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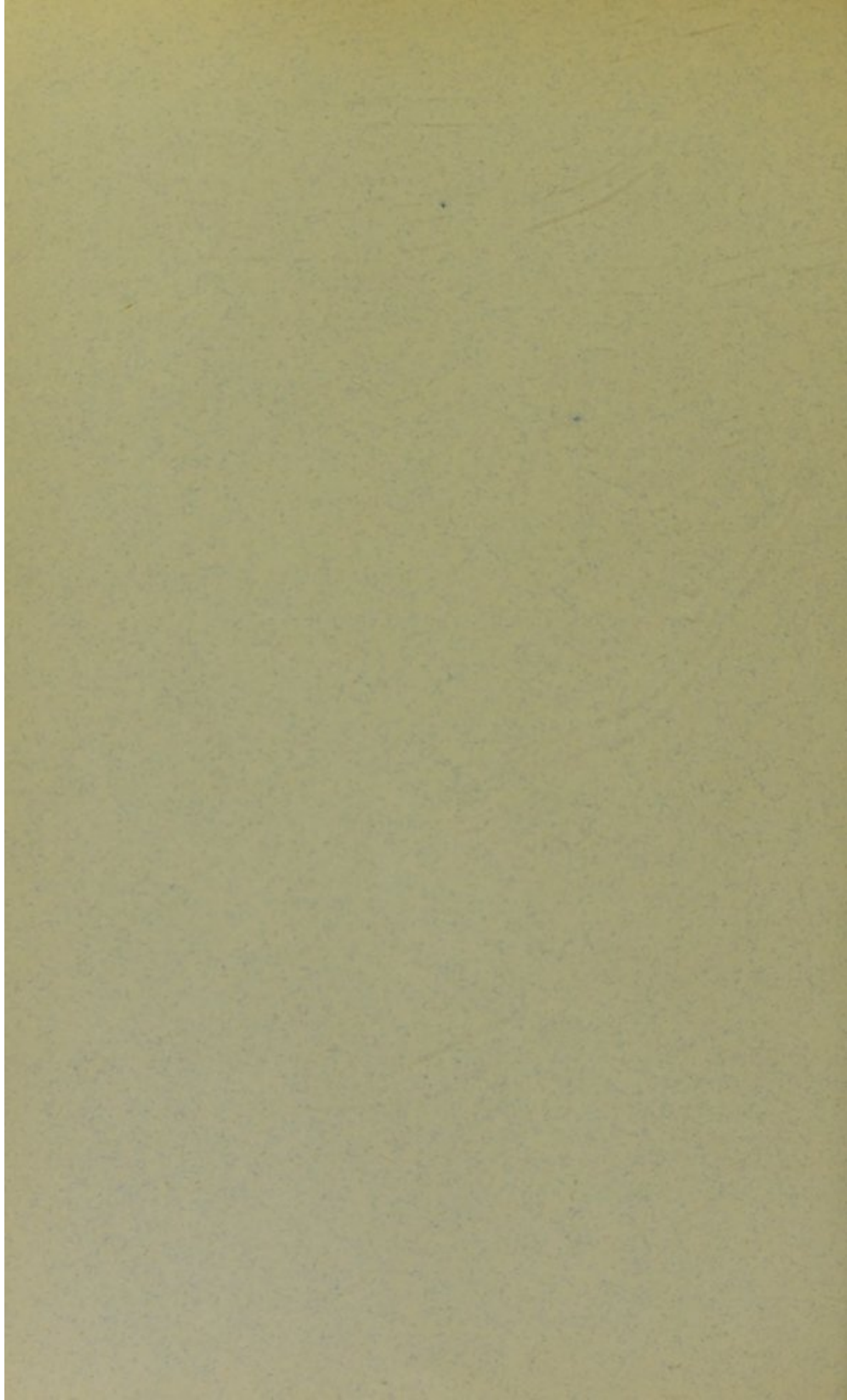
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GANGRENE OF LEG FOLLOWING DIPHTHERIA.

