Summary

The presence of the ABH and Le^a blood-group substances in the saliva of healthy schoolchildren and of cases of rheumatic fever has been studied. By the ulex test 22.9% of 669 healthy schoolchildren were non-secretors; the comparable figure for 553 rheumatic fever cases was 28.9%. Positive results with a precipitation test on the saliva with a rabbit anti-Le^a serum were obtained in 21.2% of 1,129 healthy schoolchildren and in 27.5% of 611 cases of rheumatic fever. These two differences, significant at the 2% and 1% level respectively, would be expected if rheumatic fever could develop only in those individuals who are homozygous or heterozygous for the non-secretor gene. On the basis of this hypothesis we have shown that the incidence of rheumatic fever in the parents and sibs of patients with this disease should not, on hereditary grounds, be more than 13 and 16% greater respectively than in the general population.

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The *Manual of Nutrition*, first published in 1945, was originally the work of Dr. Magnus Pyke, who was at that time a member of the Scientific Adviser's Division of the Ministry of Food. Since 1945 the rapid advance in nutritional knowledge has necessitated considerable revision of the text and tables, and the present edition, the fifth, has been prepared by present members of the Scientific Adviser's Division (Food) of the Ministry of Agriculture, Fisheries and Food in consultation with Dr. W. T. C. Berry of the Ministry of Health.

It differs substantially from the previous edition; Part I has been considerably amended to take into account the prevailing climate of opinion on the fundamental aspects of nutrition; the section on digestion in Part III has been rearranged so that the subject can be more easily explained; an expanded section has been included in Part IV on the effect of cooking on foods and nutrients, because the information is not readily available from textbooks in general use. . . . The *Manual* was originally designed to meet the needs of the caterer—for use in teaching the principles of nutrition to people already possessed of practical knowledge of cooking and catering; but its range of usefulness has been extended to teachers of domestic science and their students and pupils, and to all who are in any way concerned with public health. It has been found valuable by many of these, and by others who realize that an understanding of the scientific basis of good feeding should be part of the everyday knowledge of an educated community (*Manual of Nutrition*, H.M.S.O., 3s. net).

ANTERIOR TIBIAL SYNDROME DUE TO ARTERIAL EMBOLISM AND THROMBOSIS

ISCHAEMIC NECROSIS OF THE ANTERIOR CRURAL MUSCLES

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The anterior tibial syndrome comprises the following clinical features. There is sudden onset of severe pain in the muscles of the anterior tibial compartment. They become swollen, hard, acutely tender to pressure and to stretching, and paralysed, with resultant foot-drop. The tibialis anterior always undergoes ischaemic necrosis; the extensor hallucis longus and extensor digitorum longus usually do so. After some hours a reddish-purple discoloration, bearing some resemblance to a bruise, appears in the skin overlying the muscle bellies. The peronei, which lie outside the compartment, are not affected. Pulsation in the dorsalis pedis artery ceases for a few days or longer. A neuropathy, evidently ischaemic, of the anterior tibial nerve causes paralysis of the extensor digitorum brevis and cutaneous anaesthesia of the first interdigital cleft. During the ensuing 7 to 21 days pain and tenderness in the affected muscles subside. Movement may return to those muscle fibres in which paralysis is due to neuropathy, and to those necrotic fibres in which regeneration takes place. Paralysis may persist indefinitely; the muscles then remain indurated and undergo fibrous replacement. Histologically the affected muscle shows the changes of ischaemic necrosis (Griffiths, 1940). Much of the necrotic muscle is ingested by macrophages and undergoes replacement fibrosis.

Cases fall into three categories:

1. *Unaccustomed exertion involving the anterior tibial muscle group.*—The onset occurs a few hours later. Sixteen cases, all in healthy young men, have hitherto been reported in detail: Vogt (1943); Sirbu *et al.* (1944), one case with bilateral involvement; Horn (1945), two cases; Tillotson and Coventry (1950); and Freedman (1954)—all after marching; Phalen (1948), one case after a half-mile walk; Pearson *et al.* (1948), one case with bilateral involvement after long-jumping on a hard surface; Hughes (1948), two cases after playing football; and Carter *et al.* (1949), six cases after football and one case after marching.

