and hence they are too busy. Secondly, the training of the undergraduate does not touch on many of the above problems. Lastly, most of the iatrogenic conditions discussed in this paper are of relatively recent origin, and unless the practitioner has kept his knowledge up-to-date by reading, and by attending refresher courses, he will not be conversant with these new advances and problems.

The treatment of cardiac arrhythmias is always important and often life-saving. Many cases prove resistant to the more usual methods of treatment. It is therefore important to know of safe and effective alternative methods. Recent papers have described the use of diphenylhydantoin (DPH) in a variety of arrhythmias.

We have chosen 4 of our cases to illustrate the effect of this drug and we discuss the value and pharmacology of diphenylhydantoin.

**METHODS**

A dose of 250 mg. DPH diluted in 5 ml. solvent was administered slowly intravenously. This was equivalent to 3·5 - 5·0 mg./kg. body-weight.

Continuous electrocardiographic monitoring was maintained. If the arrhythmia persisted or recurred the initial dose was repeated. After restoration of sinus rhythm, 100 mg. t.d.s. orally was given as a maintenance dose. The optimum dosage cannot be entirely concluded from the study of experimental work on dogs, as it ranged from 5 to 200 mg./kg. body-weight. The duration of action of a single 250 mg. dose may range from 5 minutes to 12 hours. Others have shown that the duration of action is relatively short and is usually to be measured in minutes. It would appear that the best route is intravenous. Although Dreifus et al. recommend 5 - 10 mg./kg. body-weight, slowly, intravenously over a 5 - 15 min. period, with possible repetition in 2 or 3 hours, we feel that it may be dangerous to exceed an initial intravenous dose of 250 mg. because of the side-effects described later.

**CASE REPORTS**

**Case 1**

J.S., Bantu male, aged 25 years. Three-month history of left-sided chest pain and congestive cardiac failure. He had been having digoxin 0·15 mg. daily for 21 days. Heart rate was 190/min. and the murmurs of mitral stenosis were heard. His blood pressure was 105/55 mm.Hg. X-ray of the chest showed an enlarged heart and pulmonary congestion.

ECG (Fig. 1) showed an atrial tachycardia, rate 200/min. The arrhythmia was not influenced by either carotid or eyeball pressure, the Valsalva manoeuvre, or forced emesis. He was given 250 mg. DPH intravenously over 4 minutes. Within 3 minutes there was restoration to sinus rhythm. He was then given a maintenance dose of 100 mg. of diphenylhydantoin t.d.s. orally.

He developed fever and a diagnosis of subacute endocarditis (in spite of persistently negative blood cultures) was made and he was treated with large doses of intravenous penicillin. Nineteen days after admission paroxysmal atrial tachycardia recurred, but intravenous DPH failed to abolish the arrhythmia. However, carotid sinus pressure now became extremely effective, but only for hours at a time.

**Case 2**

I.S., Coloured male, aged 62 years. Six-month history of dyspnoea and loss of weight. He had bilateral upper zone bronchial breathing, and diffuse coarse crepitations over the right base. X-ray of the chest showed a large mass in the right superior mediastinum posteriorly and thickened pleura at the right apex and lateral chest wall.

On admission, pulse rate was 98/min. and his blood pressure was 95/60 mm.Hg. On the second day his pulse rose to 160/min. and the ECG now showed a paroxysmal high nodal tachycardia (Fig. 2). Eyeball pressure and exhibition of digitalis failed to restore sinus rhythm. He was then given 250 mg. DPH intravenously in 5 minutes, with immediate restoration to sinus rhythm. He was maintained on 100 mg. DPH t.d.s. orally, and remained in sinus rhythm.

**Case 3**

J.D., White male, aged 65 years. Admitted with a myocardial...
infarct, in cardiac failure with a pulse rate of 100/min. and a blood pressure of 120/80 mm.Hg. He was digitalized and treated with diuretics, but remained in intractable cardiac failure. Ten days after admission he developed a ventricular tachycardia, rate 170/min. (Fig. 3). Carotid sinuses and eyeball pressure failed to restore sinus rhythm. He was given 250 mg. DPH intravenously with restoration to a dominant sinus rhythm. DPH 100 mg. t.d.s. orally was continued for 1 month, with maintenance of sinus rhythm.

**Case 4**

H.T., Coloured female, aged 53 years. Admitted with a severe retrosternal pain associated with a tachycardia of 200/min. Her blood pressure was 140/115 mm.Hg. ECG showed supraventricular ectopic tachycardia. She was given 250 mg. DPH at the rate of 50 mg./min. After 4½ minutes she felt nauseous and faint, and her systolic blood pressure fell to 50 mm.Hg. Her arrhythmia reverted to sinus rhythm (Fig. 4) and the blood pressure immediately rose to 120/105 mm.Hg.

