosis is due to mechanical factors in which there is thickening of the lids or to extreme thinning of the lids after repeated attacks of angioneurotic oedema (blepharoclasis). Minor degrees of ptosis may be overlooked because of the wrinkling of the forehead, and elevation of the eyebrows may partially relieve drooping lids—a notable feature of the tabetic facies. In examining for ptosis, therefore, as well as testing each eye separately it is important to offset the unwitting action of the occipito-frontalis by restraining the eyebrow over the orbital ridge. The patient is first asked to close his eyes lightly, a finger is applied to the eyebrow, and then the eye is opened as widely as possible.

Ptosis is usually due to weakness of the levator palpebrae superioris. Striped fibres compose most of the muscle and are innervated by the palpebral branch of the superior division of the oculomotor nerve. Sympathetic fibres from the internal carotid plexus, which join the oculomotor nerve as it traverses the wall of the cavernous sinus, supply a small unstriped component inserted into the superior tarsus. Because of the close association of the nerve to levator palpebrae superioris with innervation of other orbital muscles, neurogenic ptosis is usually accompanied by evidence of defective ocular movement, an exception being cases of sympathetic denervation, when the slight ptosis of Horner's syndrome is accompanied by contraction of the pupil. It is important, therefore, to observe whether or not there is evidence of complicating ophthalmoplegia.

The site of a neurogenic lesion may be supranuclear, nuclear, or infranuclear. It is claimed that the lid elevator is the only ocular muscle to have its own separate cortical centre, situated in the parietal lobe,[1] but the evidence that a lesion localized here causes ptosis is questionable.[2] Ptosis may, however, be a feature of Parinaud's syndrome, in which failure of conjugate upward gaze is caused by a pineal tumour, but in most cases the site of the lesion is presumed to be at brain-stem level or distally.

Most classifications of ptosis subdivide according to whether the condition is congenital or acquired and genetic or non-gentic. This classification has some practical value, though it is clear that even in some recent classifications[3] there is confusion over the usage of the terms congenital and hereditary.

In approximately three-quarters of cases ptosis of widely varying severity is present from birth, and in about half of these the condition is an isolated symptom, mostly unilateral, and the cause is unknown. When associated with a congenital ophthalmoplegia, the superior rectus is most commonly involved, and in some patients there is a family history suggesting dominant inheritance. While the localization of the primary abnormality is uncertain in the majority of these patients, in other cases where there is an associated malformation of the lid, such as coloboma, a local cause is most likely.

A congenital ptosis can be disfiguring, but in the Marcus-Gunn phenomenon,[4] in which chewing or other oropharyngeal movements may elicit synkinetic elevation of a drooping lid ("jaw-winking"), the condition may be embarrassing as well, as in the case of the young lady[5] who "winked as fast as she ate." The cause is not known with certainty.

Trauma apart, the differential diagnosis of acquired ptosis is mostly between oculomotor palsy and ocular myopathy. Notable among the causes of paralysis of the third nerve are brain-stem glioma, aneurysms, vascular malformation of the posterior cerebral artery, compression in the cavernous sinus, encroachment on the superior orbital fissure from inflammation or neoplasm, or a retro-orbital mass. Ophthalmoplegic migraine is relatively benign but may have residual partial or complete oculomotor paralysis, probably due to involvement of the posterior cerebral artery. Diabetes as a cause of isolated and unexplained ocular palsies in adults must not be overlooked. In myasthenia gravis variable and even intermittent drooping of one or both lids may be the presenting feature and may be most resistant to treatment.

A slowly progressive hereditary ptosis in which ultimately all extrinsic ocular muscles weaken used to be considered to be of neurogenic (nuclear) origin. Though undoubtedly ophthalmoplegia may be part of certain heredo-degenerative neuraxial syndromes such as the hereditary ataxias,[6 7] or tapeto-retinal degeneration, most of the patients with progressive weakness of ocular movement and ptosis are thought to suffer from progressive ocular myopathy, for which there is electrophysiological and histological evidence.[8] But this evidence has been questioned on both clinical and experimental grounds, and the debate on the neurogenic versus the myopathic origin of the condition continues. R. B. Daroff and colleagues[9] reported on a patient who died of a degenerative neurological disease, proved at necropsy, who presented with what was at first considered to be an ocular myopathy on the evidence of biopsy. Other patients with the clinical features of ocular myopathy have been reported in whom electromyographic changes characteristic of denervation coexisted with "classical" myopathic abnormalities.[10] These clinical observations on the possible role of denervation have found support from animal studies. These have shown that section of the oculomotor nerve produced histological changes in extraocular muscles which had hitherto been considered indicative of ocular myopathy.[11] The patho-