By J. D. ROLLESTON, M.D.,

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GANGRENE OF LEG FOLLOWING DIPHTHERIA.*

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A BOY, aged 13 years, was admitted to the Grove Hospital for diphtheria on June the 19th, 1910, the seventeenth day of disease. The acute attack had been mistaken for mumps by the father, and it was not until his brother had been infected that a doctor was sent for and Klebs-Loeffler bacilli were found in the throat. About a week before admission his voice had become nasal and he had had regurgitation of fluids through the nose. On admission the tonsils showed some opacity, but the throat was free of membrane. The voice was nasal. The knee- and ankle-jerks were active, and the plantar reflex was flexor. The heart was irregular. No antitoxin was given. The same evening the right leg from the knee downwards became cold, pale, and anæsthetic. The toes could not be moved, nor the ankle flexed. The plantar reflex was lost. The circulation was re-established in about four hours. During the next week the heart became much dilated and a loud mitral systolic murmur developed. Both liver and spleen were enlarged and tender. Albuminuria was present from admission till the thirty-fifth day. On the twenty-first day both legs became cold, discoloured and numb. Pulsation was feeble in the posterior tibial and dorsalis pedis arteries. The boy also complained of tingling in both palms, but no alteration was detected in the radial pulses. On the following day the discoloration of the legs had gone. On the thirtieth day sudden pain occurred in the left leg, followed by discoloration. There was marked tenderness in the popliteal space, where the pulsation of the popliteal artery could not be felt. The femoral pulse was present in Scarpa's triangle. Gangrene rapidly developed in the left foot and leg. The photographs show the condition on the thirty-second day. The gangrene did not extend, and apart from the development of some bullæ was kept fairly dry and sweet by means of iodoform.

* Case reported to the Section for the Study of Disease in Children of the Royal Society of Medicine, October the 28th, 1910.

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On his transfer to Charing Cross Hospital, on August the 23rd, the eighty-second day of disease, the gangrenous area involved the whole of the left foot and extended on the inner side 4 in. above the lower end of the internal malleolus, on the outer side to $3\frac{3}{4}$ in. below the head of the fibula, and posteriorly to 7 in. below the popliteal space. There was still some cardiac dilatation, but the systolic murmur had disappeared. The blood-pressure, taken with C. J. Martin's modification of the Riva-Rocci sphygmo-manometer, from admission until the end of the fifth week was 80 mm. Hg., sometimes falling to 70; during the sixth week it ranged between 80 and 100, and in the seventh week and subsequently it was 100 to 96.

FIG. 1.



The voice was clear at the time of transfer, but the right knee- and ankle-jerks were lost. The vision had been frequently tested, but no ocular palsy had been detected. Amputation at the knee-joint was performed by Mr. H. S. Clogg on August the 29th, the eighty-eighth day of disease, when an organising clot was found in the popliteal artery. Subsequent recovery was uneventful.

Gangrene of the extremities as a sequel of infectious disease is relatively rare, though its occurrence has been known since the time of Thucydides, who, in his description of the plague of Athens in 430 B.C., relates that some recovered after loss of their hands and feet (Bk. ii, c. 49). The nature of the Athenian epidemic has not been satisfactorily determined, though attempts have been made by medical historians to identify it with one or other of the acute infections, but not, so far as I know, with diphtheria. Estlander, who regarded the epidemic as one of typhus, states that gangrene of the limbs was also noted in the typhus epidemics of the middle

ages, and in the sixteenth, seventeenth, and earlier part of the nineteenth centuries.

Barraud, in 1904, in an exhaustive monograph on gangrene of the extremities in young persons after infectious disease, has collected 103 cases in patients up to the age of thirty, but only 29 of these were under fourteen, *i. e.* as young as my patient. Nine of these followed typhoid fever, 5 measles, 4 scarlet fever, 2 diphtheria, and 1 each of the following diseases: typhus, pneumonia, influenza, varicella, whooping-cough, tonsillitis, appendicitis, umbilical phle-

FIG. 2.



bitis, and acute gastro-enteritis. In 27 the gangrene involved the lower, and in 2 the upper extremities.

In addition to the two cases in Barraud's list following diphtheria recorded by Hensch and Rosenthal respectively, I have been able to collect eight other cases of gangrene of one or more extremities following diphtheria, thus making a total of eleven, including the present case.

The following is a brief account of these cases arranged in chronological order. I have not been able to consult the original papers in which Cases 1, 2, 7 and 8 were described.

