up under the title "Idiopathic hypertrophic osteoarthropathy" (Camp and Scanlan, 1948; Fairbank, 1951). The radiological differences which have been described are not constant and may be a result of the difference in the rate of progress of the condition; in hypertrophic pulmonary osteoarthropathy secondary to lung cancer, for example, the process is more acute and there may be insufficient time for the new bone to fuse with the old cortex.

Clubbing of the fingers and hypertrophic osteoarthropathy are usually secondary phenomena, related to such diverse conditions as diseases of the lung (tuberculosis, fibrosis of the lung, empyema, bronchiectasis, malignant disease of lung and pleura), congenital heart disease, and intestinal disorders, such as multiple polyposis of the colon, ulcerative colitis, steatorrhoea, and cirrhosis of the liver.

The most common single cause is carcinoma of the lung; over a seven-year period Semple and McCluskie (1955) saw no case of osteoarthropathy related to any other condition. Nevertheless, the number of cases of carcinoma of the lung which show clubbing is small and those with hypertrophic pulmonary osteoarthropathy is smaller still. Jack (1952) found three fully developed cases of hypertrophic pulmonary osteoarthropathy in 668 cases of bronchial carcinoma. Wierman *et al.* (1954) reported an incidence of 5% of simple clubbing or osteoarthropathy in 481 resections for malignant lung lesions. In this connexion the family reported by de Sèze and Jurmand (1950) is of great interest. Their patient, a man of 27, presented with a 10-year history of pains in the knees and was found to show the characteristic clinical and radiological picture of pachydermo-periostosis. Investigation of his family revealed that, although his mother and two sisters were quite normal, his father suffered from bronchiectasis and had marked clubbing of the fingers. A brother, who had no chest or other illness, had clubbed fingers to a less degree. De Sèze and Jurmand suggest that the genetic element which is known to be necessary for the development of pachydermo-periostosis may also be the factor determining the development of osteoarthropathy in cases of lung disease. On this hypothesis, all cases of clubbing of the fingers or of osteoarthropathy are familial. Some are idiopathic; others require a lung lesion to bring out the syndrome.

Differential Diagnosis.—Although, as mentioned above, the large hands and feet suggest acromegaly, the normal length of the limbs and the absence of any enlargement of the tongue or jaw differentiate it from that condition. The visual fields are quite normal. Radiologically, the sella turcica is normal in size and shape, and there is no "tufting" of the terminal phalanges. Other conditions which may require differentiation are osteitis deformans and syphilis of the bone. In the former there is asymmetrical involvement of the long bones, as well as involvement of the pelvis, spine, and skull. Pachydermo-periostosis is differentiated from syphilitic periostitis by the absence of history of infection, and of other manifestations of syphilis in the skin and cardiovascular or central nervous systems. The Wassermann reaction is negative.

Prognosis and Treatment.—The prognosis as regards life is excellent, but the effect on function depends on the extent of the process and whether the bones or the skin are chiefly involved. The most-disabled patients are those with joint involvement. Treatment is of little avail in this condition. American authors—for example, Camp and Scanlan (1948)—recommend a change to a hot dry climate. Tarsorrhaphy may be required in those cases in which there is considerable hypertrophy of the eyelids. If sweating is very prominent, sympathectomy will bring about considerable symptomatic improvement.

Aetiology.—Nothing is known about the cause of the condition. A family history has been obtained in over a quarter of the recorded cases, and it seems that inheritance is mediated by a recessive or incomplete dominant gene. Attempts have been made to discover an endocrine cause, but, although in certain cases isolated features suggesting endocrine disorders have been described, they are rare, and biochemical investigation had been consistently negative.

In four cases of the pulmonary type of osteoarthropathy, Fried (1943) noted clinical features of acromegaly such as prognathism and macroglossia. Necropsy revealed enlargement of the pituitary in two cases, and the presence of adenomata in the adrenal cortex and thyroid in two cases. However, no biochemical investigations were undertaken in this series and there is no real evidence for the "dyspituitarism" that Fried invokes as the probable cause of the syndrome.

Summary

Three cases are recorded of a syndrome known as pachydermo-periostosis, in which clubbing of the fingers and toes is associated with enlargement of the extremities and thickening and furrowing of the skin over the face. The characteristic radiological appearances of the bones are described. The differentiation of this syndrome from acromegaly and its relation to hypertrophic pulmonary osteoarthropathy are discussed.

