confirmed by cardiac catheterization. There was evidence of chronic elevation of left atrial pressure apart from the raised "wedge" pressures obtained at catheterization. The electrocardiogram showed left atrial hypertrophy as in mitral stenosis, and at necropsy there was great atrial hypertrophy without dilatation in some cases. Severe left atrial hypertension is in contrast to the simple systolic type of hypertension which exists in pure rheumatic mitral incompetence in Europeans. In these patients the ventricular diastolic inflow may be impeded by stiffness of the hypertrophied myocardium associated, in some cases, with the occlusive and splinting effects of endomyocardial fibrosis. It is therefore probable that the pulmonary hypertension is, as in many cases of mitral stenosis, due to the passive effects of the high left atrial pressure coupled with a vasoconstrictive element at a precapillary level. It remains to mention the possibility that pulmonary vasoconstriction is an excessive response to the pulmonary venous hypertension because of chronic anaemia or some other unknown factor. Left atrial hypertrophy, in contrast to dilatation, parallels the absence of atrial fibrillation. It is probable that atrial systole is an essential component in the maintenance of a cardiac output sufficient to sustain life in these patients.

Finally, we wish to stress the importance of the soil in which this form of heart disease thrives. Anaemia is usual; intestinal parasitism is rampant; in addition malaria is endemic, and the dysenteries, both bacterial and protozoal, are widespread. Protein malnutrition is rife, especially in infants and children. In the presence of persistent chronic ill-health of this nature it is difficult to believe that the myocardium remains unaffected and healthy. It is probable that anaemia alone, when severe and protracted, may lead to cardiomyopathy (Somers, 1959). On top of all this it must be emphasized that these patients are always ambulant, and never rest unless it is physically impossible for them to stand and walk. This continued physical activity may have further adverse effects upon an already damaged myocardium.

Summary

The clinical, radiological, and electrocardiographic features of 50 Nigerian patients who presented with heart failure due to mitral incompetence and pulmonary hypertension have been investigated. Necropsy examination of 13 cases showed that there was severe left ventricular myocardial disease and mitral-valve disease. Most hearts showed some degree of macroscopic endomyocardial fibrosis, and histological examination revealed either a diffuse non-specific inflammatory reaction or a myocarditis with Aschoff nodules which was indistinguishable from rheumatic carditis.

It is suggested that the peculiar pattern of this disease, comprising left ventricular myopathy, mitral valvulitis, and pulmonary hypertension, may be determined not only by its primary cause, but also by the background of chronic anaemia, protein malnutrition, and chronic infestation which is present in these patients and in the population from which they are drawn.

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ADRENOCORTICAL STEROIDS IN INTERMITTENT HEART-BLOCK

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Stokes-Adams attacks, by their dramatic nature alarming to the patient and his relatives, are always a matter of grave concern when the usual treatment with sympathomimetic drugs and atropine fails. Until recently there was no other effective simple treatment. There is now, however, growing evidence of the value of adrenocortical steroid therapy in this syndrome.

Prinzmetal and Kennamer (1954), in a paper devoted to treatment of various cardiac arrhythmias, described, almost as a curiosity, the response to corticotrophin of a patient with complete heart-block and Stokes-Adams attacks. A man of 60, after an acute posterior cardiac infarct, had been having repeated and prolonged attacks of syncope for a week with no relief from ephedrine or adrenaline. As a last resort, 40 units of corticotrophin was given: the attacks ceased and normal sinus rhythm returned in a few hours. Relapse a few days later again responded almost immediately, and after 10 days' maintenance treatment heart-block did not recur. Phelps and Lindsay (1957) described a very similar case wherein intramuscular cortisone was effective.

Since then, patients with Stokes-Adams attacks of long standing, associated with chronic heart disease, have been successfully treated with corticotrophin and adrenocortical steroids.

