and parents do not consider aspirin as a drug and they should be questioned specifically about salicylate ingestion. Often it is admitted only after three or four sessions of history taking or when relatives other than parents are questioned.

Salicylates are valuable in the treatment of acute rheumatism and rheumatoid arthritis but are grossly overprescribed for relatively trivial and self-limiting conditions in childhood. The medical profession must shoulder responsibility for this, particularly those doctors who prescribe aspirin for children without examining them. Moreover, aspirin is easily obtainable without prescription and its value is constantly extolled in advertisements. The dangers of chronic aspirin ingestion by adults are well recognized and every paediatrician is aware of the perils of acute aspirin poisoning. It is

also well known that 70% of adults who take aspirin over a long period lose about 2 ml of blood per day but there have been no studies of the effects of chronic aspirin ingestion on normal children. These cases reported here emphasize that chronic aspirin ingestion in childhood is not uncommon, often goes undetected, and may cause serious anaemia.

I should like to thank Dr. R. R. Gordon, consultant paediatrician, for permission to study patients under his care, and Miss Margaret Swall for secretarial help.

Reference

Marshall, N., and Kuzemko, J. A. (1972). *British Medical Journal*, 4, 612.

MEDICAL MEMORANDA

Progressive External Ophthalmoplegia and Heart Block

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Disturbances of cardiac conduction are a well-recognized feature of some neurodegenerative disorders. We report an example of an uncommon syndrome in which complete heart block with Adams-Stokes attacks may occur at a time when the disability from the neurological condition is slight.

Case Report

A 23-year-old female laundry worker was admitted to hospital after losing consciousness suddenly at work. There were no convulsive movements. On admission her conscious level fluctuated between coma and drowsiness with response to command. Two months previously she had developed pain and difficulty in lifting her arms after unaccustomed exertion. These symptoms disappeared after one week but she felt slightly unwell, though able to continue at work, until the syncopal attack. Birth and development had been normal and the menarche had occurred when she was 14 years old. None of her family were aware of a change in her appearance but photographs showed the development of bilateral ptosis by the age of 20 years.

Information was available on 72 members in four generations of the family and there were no instances of sudden death or of progressive neurological disorders; 14 members were examined and all were of short stature—for example, the father was 63 in (160 cm) tall. Her father had evidence of healed specific choroiditis and a cousin had Down's syndrome.

Examination showed a woman of small stature (height 55 in (140 cm); weight 72 lb (32.6 kg)) and low average intelligence. There was bilateral ptosis and almost complete paralysis of voluntary and reflex eye movement in all directions. The pupils were equal, with normal light reflexes. Visual acuity was 6/6 bilaterally (Snellen). Visual fields were normal. The ocular fundi showed

fine stippling due to pigmentary degeneration. There was no facial weakness and though the limbs were thin there was no evidence of focal wasting or weakness. There was no ataxia. All tendon reflexes were present and the plantar responses were flexor. There was no sensory impairment.

An irregular bradycardia of 45-60/min was present. Brachial artery pressure was 100/70 mm Hg. The heart was not enlarged, heart sounds were normal, and there was no evidence of congestive cardiac failure.

On investigation the blood count, result of urine analysis, urea and electrolytes, serum proteins and electrophoretic pattern, and serum creatine phosphokinase were all normal. The serum enzymes were: SGOT 36 U/ml, SGPT 26 U/ml. Serology was negative for syphilis. The chest x-ray picture was normal. Chromosome analysis showed a normal female karyotype. E.E.G. showed a slight paroxysmal tendency but no persistent focal or specifically epileptic abnormalities. Audiology showed a mild sensorineural deafness.

E.C.G. showed complete heart block with multifocal ventricular pacemakers. There were runs of ventricular tachycardia and episodes of ventricular fibrillation (see fig.).

E.C.G. showing runs of ventricular tachycardia and episodes of ventricular fibrillation.

She was resuscitated successfully from several episodes of ventricular fibrillation, after which a temporary transvenous pacing catheter was inserted. She was treated with prednisolone 30 mg daily for five weeks but there was no sign of recovery of atrio-ventricular conduction and a permanent pacemaking system (Lucas) was implanted. Apart from a short period during which exit block occurred she remained well and continued to be paced satisfactorily. Twenty months later there was no progression of her neurological disability.

Comment

Cases of progressive external ophthalmoplegia with complete heart block have been described by Sandifer (1946), Jager *et al.* (1960), Kearns (1965) (three cases), Daroff *et al.* (1966), Drachman (1968) (two cases), Ross *et al.* (1969), and Shastri *et al.* (1971)—a total of 10 cases, in eight of which patients experienced Adams-Stokes attacks, three eventually dying during an attack. Three were treated successfully with cardiac pacemakers.