2. *Local exogenous mechanical factors causing a rise in intracompartmental pressure.*—Sirbu *et al.* (1944) describe the occurrence of the syndrome after repair of a small muscle hernia. Carter *et al.* (1949) describe two cases apparently due to blood from a transfusion tracking extravasously into the compartment.

3. *Embolic or thrombotic occlusion of the anterior tibial artery or parent trunk.*—Hughes (1948) describes a case occurring in a young man with polyarteritis nodosa, and Watson (1955) two cases, the first (embolic) occurring in a woman aged 51, with mitral stenosis,

aortic valve incompetence, and auricular fibrillation, and the second (described as embolic, but possibly thrombotic) in a woman aged 70 with hypertension, auricular fibrillation, and peripheral arteriosclerosis.

As the syndrome is uncommon, it was thought desirable to introduce this paper with a summary of the main clinical features. Five cases are reported—two due to embolism and three to thrombosis.

Case 1

On March 22, 1950, a housewife aged 63 experienced severe pain and loss of power which came on rather suddenly in the right leg, with some numbness in the right foot. This was followed a few minutes later by mild transient pain in the left leg. On examination two days later the tibialis anterior muscle and the long extensor muscles of the right leg were swollen and hard, excruciatingly tender to pressure and stretching, and completely paralysed, with consequent foot-drop. The overlying skin was purplish red. The patient lay supine with her affected limb flexed at hip and knee. In this position foot-drop was prevented by pressure of the sole on the couch. Attempts to straighten her knee and lower it to the couch caused intense exacerbation of the pain; this was due to consequent foot-drop and stretching of the affected muscles. Pulsation was absent from the right dorsalis pedis artery and present in the other arteries of both lower limbs. The skin of the feet and toes was normal in colour and temperature. Cutaneous sensibility was impaired in the first interdigital cleft. No inflamed veins were seen or felt, and there was no oedema.

Signs of mitral stenosis, cardiac enlargement, and auricular fibrillation were present; the ventricular rate was 74 and the blood pressure 160/95. There was no cardiac failure, nor was there evidence of disease elsewhere.

By the sixth day, when we were able to admit her, the pain had somewhat abated, but the discoloration, induration, paralysis, and hypaesthesia were unchanged. Faint pulsation was discernible in the right dorsalis pedis artery, and a day later it was of normal strength. On the 11th day Mr. A. N. McCrea performed decompression by means of an incision 10 in. (25 cm.) long into the deep fascia overlying the swollen muscles, but they bulged only slightly. Three biopsy specimens were taken. The superficial fibres were normal in colour, but the deeper ones were buff-coloured and avascular. Twenty-one days after the onset a very faint trace of voluntary contraction was detectable in the tibialis anterior and extensor hallucis longus. She was apyrexial throughout the acute stage.

Electrical Reactions (35th day).—Faradism—no response in the tibialis anterior, extensor digitorum longus, extensor hallucis longus, and extensor digitorum brevis; normal response in the peroneus longus and peroneus brevis. Interrupted galvanism—all these muscles responded. Pain, tenderness, and discoloration were now absent, though induration persisted.

By the 45th day dorsiflexion of the ankle and toes was present, though it was very weak. The patient was treated with interrupted galvanism and faradism, and a plaster back-splint was applied to minimize foot-drop. By the 60th day fairly strong dorsiflexion of the ankle and toes was possible, and contraction and relaxation of the muscles could be seen and felt, except for the medial half of the tibialis anterior, which remained indurated and functionless. A few days later she started to walk. Electrical tests on the 64th day showed response to faradism in all the muscles in which it had been previously absent; response to interrupted galvanism was likewise present. When seen again at the eighth month she reported that she was able to carry out ordinary household duties. All the previously affected muscles were found to contract firmly, except for the medial half of the tibialis anterior, which was still indurated. Cutaneous sensibility was still impaired in the first interdigital cleft.