Litchfield *et al.* (1958), using corticotrophin, obtained immediate and permanent freedom from attacks in a man of 35 with ankylosing spondylitis who developed right bundle-branch block and intermittent complete heart-block. The attacks had occurred for nine months, continuing despite ephedrine and frequent injections of adrenaline during six weeks in hospital. A second patient, a man of 45 with rheumatic aortic valvular disease and paroxysmal complete heart-block, had

suffered from Stokes-Adams attacks for five months. They ceased immediately on treatment with corticotrophin, 120 mg. daily, and for five months could be prevented by maintenance dosage above a critical level. Their third patient, a woman of 35 apparently suffering from an acute carditis with a varying degree of atrioventricular block, had had increasingly severe Stokes-Adams attacks for two months. Within six hours of a first injection of corticotrophin complete heart-block was replaced by 2:1 heart-block and in 48 hours atrioventricular conduction was normal.

Caramelli and Tellini (1960) gave prednisone to 31 patients with heart-block, irrespective of its aetiology or degree, and reported the electrocardiographic changes. Conduction returned to normal in five out of seven patients with intermittent complete block, in both of two patients with 2:1 heart-block, and in seven out of ten patients with an abnormally prolonged P-R interval. The rhythm was unaffected in 10 patients with established complete heart-block. Positive results, when obtained, always appeared rapidly, and they thought it pointless to persevere with treatment if there was no effect within four to five days.

Friedberg *et al.* (1960) reported six patients with chronic ischaemic heart disease, in all of whom Stokes-Adams attacks ceased within 48 hours of starting treatment with prednisone, and thereafter could be prevented by an adequate maintenance dose. In all, standard treatment had proved ineffective or at best of transient benefit. Relief of attacks in five out of the six patients was accompanied by a return of normal conduction in the electrocardiogram.

We report here our experience of six patients with Stokes-Adams attacks treated with oral prednisolone.

Case 1

An estate manager aged 72 began, in August, 1959, to suffer from attacks of faintness three to eight times a day. After a momentary disagreeable sensation in the head he would fall to the ground, but was able to get up again immediately. He was unconscious on one occasion only. Sometimes he was able to avoid falling by sitting down. No colour change had been noticed by witnesses. He denied any chest pain or shortness of breath.

He was admitted to hospital some six weeks after the onset. There were no abnormal physical signs except that his heart rate alternated between 40 and 70, with occasional periods of pulselessness lasting for five seconds and accompanied by faintness. An electrocardiogram showed predominant sinus rhythm with a normal P-R interval, right bundle-branch block, and periods of complete atrioventricular block. The attacks continued for a week unaffected by sublingual isoprenaline, 20 mg. four times a day.

Prednisolone, 80 mg. a day, was then begun. He had his last attack 36 hours later, and after two days' treatment his electrocardiogram showed sinus rhythm. After nine days the dose of prednisolone was reduced in stages and he returned home. He has remained entirely well for the past year on a maintenance dose of 10 mg. a day. His electrocardiogram is unchanged, the right bundle-branch block persisting.

Case 2

A retired gardener of 68 began, in October, 1957, to suffer from attacks of loss of consciousness, gradually becoming more frequent until he was averaging four a day. He also experienced frequent feelings of "dizziness" without unconsciousness.

He was admitted to hospital six months after the onset, and typical Stokes-Adams attacks lasting up to 45 seconds,

with unconsciousness and twitching and followed by flushing, were repeatedly observed. He had free aortic incompetence with moderate left ventricular enlargement and a blood-pressure of 200/65 mm. Hg. His blood Wassermann reaction was negative. An electrocardiogram showed a P-R interval of 0.24 second and right bundle-branch block.

Attacks averaged five a day for the first 10 days after admission despite ephedrine and adrenaline. Prednisolone, 80 mg. daily, was then started. In the next 24 hours he had about 40 attacks, the next day three, and thereafter none. An electrocardiogram nine days from the starting of treatment showed a P-R interval of 0.2 second and right bundle-branch block. When he had been free from attacks for three weeks he returned home, then receiving prednisolone, 20 mg. a day. Two months later the right bundle-branch block pattern had disappeared. Steroids were given in decreasing doses for a further five months and then stopped.

Three months later syncopal attacks recurred, but these again ceased when he took prednisolone 15 mg. daily. He remained well for a further 18 months, and then was admitted to another hospital with left ventricular failure, complete heart block, and right bundle-branch block, and died next day.