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PAROXYSMAL AURICULAR TACHYCARDIA WITH AURICULO- VENTRICULAR BLOCK

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Heyl (1932) first drew attention to paroxysmal auricular tachycardia associated with auriculo-ventricular block, leading to disturbance in the ventricular rhythm, arising as a complication of digitalis administration. Lown and Levine (1955) point out the serious nature of this disturbance of the auricular rhythm as a manifestation of digitalis toxicity. It is an example of a rapid heart rate due to this cause (Levine, 1948). The arrhythmia can easily be produced experimentally by the pharmacological action of digitalis on the normal heart, in contrast to the difficulty in producing ventricular arrhythmias (Scherf and Schott, 1953). Fig. 1 illustrates such an experiment. Acetyl strophanthidin was used as the digitalizing agent on account of its extremely rapid action (Lown and Levine, 1955). The drug was administered intravenously to a normal dog (weight 12 lb.;

FIG. 1.—Experimental paroxysmal auricular tachycardia with auriculo-ventricular block produced in a normal dog with acetyl strophanthidin. TH=Thoracotomy.

5.4 kg.) anaesthetized with 6 mg. of intravenous pentobarbitone sodium. Paroxysmal auricular tachycardia with auriculo-ventricular block occurred as a terminal complication when 3.2 mg. of acetyl strophanthidin had been given. We describe below four cases of this serious complication of digitalis therapy, with particular reference to diagnosis and treatment.

Case Reports

Case 1.—A man aged 49 was admitted to hospital with intractable congestive heart failure due to coronary artery disease. Prior to admission he had been receiving 0.25 mg. of digoxin thrice daily, and 2 ml. of mersalyl twice weekly for an indefinite period, but he failed to improve. The pulse was rapid and irregular, and he was thought to have uncontrolled auricular fibrillation. Consequently 1 mg. of digoxin was administered orally, and thereafter 0.5 mg. every six hours. Twenty-four hours later his condition was unchanged, and the pulse remained rapid and irregular. An electrocardiogram confirmed the presence of paroxysmal auricular tachycardia with auriculo-ventricular block (Fig. 2). Digitalis was immediately stopped and further diuretic treatment suspended. Potassium chloride, 5 g., was given daily in divided doses by mouth for four days. This restored a slow sinus rhythm, with marked improvement in the patient's condition. One week later the abnormal auricular rhythm recurred, and on this occasion sinus rhythm was effectively restored with procaine amide, 0.5 g. twelve-hourly for four doses.

Case 2.—A woman aged 71 was admitted to hospital with advanced congestive heart failure due to coronary artery disease. She had been receiving digitalis and diuretic treatment for some months previously. The heart rate was rapid and irregular, and she was thought to have uncontrolled auricular fibrillation. Consequently digitalis foliata, 1 gr. (65 mg.) six hourly, was administered. No improvement occurred after three days. An electrocardiogram confirmed

that she had paroxysmal auricular tachycardia with auriculo-ventricular block (Fig. 2). Digitalis was omitted, and 5 g. of potassium chloride was administered orally in divided doses. On the fifth day normal slow sinus rhythm was restored, with improvement in the patient's condition. After further treatment she was discharged ambulant.

Case 3.—A woman aged 83 sustained a fresh myocardial infarction and was treated with 0.25 mg. of digoxin six-hourly until admission five days later with congestive heart failure. An electrocardiogram confirmed that she had paroxysmal auricular tachycardia with auriculo-ventricular block (Fig. 2). Potassium chloride, 5 g., was given orally in divided doses each day. Three days later normal sinus rhythm was restored.

Case 4.—A man aged 50 developed a fresh myocardial infarction, and had been treated with 0.25 mg. of digoxin every six hours for five days before admission to hospital. An electrocardiogram taken just before death confirmed the presence of paroxysmal tachycardia with auriculo-ventricular block, most likely related to digitalis therapy.

Discussion

Paroxysmal auricular tachycardia with auriculo-ventricular block cannot be distinguished from uncontrolled auricular fibrillation on clinical examination. In both conditions the ventricular rate is rapid and irregular. Differentiation is important during the course of digitalis therapy, for whereas

FIG. 2.—Paroxysmal auricular tachycardia with auriculo-ventricular block. Case 1 shows 2:1 block. Reversal to sinus rhythm with potassium treatment is shown in Cases 1 and 2.

increased dosage of digitalis is required for uncontrolled auricular fibrillation, such treatment may be disastrous in the presence of the toxic arrhythmia. Even electrocardiographic analysis may be difficult. Well-defined P waves are helpful, and should be sought in all leads. Oesophageal leads may be necessary (Brown, 1936). Our patients were thought to have auricular fibrillation in the first instance. Cuttings from appropriate leads showing P waves were selected for the figures. An isoelectric interval between successive P waves helps to differentiate paroxysmal auricular tachycardia with auriculo-ventricular block from auricular flutter. Such electrocardiographic diagnoses as "impure flutter" and "impure fibrillation" should be regarded with suspicion, especially if the patient is receiving digitalis. It is doubtful if they have any fundamental meaning, and they may conceal the serious disturbance of auricular rhythm under review. In our cases the auricular rate varied between 195 and 230 a minute.