In December, 1950, she developed a left hemiplegia, attributable to a cerebral embolism, from which she made a fairly good functional recovery.

Fourteen months after the onset a second biopsy of the tibialis anterior muscle was performed. The superficial part was pale greyish pink. It did not bleed or contract on incision except for the deeper fibres of the medial portion, which appeared normal.

Histological Findings

First biopsy, 11 days after the onset.—The material consisted of three small fragments of necrotic muscle. In two of the fragments the muscle fibres retained their normal size and shape, although most of the nuclei had disappeared (Fig. 1). A section stained by Mallory's phosphotungstic

FIG. 1.—Case 1. Necrotic muscle in longitudinal section, showing accentuation of transverse markings, early fragmentation, and disappearance of nuclei. A collection of extravasated erythrocytes is shown in the interstitial tissue. (Haematoxylin and eosin $\times 110$.)

acid haematoxylin showed the transverse striae to be normal in a few fibres, while in others they were obscured or replaced by a diffuse granularity. Many fibres showed accentuation and widening of the transverse markings, Hensen's lines being clearly visible, and this change was seen to progress to transverse fragmentation with separation of the sarcomeres. A few fibres had begun to split longitudinally into separate myofibrils. Between the fibres there were thin deposits of finely granular basophilic debris, sparsely infiltrated by polymorphonuclear leucocytes. In many areas of the third fragment the dead fibres were undergoing invasion and phagocytosis by macrophages, a few of which had two or more nuclei; fibroblasts were also present in small numbers, but there was no collagenous fibrosis. All stages could be found between fibres of normal size which had retained their structural outlines and contracted endomysial sheaths within

which recognizable muscle substance had been completely replaced by swollen macrophages (Fig. 2). A reticulin impregnation showed that, as the muscle substance disappeared, the endomysial framework shrank *pari passu* but remained essentially intact. The arterioles appeared contracted but structurally normal. Capillary engorgement and extravasation of erythrocytes were seen in many areas, but the latter was possibly an operative artifact. Traces

FIG. 2.—Necrotic muscle in transverse section, showing phagocytosis of dead fibres. (H. and E. $\times 110$.)

of free iron were found, mostly within necrotic muscle fibres. No evidence of regeneration of muscle was seen. The appearances were those of acute ischaemic necrosis of recent origin.

Second biopsy, 14 months after the onset.—The excised fragments of muscle showed moderate diffuse collagenous thickening of the endomysial and perimysial connective tissue. As a result the architectural pattern was slightly irregular, but the appearance of the muscle fibres themselves was within normal limits.

Case 2

A housewife aged 50, known to have had mitral stenosis and auricular fibrillation without symptoms for at least one year, was seized on the evening of July 1, 1952, by severe pain in the front of the left leg. Two hours later her family doctor found diminished pulsation in the dorsalis pedis and posterior tibial arteries, and cutaneous anaesthesia of the toes on the affected side. He administered morphine. Two hours later the pain and anaesthesia had gone and pulsation was normal. The following morning, however, the pain and anaesthesia returned, the foot was cold, and dorsiflexion was impaired.

The following signs were present on the affected side when she was admitted to hospital that afternoon: the anterior tibial muscles were painful, slightly swollen, moderately indurated, tender to pressure and stretching, and paralysed; there was cutaneous anaesthesia of the first and second interdigital clefts, and the skin of the foot was cold and coloured a dusky pink; the dorsalis pedis and posterior tibial arteries did not pulsate, while those in the healthy leg were normal.

The next day there was a little return of movement, though the induration was greater. The temperature was 98.8° F. (37.1° C.) during the first week, and normal thereafter. The neutrophils numbered 13,800 per c.mm. in a total white-cell count of 17,000 during the first week; the E.S.R. was 28 mm./hour (Wintrobe). All affected muscles responded to faradism, but the current required was greater than normal. Peripheral pulsation became detectable during the third week; it always remained feeble and was sometimes impalpable. Fasciculation was seen in the affected muscles. During the ensuing weeks the tibialis anterior muscle remained hard, and limitation of plantar flexion suggested that this was due to fibrosis.