Case 3

A woman of 82 had a series of syncopal attacks, many times a day, for several weeks in 1955. Her doctor noted her pulse rate at times to be below 40. At one time, when the attacks were particularly frequent, she had a temporary left hemiparesis. She was then well for two years, when attacks returned at intervals of a few days. She usually had a brief warning, and then became pale and pulseless, sometimes with involuntary movements. On examination her heart was in regular rhythm at a rate of 90, the left ventricle was moderately enlarged, and her blood-pressure was 210/110 mm. Hg. She had an aortic systolic murmur conducted to the neck and a widely split pulmonary second sound. Her cardiogram showed right bundle-branch block and a P-R interval of 0.2 second. She was treated for 15 months with ephedrine and adrenaline with some temporary improvement.

In July, 1958, she was having three or four attacks a day, usually consisting of "dizziness" only, but with loss of consciousness in about one in ten.

Prednisolone, 80 mg. a day, was then begun. In the first three days she had three attacks, none, and one attack respectively, and thereafter they ceased. The prednisolone was gradually reduced to 15 mg., and she has remained well for over two years.

Case 4

A woman of 58, a high-grade mental defective, complained in 1956 of occasional feelings of faintness, and her pulse was said to have been irregular. Clinically her heart was normal. An electrocardiogram showed non-specific T-wave changes, thought to indicate degenerative heart disease, with normal conduction. On the supposition that her sensations were due to a paroxysmal tachycardia, quinidine, 5 gr. (0.32 g.) t.d.s., was advised. After a few doses her doctor noticed that her pulse rate had fallen to 40, and the drug was abandoned.

She was next seen and admitted in August, 1958, apparently *in extremis*, having suffered for three days from attacks of unconsciousness and twitching every few minutes. She was pale and sweating, and typical Stokes-Adams attacks lasting 15 to 45 seconds were observed every two to three minutes. Her pulse was irregular at about 30 between the periods of standstill. Dissociated atrial waves could be seen in her jugular pulse. Her electrocardiogram showed complete heart-block. There was no improvement with adrenaline.

Hydrocortisone hemisuccinate, 100 mg., was given intravenously and repeated in six hours; and prednisolone,

80 mg. a day, was started by mouth when she could swallow. Fifteen hours after the starting of treatment she was in sinus rhythm with a normal P-R interval, the attacks had ceased, and the improvement in her general condition was dramatic.

After a week the prednisolone was reduced in steps to a maintenance dose of 10 mg. daily, and eventually discontinued in December, 1958. She has remained well for two years, apart from occasional mild "giddiness" of doubtful significance.

Case 5

A lorry-driver of 55 was admitted to hospital in May, 1959, with an acute anteroseptal cardiac infarct. He was severely ill, and during the first 10 days had a number of attacks of paroxysmal tachycardia for which he was given quinidine and later digoxin. These attacks ceased, but were replaced by periods of ventricular asystole, his electrocardiogram showing a P-R interval of 0.24 second and right bundle-branch block. Twelve days after admission he was having Stokes-Adams attacks every five to ten minutes, beginning with olfactory and auditory hallucinations followed by confusion and flushing without loss of consciousness. Digoxin was stopped, but the attacks continued unabated for three days.

Prednisolone, 40 mg. a day, was started, and the attacks ceased within 24 hours. His electrocardiogram then showed normal A-V conduction and right bundle-branch block.

He was discharged home after six weeks in hospital, but was able to live only a very restricted life owing to breathlessness and effort angina. A maintenance dose of prednisolone was continued for a year and then stopped. Three weeks later he died suddenly.

Case 6

A widow of 77 was admitted to hospital in August, 1960, with a six-weeks history of increasingly frequent attacks of loss of consciousness. Bradycardia had been noted for six months. She was moderately short of breath, and during the week before admission had been given an oral diuretic but no digitalis.

On admission she was in mild congestive heart failure with moderate left ventricular enlargement, a ventricular rate of 33, and easily audible dissociated atrial sounds. About 10 typical Stokes-Adams attacks were observed in the first 24 hours in hospital, and there was no response to adrenaline.