**PHARMACOLOGY**

DPH was introduced for use in the treatment of epilepsy by Merritt and Putnam in 1938. It has been postulated that it might act through enhancing intracellular sodium transport across the cell membrane, so that there is a net outward movement of intracellular sodium and then an inward movement of potassium, thereby raising the threshold to stimulation in heart and skeletal muscle, and in the brain to seizure activity.

DPH lowered the acetylcholine content of both brain and heart. Harris and Kokernet, in 1950, found DPH to be effective in abolishing ectopic ventricular tachycardia, after experimental myocardial infarction in the dog and Mosey and Tyler successfully used DPH to terminate ouabain-induced ventricular tachycardia in dogs. Electrocardiographic changes consisted of prolonged PR interval, widening of the QRS complexes, and ST segment and T wave changes. Non-specific T wave changes may occur in the absence of toxicity.

In dogs, cardiac standstill may result from doses of 66 to 69 mg./kg. body-weight. Ventricular extrasystoles may appear at the height of the pharmacological effect. The side-effects of acute administration include in man, hypotension (our case 4 and Conn) and in dogs, acute peripheral vasodilatation and myocardial depression and emesis.

Using divided cardiopulmonary and systemic circulations in dogs, it has been shown that the most pronounced cardiovascular effect of DPH is a direct myocardial depression resulting in reduction of the contractile force. There is a patent and direct peripheral vasodilatory effect of DPH, directly on the vasculature. These mechanisms explain the hypotension which occasionally accompanies intravenous administration of DPH in clinical use. Slow administration of the drug is advised, to avoid this
ventricular ectopic tachycardias and 1 case of ventricular tachycardia, with the development of transient hypotension in 1 case (case 4). In another case (case 1), the arrhythmia recurred after 29 days and DPH rendered the carotid sinus extremely sensitive to touch, whereas previously it had been insensitive. The use of DPH appears to be a significant and comparatively safe addition to the armamentarium of drugs used in the treatment of certain arrhythmias.

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REFERENCES

RECURRENT SPONTANEOUS PNEUMOTHORACES COINCIDENT WITH MENSTRUATION

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A recent report by Kovarik and Toll describes a case of recurrent spontaneous pneumothoraces coincident with menstruation which at thoracotomy was found to be caused by endometrial tissue present on the diaphragm on the right side, and in the right upper lobe. The authors stated that, to their knowledge, only 10 cases of thoracic endometriosis had been reported previously, and one of these, involving the diaphragm on the right side, was the only reported case of recurrent spontaneous pneumothoraces coincident with menstruation.

The following case report is of interest because, although histological confirmation of the diagnosis has not been obtained, the history of recurrent spontaneous pneumothoraces occurring at the time of menstruation, always on the right side, closely parallels the experience of Kovarik and Toll.

CASE REPORT

The patient is a 36-year-old White female, gravida 3, para 2. Her first pregnancy terminated at 7 months in 1946, after which uterine curettage was performed. The surviving children were born in 1948 and 1949.

In August 1956 she had an appendicectomy, and at the same time an ovarian cyst was removed. Further particulars of this operation are not available. One week later she developed pleuritic pain on the right side, followed by a small haemoptysis. According to information supplied by her medical attendant, an X-ray of the chest 3 weeks later showed 'bronchitis' at the right base.

She was admitted to Addington Hospital in February 1957, with right-sided chest pain. According to the hospital records, a pneumothorax was present on the right side, and no underlying pathology was noted. A month later, several days after another episode of pain on the right side of the chest, a radiological examination at the Durban Chest Clinic showed no abnormality. Further admissions to Addington Hospital occurred in June 1958 and October 1959, and on each occasion pneumothorax on the right side was shown to be present.

Subsequent episodes of right-sided pneumothorax were recorded in January 1960 (at Addington Hospital) and again in October of the same year (at the Durban Chest Clinic), when bronchoscopy and bronchography, undertaken at Wentworth Hospital, disclosed no abnormality.

She was seen by me for the first time in February 1964, again presenting with a pneumothorax on the right side. It was at this time that the association of these episodes with menstruation was noted. She stated that the pain usually commenced on the first day of menstruation, but sometimes a day before the onset of bleeding. The pain was of moderate severity, pleuritic in nature, and lasted 3-4 days. Sometimes she experienced a 'bubbling' sensation at the base of the right lung. Her cycle was regular.