Two years later she was readmitted with a left hemiplegia, ascribed to cerebral embolism, from which she made a good functional recovery. It was noted that pulsation in both dorsalis pedis arteries was normal and equal.

Case 3

A chronic alcoholic barman aged 53 was admitted to hospital on March 3, 1957, with a history of melaena for two days. He was profoundly anaemic, the haemoglobin being 2.4 g./100 ml. (16% Haldane). The blood pressure was 120/60. Scattered crusted sores and skin pigmentation gave evidence of self-neglect. Three pints (1.7 litres) of blood was transfused. Two days later he had a severe recurrence of bleeding, the haemoglobin falling to 2.7 g./100 ml. (18% Haldane) and the blood pressure to 60/40. A further 5 pints (2.8 litres) of blood was transfused, and, as regards the intestinal bleeding, he made a fluctuating but ultimately good recovery on Hurst's dietary regimen, iron, and antacids. A barium-meal examination at the third week showed evidence of duodenal ulceration, but none of oesophageal varices.

On March 5, very shortly after the recurrence of bleeding and oligæmic shock, and before receiving his second transfusion, he complained of persistent cramp-like pain in the front of his left leg. Seven days later all muscles in the anterior tibial compartment were hard, tender, and paralysed; the overlying skin was a dusky red, and there was impaired cutaneous sensibility in the first interdigital cleft. A plaster back-slab was applied to correct the foot-drop. During the next four weeks the overlying skin became bright red, with extension of the discoloration to the dorsum of the foot. The entire anterior tibial muscle group underwent softening and was soon fluctuating. He had a number of pustules and boils in the scapular region and a large one on the right buttock, but there were none on the affected leg. Mr. A. N. McCrea made an incision 4 in. (10 cm.) long into the upper third of the fluctuating area. The compartment was evacuated, leaving a cavity bounded by tibia, fibula, and interosseous membrane. It contained pus, from which coagulase-positive *Staphylococcus aureus* was grown, and pink necrotic muscle having the consistency of blancmange. After a number of weeks the cavity was clean and lined by healthy granulations.

On June 4, he was transferred to St. Charles' Hospital with a view to skin grafting, but his general condition, at all times poor, deteriorated further. Mr. N. D. Ashe reported that an above-knee amputation was performed on August 7, and that this was followed by gangrenous patches on the right leg and later congestive heart failure, from which the patient died on September 29.

Case 4

A woman aged 77 was undergoing in-patient medical treatment for haematemesis due to gastric and duodenal ulceration. There was no shock or anaemia. She also had auricular fibrillation and left ventricular hypertrophy due to hypertension, uncomplicated by cardiac failure. A few days before admission she had been aphasic, but speech was almost normal when she was admitted on August 6, 1957.

Eleven weeks after admission she experienced pain in the left leg. On examination, 18 hours after the onset of pain, the left tibialis anterior muscle was tender, indurated, and paralysed. Pulsation was absent from the left dorsalis pedis artery. All other arteries of the lower limbs pulsated normally, the long extensor muscles were intact, and, so far as could be determined with her impaired co-operation, sensibility was likewise intact. The next day the skin overlying the tibialis anterior was reddened, the foot maintaining normal colour and temperature. Heparin was given initially and followed by a course of phenindione, but without noticeable benefit.

Biopsy of the tibialis anterior muscle was performed by Mr. N. Samuels nine days after the onset of crural symptoms. When the overlying fascia was incised dark blood oozed out. The infarcted muscle was a dark greyish blue and failed to contract on being cut. Three months later the induration, paralysis, and absence of arterial pulsation were unchanged.

Histological Findings

Examination of the biopsy specimen taken nine days after onset gave the following results. The two fragments consisted mainly of mature collagenous fibrous tissue in which were many small muscle fibres. These fibres showed a tendency to parallel arrangement but were widely separated by collagen. They varied greatly (from 6 to 38 μ) in diameter, and most of them had numerous sarcolemmal nuclei. Most of these fibres were deeply stained with Mallory's phosphotungstic acid haematoxylin and showed clearly the individual myofibrils, but transverse striae were visible only in a few. The ambient fibrous tissue was sparsely infiltrated by lymphocytes, and traces of free iron were found in it; recent extravasation of blood had occurred in some areas. The appearances suggested a slowly progressive ischaemic atrophy with replacement fibrosis and some regeneration of the muscle fibres.