(1) 1875. Moroni's case. Gangrene of an extremity following diphtheria.

(2) 1878. Menzel's case. Gangrene of leg after faucial diphtheria; amputation at upper third of leg.

(3) 1879. Vedder's case. Boy, aged 8 years. Thirteen days after onset of severe faucial and nasal diphtheria gangrene of right

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leg developed, followed in three days by transient right hemiplegia and aphasia. Two days later pain in left leg. Death two days afterwards. No necropsy.

(4) 1883. Poupon's case. Girl, aged $7\frac{1}{2}$ years; laryngeal diphtheria, tracheotomy, albuminuria. Discharged in apparently good health fourteen days after admission. Re-admitted ten days later with great dyspnoea. Pulmonary embolism diagnosed. Signs of right popliteal embolism next day. Violet patches on right foot. Death on following day. Necropsy: Clot in femoral artery extending from opening in adductor magnus to middle of popliteal artery. Lungs not examined.

(5) 1890. Henoch's case. Boy, aged 8 years; very severe diphtheria. Gangrene of lower limbs. Necropsy: Thrombosis of both iliac arteries.

(6) 1890. Rosenthal's case. Girl, aged 2 years; severe diphtheria. Gangrene of both legs. Necropsy: Thrombosis of common iliac arteries.

(7) 1894. Munn's case. Embolus following diphtheria. Gangrene of left leg; amputation; recovery.

(8) 1894. Ward's case. Gangrene of left leg caused by an embolism the result of diphtheria.

(9) 1902. Breton's case. Girl, aged 3 years; moderate attack of diphtheria treated with antitoxin. Seventeenth day: Heart irregular; complete left hemiplegia and signs of thrombosis in left foot. Nineteenth day: Discoloured patches on right leg, ankle, and heel. Twenty-first day: Generalised convulsions. Twenty-third day: Nasal voice; another discoloured patch on metatarso-phalangeal joint of right hallux. Slough formed on heel, but other patches disappeared. Recovery.

(10) 1910. Bendix's case. Boy, aged 10 years; severe diphtheria; extensive gangrene of right index and middle fingers; operation; recovery.

This list does not contain two cases of Raynaud's disease following diphtheria, one in a boy, aged 7 years, reported by Chevron, and the other in a man, aged 48 years, recorded by Powell. In another two cases signs of femoral embolism occurred, but death took place before gangrene had had time to develop, in a case related by Escherich, to be described below, and in the following case reported by Auché: Child, aged $4\frac{1}{2}$ years; severe faucial, nasal and laryngeal diphtheria; tracheotomy; repeated injections of antitoxin. After eight or nine days the general condition became worse and signs of embolism developed in the lower limbs. Death. Necropsy: Apical

thrombi in both ventricles; very intense myocarditis and slight parietal endocarditis; Gram-positive diplo-streptococcus in endocardial clots. Two thrombi, one 5 cm. long in left external iliac and femoral arteries, the other $2\frac{1}{2}$ cm. long in the right femoral artery.

It is noteworthy that all the cases of gangrene of the extremities following diphtheria have occurred in children, in striking contrast to the gangrene following other infectious diseases, especially typhoid and typhus.

In the few cases in which the date of onset is given the gangrene is stated to have appeared in convalescence, as in the present case. In three cases there was evidence of multiple embolism, which probably also occurred in my case.

In most of the previous cases the character of the initial angina was severe. In the present case the throat was clean on admission to hospital, but a retrospective diagnosis of severe angina could be made on the following grounds: (1) The disease was mistaken by the father for mumps—an error frequently committed with disastrous results in the early stage of malignant diphtheria; (2) the occurrence of two phenomena almost exclusively confined to severe attacks, viz. early palatal palsy and enlargement of the liver; (3) though by no means conclusive, the character of the brother's angina is suggestive owing to the frequency with which severe attacks of diphtheria affect members of the same family. Thus in fifty-one out of 133 families, or in 38.3 per cent. suffering from diphtheria, I have noted that two or more members of the same family had an angina of equal severity.