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The common features of these cases are the development of ptosis at an early age (under 20 years) and small stature. Retinal pigmentary degeneration was seen in all except the cases of Sandifer and Ross *et al.* The pigmentary epithelium appears thin and atrophic and there is diffuse mottling of the pigment epithelium, greatest in the peripapillary zone. There is diffuse stippling of pigment over the retina and heavier pigmentation in the macula without serious impairment of central vision (Kearns, 1965). Sensorineural deafness of varying severity was reported in six cases. Muscular weakness occurred in seven cases, sometimes involving only the orbicularis oculi, but in one leading to dysphagia and in another to shoulder-girdle wasting. The cerebrospinal fluid was examined in five cases and the protein was found to be raised in all (70–166 mg/100 ml).

Progressive external ophthalmoplegia was thought to be due to degeneration of the oculomotor nuclei until Sandifer showed myopathic changes in the lateral rectus muscle of his case. More recently, however, the difficulties of distinguishing between myopathic and neuropathic changes in ocular muscles have been recognized. (Rosenberg *et al.*, 1968); and Drachman *et al.* (1969) showed that apparent myopathic abnormalities can be produced by section of the oculomotor nerve in dogs. It is now generally believed that the ophthalmoplegia is neuropathic in origin.

Necropsy was performed in the three patients who died. In the case reported by Jager *et al.* no abnormality was found in the central nervous system, whereas in that of Daroff *et al.* there was vacuolation and decrease of neurones in the oculomotor nuclei, mammillary bodies, and habenular nuclei, and in Kearns's case there was siderosis and loss of neurones in the substantia nigra and vestibular nuclei but no abnormality of the oculomotor nuclei. The heart showed no abnormality in the cases of Jager *et al.* and Daroff *et al.* and only slight subendothelial fibrosis and slightly thickened endocardium in Kearns's case.

The disability produced by the neurological disorder in these patients is slight, and apart from cosmetic considerations there may be no symptoms. Diplopia rarely occurs. The development of heart block radically alters the progress of an otherwise relatively benign syndrome. Complete heart block is often preceded by the E.C.G. pattern of partial bilateral bundle-branch block shown by marked left axis deviation in standard leads and right bundle-branch block in precordial leads (Lasser *et al.*, 1968).

When a patient with progressive external ophthalmoplegia presents with episodes of disturbed consciousness the possibility of Adams-Stokes attacks should be carefully considered. If heart block is shown implantation of an artificial cardiac pacemaker now represents a safe and effective method of treatment.

We wish to thank Dr. H. A. Fleming and Dr. M. F. T. Yealland for their encouragement to report this case.

References

- Daroff, R. B., Solitair, G. B., Pincus, J. H., and Glaser, G. H. (1966). *Neurology, (Minneapolis)*, 16, 161.
 Drachman, D. A. (1968). *Archives of Neurology*, 18, 654.
 Drachman, D. A., Wetzel, N., Wasserman, M., and Naito, H. (1969). *Archives of Neurology*, 21, 170.
 Jager, B. V., Fred, H. L., Butler, R. B., and Carnes, W. H. (1960). *American Journal of Medicine*, 29, 888.
 Kearns, T. P. (1965). *Transactions of the American Ophthalmological Society*, 63, 559.
 Lasser, R. P., Haft, J. I., and Friedberg, C. K. (1968). *Circulation*, 37, 429.
 Rosenberg, R. N., Schotland, D. L., Lovelace, R. E., and Rowland, L. P. (1968). *Archives of Neurology*, 19, 362.
 Ross, A., Lipschutz, D., Austin, J., and Smith, J. (1969). *New England Journal of Medicine*, 280, 313.
 Sandifer, P. H. (1946). *Journal of Neurology, Neurosurgery and Psychiatry*, 9, 81.
 Shastri, S. D., Tulgan, H., Budnitz, J., and Colker, J. L. (1971). *New York State Journal of Medicine*, 71, 587.

Cullen's Sign, a Feature in Liver Disease

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Cullen's sign, a discoloration caused by blood around the umbilicus, has been described many times in association with a ruptured ectopic pregnancy or acute pancreatitis (Smith and Wright, 1935; Fallis, 1937). Though Hofstätter first reported its occurrence in 1909, he did not relate it to any underlying disorder, and it was Cullen (1918) who first recognized its relevance to ruptured ectopic pregnancy. A similar discoloration in the flanks was also described in acute pancreatitis by Turner in 1920, and this particular sign now bears his name.

Cullen's sign has rarely been described except in these conditions. In 1922 Sternberg reported it in association with a case of adenocarcinoma of the liver, and it was described in a case of possible cirrhosis with portal hypertension by Hellendal in 1934. We report its occurrence in two patients who were admitted to Harare Hospital within six months of each other, both diagnosed as having primary carcinoma of the liver.

Though ectopic pregnancy is commonly encountered in this hospital, and also acute pancreatitis, but to a lesser degree, no occurrence of Cullen's sign in association with them has been recorded over the past five years (1968–72).

Case 1

A 32-year-old man was admitted to hospital with a two-week history of pain in both hypochondria and a feeling of fullness in the abdomen.

FIG. 1—Case 1. Photograph showing extent of discoloured area.

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