At the edge of both fragments were a few small areas (the largest only 1.8 mm. in diameter) of architecturally intact muscle showing signs of recent necrosis. The fibres here were normal in diameter (40 to 52 μ) and many of them showed normal transverse striation, although the normal staining reaction with Mallory's phosphotungstic acid haematoxylin had been completely lost or greatly impaired. Some but not all of the sarcolemmal nuclei had disappeared. Extravasated red cells occurred in some of the endomysial spaces, but there was no leucocytic infiltration. The appearance of these small areas suggested acute ischaemic necrosis of very recent origin. The few arterioles and small arteries in the sections appeared contracted but structurally normal.

Case 5

A man aged 79 was admitted to hospital on November 7, 1957, having had a brief attack of impaired or lost consciousness earlier the same day. On admission he had fully recovered from the attack and was found to have gross left ventricular hypertrophy, a regular pulse of 38 a minute, a blood pressure of 130/75, and signs of right and left ventricular failure. Electrocardiography demonstrated complete A-V block. It seemed that the episode that occasioned his admission was either a Stokes-Adams or a "cerebrovascular" attack. He was digitalized and eventually made a satisfactory recovery from the failure.

On November 11 he developed acute bronchitis, for which he was given tetracycline. Two days later he complained of pain in the left leg. The front of the leg and the dorsum of the foot were cold and cyanotic. All arterial pulses on that side, other than the femoral, were absent. On the fourth day after the onset of pain in the leg the left tibialis anterior muscle was found to be hard, acutely tender to pressure and stretching, and paralysed; the other muscles were intact. Cutaneous sensibility was impaired in the first interdigital cleft. The skin over the tibialis anterior muscle was slightly reddened and that over the dorsum of the foot slightly cyanotic. He was given several injections of tolazoline and nylidrine hydrochloride ("perdilatal") into the femoral artery without benefit.

Mr. E. D. Morris performed a biopsy 10 days after the onset and described the tibialis anterior muscle as dark blue in colour. On incising it there was dark venous oozing. The muscle failed to contract on being pinched or cut. During the ensuing weeks the cutaneous erythema deepened and the induration and paralysis persisted. In January, 1958, lobar pneumonia developed, from which he died. Post-mortem examination by Dr. S. A. Kahn showed: thrombotic occlusion of the femoral artery distal to the origin of the profunda femoris; pneumonic consolidation of the left lower lobe; fibrosis of ventricular septum; left ventricular hypertrophy; and widespread atherosclerosis.

Histological examination of the biopsy specimen taken 10 days after the onset gave the following results. The material consisted of a fragment of necrotic muscle. The muscle fibres were abnormally hyaline and some of them

were swollen. They stained deeply with Mallory's phosphotungstic acid haematoxylin, but most of them had lost their transverse striation. Nearly all of the sarcolemmal nuclei had disappeared. The endomysial spaces were infiltrated by polymorphonuclear leucocytes and contained a little granular basophilic debris and a few extravasated red cells. The section included a few very small arterioles, which were histologically normal.

Discussion

It was pointed out earlier that the anterior tibial syndrome can be caused by three different and unconnected agencies: (1) unaccustomed exertion involving the anterior tibial muscles in healthy subjects; (2) local exogenous mechanical factors causing a rise in pressure within the anterior tibial compartment; and (3) occlusion of the anterior tibial artery or a parent trunk by embolism or thrombosis.

In order to understand the peculiar vulnerability of the contents of the anterior tibial compartment we must consider its anatomy. The tibialis anterior, extensor hallucis longus, and extensor digitorum longus are contained within a relatively rigid compartment bounded by the tibia, fibula, interosseous membrane, and overlying fascia. The anterior tibial artery, veins, and nerve also lie within this compartment. The arterial supply of these muscles has been studied by the injection of radio-opaque suspensions (Blomfield, 1945, 1948; Hughes, 1948).