Our cases were receiving digitalis when they developed paroxysmal auricular tachycardia with auriculo-ventricular block. The response to potassium treatment supports the view that digitalis was the causative agent (Cases 1, 2, and 3; Lown and Levine, 1955). An excessive dose of the drug may cause the arrhythmia, but it is important to realize that it may occur when the heart muscle is sensitized to digitalis by potassium loss (Lown, Salzberg, Enselberg, and Weston, 1951). Thus in intractable heart failure prolonged diuresis may render a therapeutic dose of digitalis a toxic dose, and thereby cause paroxysmal auricular tachycardia with auriculo-ventricular block.

Prompt treatment is essential in paroxysmal auricular tachycardia with auriculo-ventricular block due to digitalis toxicity. The drug, of course, must be stopped, and diuresis, paracentesis, and other measures aimed at diminishing the load on the heart must be suspended, to conserve body potassium. Potassium is the specific remedy (Lown and Levine, 1955). In urgent cases it may be given intravenously. We used oral therapy in Cases 1, 2, and 3—5 g. of potassium chloride being given daily in divided doses under continual electrocardiographic control until sinus rhythm was restored. Lown and Levine (1955) note that auriculo-ventricular block is abolished before the ectopic auricular centre is suppressed by potassium. Thus the ventricular rate increases before the sudden restoration of sinus rhythm. Procaine amide is also effective (Case 1). We prefer the intramuscular route, 0.5 g. of the drug twelve-hourly, until sinus rhythm is restored. Two of our cases had fresh myocardial infarction (Cases 3 and 4). One of them recovered with potassium treatment; the other, who received no specific treatment, died. The digitalis treatment of fresh myocardial infarction requires special care with regard to its toxic action causing this serious disturbance of auricular rhythm.

Finally, more rarely, paroxysmal auricular tachycardia with auriculo-ventricular block may occur spontaneously—in the absence of digitalis administration (Lown and Levine, 1955; Friedberg, 1949). It appears to be a benign condition, and, paradoxically, digitalis is the treatment of choice.

Summary

Paroxysmal auricular tachycardia with auriculo-ventricular block is a serious complication of digitalis toxicity that cannot be differentiated clinically from auricular fibrillation. Four cases are described; the importance of diagnosis depends upon the identification of well-defined P waves in any appropriate lead separated by isoelectric intervals.

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TWO CASES OF ALKAPTONURIA

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Alkaptonuria results from an inherited inability to metabolize homogentisic acid, a breakdown product of tyrosine, which undergoes oxidation in alkaline urine to form pigments, giving the urine its characteristic brown or black appearance. The condition is relatively rare; only about 200 cases have been described (Martin *et al.*, 1952). Hogben *et al.* (1932) calculated the incidence of the condition to be about one in ten million.

Apart from constituting an interesting metabolic disorder, alkaptonuria is important in that cases may be misdiagnosed. Thus the presence of a reducing substance (homogentisic acid) in the urine may lead to a diagnosis of diabetes mellitus, whilst the complication of ochronotic arthritis may be diagnosed as some other arthritic condition.

For this reason we are prompted to describe two new and apparently unrelated cases which illustrate diagnostic pitfalls.

Case 1

A 12-year-old schoolgirl was admitted to the professorial surgical wards of the Royal Infirmary, Edinburgh, on May 4, 1956, for the investigation of intermittent attacks of lower abdominal pain. When several months old she had been admitted to another hospital for the investigation of a red coloration of the urine; a diagnosis of pyelonephritis was made, although there is no record of bacteriological examination of the urine or the presence of red cells on microscopy. During the whole of the patient's childhood the mother had often observed brown staining of the diapers and undergarments.

The child was normally developed and no abnormalities were detected on physical examination apart from a generalized brown pigmentation of the skin. Barium-meal and x-ray examination of the skeletal system failed to reveal anything abnormal. The Wassermann and Mantoux reactions were negative. Her urine when freshly voided was acid and usually a normal colour, although occasionally there was a faint red coloration; on standing exposed to the air for several days, however, the urine became alkaline and gradually turned a deep brown colour. Tests for homogentisic acid were positive (see below). Over a seven-day period the excretion of homogentisic acid averaged 2.4 g. in 24 hours.

A diagnosis of alkaptonuria associated with non-specific mesenteric adenitis was made. When seen four months after discharge from hospital she was asymptomatic. A search for other cases of alkaptonuria among relatives was unsuccessful.

Case 2

A coal-miner aged 53 was seen at the Industrial Chest Unit, Bangour Hospital, on July 25, 1956, complaining of breathlessness on exertion. In 1938 he had been admitted to another hospital for the investigation of intermittent lower back pain. At that time there were no abnormalities on physical examination, but an x-ray film of the lumbar