Prednisolone, 80 mg. daily, was then begun. About 16 attacks occurred in the next 36 hours and then they ceased. Complete heart-block persisted and there was no significant change in her electrocardiogram. After three weeks in hospital she was returned home on prednisolone, 15 mg. daily, and so far has remained free from attacks for three months.

Discussion

Six patients with heart-block and frequent Stokes-Adams attacks have been treated with prednisolone after adrenaline and related drugs had proved ineffective. In all of them the attacks ceased within 48 hours, and, apart from one patient with established complete heart-block, regular sinus rhythm returned. The clinical improvement was reflected in the electrocardiograms of four patients, with the disappearance of paroxysmal complete block in two and the return to normal of a prolonged P-R interval in two others.

It is well known that patients with Stokes-Adams syncope may improve spontaneously at any time, and that extraneous factors may modify the frequency of attacks. Thus in Case 5 spontaneous recovery was very likely, both because the heart-block appeared 10 days after the onset of cardiac infarction and because it may

have been precipitated by digitalis. In Case 6 the attacks became more frequent while the patient was receiving an oral diuretic, and though her serum potassium was normal on admission the possibility of some electrolyte disturbance cannot be excluded. In Cases 1, 2, 3, and 6 Stokes-Adams attacks had been recurring for weeks or months without relief by adrenaline, ephedrine, or isoprenaline, and their prompt cessation can be attributed to prednisolone with some confidence. In Case 4 the duration was a mere three days, but attacks were recurring so often that death seemed imminent, and steroid therapy appeared to be life-saving.

Three possible mechanisms for the effectiveness of corticotrophin or adrenocortical steroid therapy have been suggested.

Prinzmetal and Kenamer (1954) used corticotrophin in the belief that it would suppress inflammation involving the conducting system at the periphery of a cardiac infarct. If this assumption is correct, there is a logical indication for steroid therapy when heart-block complicates myocardial infarction, as there might be if it appears in patients with acute carditis.

Lown *et al.* (1955) presented evidence that cortisone accelerates atrioventricular conduction in the normal heart. They observed that, compared with normal controls, patients with Addison's disease had a significantly prolonged P-R interval in the electrocardiogram, 20% showing first-degree heart-block at some stage. In most cases the P-R interval was shortened by treatment with cortisone. These effects did not appear to result from electrolyte disturbance, for neither in Addisonian crisis nor on treatment with a mineralocorticoid such as deoxycortone was conduction affected. Conversely, the electrocardiograms of patients with Cushing's syndrome tend to show a shortened P-R interval, sometimes of sufficient degree to resemble Wolff-Parkinson-White syndrome. Adrenalectomy is usually followed by a return towards normal. Subsequent writers were aware of these observations, though Phelps and Lindsay (1957) and Litchfield *et al.* (1958) used cortisone and corticotrophin primarily for their anti-inflammatory effect.

Friedberg *et al.* (1960) pointed out that in their patients syncopal attacks from ventricular standstill might cease before there was any change in the basic rhythm, and, indeed, heart-block might later recur and even progress in degree during clinically effective maintenance treatment. They ascribed this to a favourable effect of prednisone on the arousal and stabilization of ventricular pacemakers. Such a mechanism must be assumed for the effect of prednisolone in Case 6, who had permanent complete heart-block.

Our dosage has been empirical, and the optimum must vary from patient to patient and at different stages of the disease. Caramelli and Tellini (1960) found that 40 mg. of prednisone a day was required to produce a full response where one could be obtained, and in their patients larger doses showed no advantage.

Maintenance treatment for a long period is likely to be needed by patients with chronic heart disease, and we have found that 10 to 15 mg. of prednisolone daily suffices. In Case 4 it was stopped after five months without a return of attacks. When maintenance prednisolone was stopped after seven months, Case 2 relapsed, but the attacks again responded to 15 mg. daily. In one of the patients reported by Litchfield *et al.* (1958), 60 mg. of prednisone or 200 mg. of

cortisone was insufficient to control attacks, although corticotrophin, 50 mg. daily, was effective.