The tibialis anterior is supplied solely by the anterior tibial artery through a series of about 12 segmental branches except for the proximal third, which is also supplied by the anterior tibial recurrent artery. There is no effective anastomosis between these vessels. The extensor digitorum longus is supplied by the anterior tibial, and by three perforating branches of the posterior tibial and by the perforating peroneal arteries. These arteries anastomose within the muscle. The extensor hallucis longus is supplied by the anterior tibial and perforating peroneal arteries. According to Campbell and Pennefather (1919) intramuscular anastomoses are so fine that the main muscular branches can be regarded as end-arteries. Ligation of the anterior tibial artery at various levels below its point of entry into the compartment results in cutting off the supply to the muscles distal to the ligature. A localized occlusion of the anterior tibial artery is unlikely on anatomical grounds to cause necrosis of all three muscles, the long extensors being less vulnerable than the tibialis anterior. This is confirmed by clinical experience.

There is little doubt that, when the syndrome follows unaccustomed exertion post-exertional swelling of the muscles compresses the anterior tibial artery and its branches, obliterating their lumina. The muscular pain and stiffness that so commonly follow unaccustomed activity are probably due to oedema and microscopic haemorrhages within the muscle. A substantial increase in muscle volume can occur in these circumstances. Barcroft and Kato (1915) found that 15 minutes' intermittent faradic stimulation of a dog's gastrocnemius and digastric muscles, in a manner simulating normal activity, resulted eight hours later in a 19% increase in weight of the muscle due to oedema. Weight-lifting can cause in half an hour a temporary increase of as much as 1½ in. (3.8 cm.) in the circumference of the upper arm (MacQueen, 1954). Small interfibrillary and interfascicular haemorrhages may also occur (Lorenz, 1898; Meyenburg, 1929) and contribute to enlargement of the muscle.

A pressure of about 50–60 mm. Hg, much lower than that required to collapse the main artery, will, when exerted direct upon a muscle itself, collapse its capillaries and completely arrest the flow (Lewis, 1936). Where muscles are free to expand no harm is done. Expansion of the anterior tibial muscles, however, is limited by the relatively rigid walls of the compartment within which they lie. Comparatively slight swelling may therefore raise the pressure within the compartment enough to obliterate the blood supply. The perforating arteries which supply the long extensors run a shorter course within the compartment and are less subject to compression. Hence these muscles are less vulnerable.

When the syndrome is due to a local expanding lesion—for example, trauma or infusion of fluid—the effects of a rise in intracompartmental pressure are similar.

In cases of the third category, five of which are here reported, the effects of an arterial block by embolism or thrombosis and the extent of the infarction are dependent on the site of the block, on the degree of impairment of the collateral circulation by atherosclerosis, and on the amount of swelling in the muscle that follows its infarction. Post-infarctional swelling tends to obliterate collateral vessels and thereby increase the ultimate mass of necrotic muscle.

In Case 1 pulsation was present in the posterior tibial artery and absent from the dorsalis pedis artery, indicating a block in the anterior tibial artery. All muscles within the compartment were paralysed. Biopsy on the 11th day showed ischaemic necrosis. The piece taken 14 months later showed evidence of regeneration. The electrical reactions on the 35th day indicated neuropathic paralysis of those muscles which had not undergone necrosis. The return by the 60th day of contractility and faradic response to the greater part of the muscle group is attributable to recovery from the neuropathy and to regeneration in some of the necrotic muscle fibres. Regeneration has been reported in this syndrome by Pearson *et al.* (1948) and by Hughes (1948), and has been observed experimentally by Le Gros Clark (1946).