Though recent research has shown that gangrene of the extremities following infectious disease is, as a rule, caused by autochthonous thrombosis due to acute arteritis—in only 10.7 per cent. of Barraud's and 5.7 per cent. of von Wartburg's cases was there definite evidence of embolism—in the present case the origin of the gangrene was almost certainly embolic. In the first place there was a well-marked cardiac lesion. Secondly, emboli were also probably present in situations where primary arterial thrombosis is uncommon, viz. the spleen and kidneys, as well as in the femoral and popliteal arteries of the opposite limb, in which, however, the circulation was re-established. The excessive tenderness and enlargement of the liver were possibly due to hepatic embolism, but these signs are fully explained by the hepatomegaly which frequently accompanies severe diphtheria without any infarction, and is due partly to congestion and partly to fatty change. Thirdly, the diagnosis of embolism in diphtheria

has frequently been verified at the necropsy. Thus in 59 post-mortem examinations I found infarcts in 7, or 11·8 per cent. In four they were situated in the lungs only, in one in the left kidney, in one in the liver, and in one cerebral embolism was associated with renal infarction.

In this connection it may be stated that cerebral embolism, which the present case fortunately escaped, is much more frequent in diphtheria than embolism of the extremities. Though some cases of post-diphtheritic hemiplegia, of which about seventy cases have been recorded, may have been due to thrombosis or encephalitis, in the great majority of fatal cases evidence of embolism has been found.

Escherich has recently published a case of a boy, aged 2 years, admitted to hospital on the sixth day of a severe attack of faucial diphtheria with broncho-pneumonia. Right hemiplegia developed the same day. The next day generalised convulsions occurred. On the eighth day the thighs became livid, cold, and devoid of sensation, and no pulse could be felt in the popliteal and dorsalis pedis arteries. Death took place the same day. The necropsy revealed a thrombus adherent to the ventricular surface of the mitral valve, embolism of the left middle cerebral artery, and softening of the left cerebral hemisphere. Emboli were also found in the left common iliac artery at its bifurcation and in the right femoral artery. Small recent infarcts were present in the right kidney and liver.

Other instances of embolism following diphtheria will be found in the writings of Professor Marfan and his pupils Deguy and Detot.

The sudden onset in this case, though suggestive, is not, as was once thought, pathognomonic of embolism.

The exact situation of the embolus which was the cause of the gangrene in this case it is impossible to determine. As stated above, an organising clot was found in the popliteal artery, but Mr. W. S. Fenwick, surgical registrar of Charing Cross Hospital, has kindly informed me that the lumen of the vessel was not obliterated, so that the embolus which was the cause of the gangrene must have been higher up.

Of the sixty-two cases collected by Barraud in which the site of the arterial obstruction was determined, unilateral femoral thrombosis was the commonest finding, being noted in thirteen cases, and was closely followed by unilateral popliteal thrombosis, which occurred in twelve cases. It is probable, however, as Barraud

remarks, that the latter figure is too high, for in amputation cases which recovered no exact knowledge was obtained as to the extent of the thrombosis, which may, as in my case, have been present in the femoral as well as in the popliteal artery.

It is probable that the excessively low blood-pressure helped to prevent the establishment of a collateral circulation.

The prognosis in gangrene of the extremities following infectious disease is grave, but by no means hopeless. The mortality among Barraud's 103 cases was 51.6 per cent., but many of these date from the pre-antiseptic period. Of the 29 cases in children under fourteen years of age, 13 died, 11 recovered, and in 5 the issue was not recorded. Of the 8 cases following diphtheria in which I have been able to ascertain the issue, 4, including the present case, recovered and 4 died.

Prophylaxis is important, and should consist of large doses of antitoxin and prolonged rest in bed in severe cases of diphtheria. The history of this patient's brother furnishes an instructive example of the value of this treatment. He was admitted with severe angina on the seventh day of disease, when he received 16,000 units of antitoxin. Complete recovery took place, and no complication ensued beyond albuminuria and ciliary palsy. It is noteworthy that in only 1 of the 11 cases of gangrene following diphtheria, viz. that recorded by Breton, had antitoxin been employed.

Finally, I would draw attention to the fact that though more than eight weeks elapsed between the occurrence of the gangrene and the amputation, no harm resulted from the delay. An earlier operation was considered inadvisable owing to the boy's general enfeeblement and his cardiac condition. For the first fortnight following the onset of the gangrene the temperature ranged between 96° and 100° F., but subsequently it remained practically normal.

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