Steroid therapy has so far proved safe in these patients. The usual accepted contraindications were absent. It is, however, interesting that, in Case 2, Stokes-Adams attacks occurred with greater frequency during the first day after starting treatment. Such a phenomenon has not been noted before. There is a theoretical possibility that steroids might interfere with the process of healing after cardiac infarction, but this does not seem to be the case in experimental infarcts in laboratory animals. Furthermore, in such cases treatment for a few days only may be enough.

Summary

Six patients with heart-block and Stokes-Adams attacks have been treated with prednisolone after the failure of conventional measures, and in all six the attacks ceased within 48 hours. Subsequently all patients have remained free from episodes of syncope for a long period.

Similar results have been reported by others, and treatment with adrenocortical steroids appears often to be useful when sympathomimetic drugs are ineffective. In general, a favourable response is most likely when Stokes-Adams attacks occur in a patient with atrio-ventricular block which is unstable. In such cases a return to normal rhythm can be hoped for. Once complete heart-block is established, the rhythm is usually unaffected by steroid treatment, but if it is complicated by syncopal attacks from ventricular standstill, steroid therapy may still relieve them. Prolonged maintenance treatment is suggested in patients with chronic ischaemic heart disease.

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Dr. J. A. SCOTT, the London County Council's Medical Officer of Health, reports that the number of emergency calls received by the London Ambulance Service increased by more than 10,000 between 1958 and 1960. In 1958 the number of calls was 99,188; in 1959 104,983; in 1960 109,551. Despite the extra journeys the average time taken by ambulances to reach the scenes of accidents was only a fraction of a minute longer than in previous years—6.5 minutes in 1958, 6.8 minutes in 1960. On average, patients were admitted to hospital 21.6 minutes after the calls for help were received. As usual, women about to give birth outnumbered all other kinds of patients (25.2% of the total). Street accident cases came next (20%), displacing from second position cases of illness in public places. There were 22,709 patients who had been involved in street accidents, 1,000 more than in 1959. The number of patients who had been victims of assault rose by nearly 700 to 4,107.

HYPERBILIRUBINAEMIA AND PERCEPTIVE DEAFNESS

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The association between kernicterus and perceptive deafness has been well known since Crabtree and Gerrard (1950) demonstrated that deafness was present in 16 out of 20 cases of athetoid cerebral palsy.

After the identification by Claireaux, Cole, and Lathe (1953) of bilirubin as the pigment in the brain cells in kernicterus, evidence accumulated to incriminate bilirubin as the principal factor in the causation of neurological complications in haemolytic disease of the newborn. This evidence has been reviewed by Lathe, Claireaux, and Norman (1958) and by many others, and hardly needs to be recapitulated. It seemed of importance, therefore, to ascertain by a prospective type of investigation how often perceptive deafness might occur as the sole result of hyperbilirubinaemia and whether this could occur at a bilirubin level lower than necessary to cause athetoid cerebral palsy.

Material

The children selected for this study were infants born at Queen Charlotte's Maternity Hospital between the end of 1953 and the middle of 1957 who suffered from hyperbilirubinaemia.

From the middle of 1954 at Queen Charlotte's Hospital regular daily estimations of total bile pigments and conjugated bilirubin have been performed on all babies showing any sign of jaundice at all, and are repeated on each baby until the bilirubin level begins to fall.

An adaptation of the Evelyn and Malloy technique, as described by Lathe and Ruthven (1958), has been used, but at the beginning of 1957 the factor employed in calculating the bilirubin was altered, as it was found that the readings had been too high by about 20%. The figures given in this paper have therefore been adjusted to make them comparable to the more recent estimations. Accordingly, out of 107 infants, after adjustments as mentioned above, it was found that only 20 reached a bilirubin level of 20 mg./100 ml.

For the purposes of this investigation it was possible to examine 50 children completely. Full assessment of their hearing was carried out, and this study of the relationship of hyperbilirubinaemia to perceptive deafness is based on the special investigation of these 50 children. In this group were 13 with a bilirubin concentration of over 20 mg./100 ml.

Results of Hearing-tests

All these children had a detailed audiological examination, and perfectly normal hearing was found in 41 out of 50. In three there was a significant impairment of hearing of conductive type, but this is not relevant in this context.

In six children bilateral perceptive partial deafness was detected. As seen from the audiographs (see Chart), the