At the onset, transient pain was complained of in the opposite leg. This, too, may have been ischaemic and due to contralateral arterial spasm. Atlas (1942) has noted that in cases of embolic occlusion of a small artery of a lower limb the ensuing arterial spasm may be so widespread as to involve the opposite limb. Barnes and Trueta (1942) applied a tourniquet to a rabbit's thigh for several hours. In addition to widespread ipsilateral arterial spasm, they noted occasional spasm in the contralateral limb beginning at the same level as the tourniquet. Arterial spasm following embolism and its subsequent relaxation might explain the return of pulsation to the dorsalis pedis artery. The decubitus, with affected limb flexed at hip and knee, was also noted by Pearson *et al.* (1948), and its cause was discussed in the report on Case 1.

In Case 2 pulsation was absent from the posterior tibial and dorsalis pedis arteries on the affected side, indicating a block, clinically embolic, of the popliteal artery or its bifurcation; yet evidence of ischaemia was confined to the specially vulnerable muscles of the anterior crural group.

Case 3, ascribed to thrombosis, was remarkable for the liquefaction undergone by the contents of the

compartment. As the skin overlying the compartment was not infected, the infection within was probably derived from one of the patient's many boils. No other foci were found. It is puzzling to see how blood-borne organisms could have reached an avascular region. Possibly they were in transit at the moment of infarction. Although arterial thrombosis presumably occurred on a basis of atherosclerosis, infarction was precipitated by profound anaemia and oligaeamic shock. Bedford (1956) has reported cases of cerebral infarction following shock due to severe gastro-intestinal haemorrhage, and Master *et al.* (1950) have reported cases of myocardial infarction of similar origin.

In Cases 4 and 5 the patients were old, and cerebral and cardiac signs indicated the presence of widespread and severe atherosclerosis. Here arterial thrombosis was the immediate cause of the syndrome. The slowly progressive ischaemic atrophy and fibrosis seen histologically gave rise to no clinical signs.

Treatment

It seems logical to treat post-exertional cases by decompressing the compartment with a long incision dividing the deep fascia over the muscles. Promptitude is essential, as muscle deprived of its blood supply will undergo necrosis unless the ischaemia is relieved within a few hours of the onset of symptoms. Decompression after necrosis has occurred may aid regeneration. Despite the failure of limited medical measures in Cases 4 and 5, we suggest that the simultaneous administration of papaverine, nylidrine hydrochloride, and anticoagulants offers hope of resolution in cases due to arterial thrombosis or embolism.

Summary

The clinical features of the "anterior tibial syndrome" are described. The main features are ischaemic necrosis of the tibialis anterior muscle and, in greater or less degree, the extensor hallucis longus and extensor digitorum longus muscles; these three muscles occupy the rigid-walled anterior tibial compartment. The immediate cause of the syndrome is occlusion of the anterior tibial artery or its parent trunk. This may be due to (1) swelling of the muscles following unaccustomed exertion, and consequent rise in intracompartmental pressure above the arterial blood pressure; (2) local expanding lesions within the compartment, with similar effect; and (3) embolism or thrombosis of the anterior tibial artery or its parent trunk.

Five cases are reported, of which two were due to embolism, one to thrombosis following haemorrhagic shock, and two to thrombosis associated with senile atherosclerosis.

Our thanks are due to the surgeons who obtained biopsy specimens of muscle.

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HYPERCALCAEMIA AND RENAL FAILURE IN MULTIPLE SECONDARY CARCINOMA OF BONE

REPORT OF A CASE

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The association of hypercalcaemia and renal failure is familiar from such examples as hyperparathyroidism (Albright and Reifstein, 1948; Cohen, FitzGerald, Fourman, Griffiths, and de Wardener, 1957), calciferol overdosage (Danowski, Winkler, and Peters, 1945), and sarcoidosis (Dent, Flynn, and Nabarro, 1953; McSwiney and Mills, 1956). It has also been described in secondary carcinoma of bone (Albright and Reifstein, 1948; Swyer, Berger, Gordon, and Laszlo, 1950; Snelling, 1952; Couch and Lewis, 1953). The mechanism of the hypercalcaemia in the latter group of cases seems clear enough; it is generally agreed to be due to release of calcium into the blood stream through the destruction of bone by the secondary deposits of carcinoma. Agents which accelerate this process raise the serum calcium; agents which retard the process cause the serum calcium to return towards normal (Pearson, 1957). The mechanism of the renal failure is less certain. It might, for example, be due to the blocking of renal tubules by casts of calcium salts; on the other hand, rapid fluctuations of serum calcium level are sometimes followed so closely by corresponding changes in blood urea that this explanation seems improbable.

Detailed renal function studies in this condition have not often been made; those recorded here do not indicate the exact mechanism of the functional disorder, but because of the sparseness of such information they are presented in the hope that they will stimulate further observations.

Case Report

The patient was a married woman aged 49 whose periods had ceased three years previously. Four months before admission she noticed a swelling in the left breast. On examination a hard mass attached to the skin was found. This was removed at a radical mastectomy. Histology showed trabecular and solid alveolar polygonal-cell

carcinoma, with extension to the axillary glands. She was given post-operative x-ray therapy to the chest wall and axilla.

Two months after the operation she began to notice pain in the lower back. X-ray films showed probable secondary deposits in the right ischium. Further x-ray therapy was given, to the pelvis and lumbar spine, and testosterone, 100 mg. twice weekly, was prescribed. Two weeks later the pain was much worse and the patient appeared mentally confused. Testosterone therapy was stopped, a total of 400 mg. having been given, and the patient was admitted to hospital on March 12.

On admission she appeared slightly confused and fatuous; cerebral secondary deposits were suspected, but there were no localizing neurological signs. An E.E.G. (Dr. Neil Gordon) was reported on as follows: "This record is grossly abnormal. The abnormalities were generalized and consisted of irregular moderate-voltage slow waves in both the theta and delta ranges. There was no regular alpha rhythm, and eye opening did not cause any significant change in the trace. In fact, the background of the record between the slow waves was remarkably flat. There was a slight increase in synchrony on overbreathing. Conclusions: The findings would be compatible with a gross generalized disturbance of cerebral function. The abnormalities were non-specific, but were so marked that if they were due to raised intracranial pressure one would have expected unequivocal clinical evidence of this. This raises the possibility that they are due to a metabolic disorder." Investigation of blood chemistry the next day showed alkalosis, potassium depletion, and uraemia (see Table).

Blood Chemistry

	March					
	13 V	14 V	15 A	17 A	19 V	20 V
Plasma sodium (mEq/l.)	139.5	—	140	138	—	—
Plasma potassium (mEq/l.)	3.4	—	2.9	3.1	4.55	4.8
Plasma chloride (mEq/l.)	91.0	—	94.0	100.0	—	—
Plasma total CO ₂ (mEq/l.)	38.0	—	34.0	27.3	—	—
Blood pH	—	—	7.47	7.465	—	—
Blood urea (mg./100 ml.)	150	—	149	122	106	—
Serum calcium (mg./100 ml.)	—	16.6	16.6	14.2	13.0	12.5
Serum inorganic phosphorus (mg./100 ml.)	—	—	4.5	4.7	—	—

A=Arterial. V=Venous.

The elevated plasma urea, coupled with probable secondary deposits in the skeleton, raised the possibility of hypercalcaemia; the serum calcium was found to be 16.6 mg./100 ml. Subsequent blood chemistry results are shown in the Table and the Chart. The alkalosis and potassium depletion were corrected by the administration of 4 g. of potassium chloride daily: by March 20, when the serum potassium was 4.8 mEq/l., a total of 96 mEq of potassium had been retained, suggesting that originally the potassium depletion was of slight degree only. As may be seen, the serum calcium and blood urea levels fell steadily; the former reached a normal figure by March 27, but the blood urea continued to be moderately raised.

A further E.E.G. on March 18, when the potassium depletion had been nearly, and the alkalosis fully, corrected, but when the serum calcium was still elevated, showed great improvement but was still not quite normal, with poorly formed alpha rhythm and little change on eye opening. The patient's mental state at this stage appeared quite normal. E.E.G. examinations on March 26 and April 2 showed further improvement, the last record being reported as completely normal.