ACROCYANOSIS.*

By EDWARD SAMUEL STERN, M.A., M.D., B.Ch.Cantab., M.R.C.P., D.P.M.,
Assistant Medical Officer, Napsbury Mental Hospital.

INTRODUCTION.

WHEN normal human skin is moderately cooled it goes blue, owing to a contraction of the arteries and arterioles, and a relaxation of the capillaries and subpapillary venous plexus of the epidermis. This blueness is light in colour. In certain individuals, however, it is deep, or relatively saturated, in the hands or feet or both; these include cases of acrocyanosis (ἄκρον = extremity, κυάνεος = dark blue). This condition, though rare in the general population, is common among the inmates of mental institutions.

The latter fact has long been familiar to alienists, and is mentioned in the standard text-books. Stoddart (36) states that in stupor the extremities are often cold and blue, and Henderson and Gillespie (12) note that in schizophrenia the hands, feet, nose and ears (*sic*) show cyanosis and œdema. Similar conditions are found in mental defectives, Tredgold stating (37) that in "mongols" cyanosis and coldness of the extremities are prevalent.

Various hypotheses have been proposed as to its ætiology, course and pathology, but none has seemed satisfactory. It was therefore decided to re-investigate the condition.

It was found that the existing clinical descriptions were incomplete and that nothing further was certainly known. The reasons for previous shortcomings seem to lie in the study of insufficient numbers of cases observed for an insufficient length of time, and a failure to appreciate the mechanics of the small blood-vessels or to make histological examinations.

In this investigation some hundreds of cases of the disorder have been examined, and, in many of these, careful observations have been made over a period of years. Theoretical considerations early led to the prediction of certain morbid histological changes and this was confirmed. A special examination of the blood has also been made in six cases. All the results have been consistent with the same conclusions.

It will be shown that acrocyanosis is due to certain changes in the arterioles caused by continual cooling of the parts, and that the condition is not always permanent. In order to detect it in all cases, special methods have had to

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be used, revealing that it is more prevalent than has been thought. It is approximately symmetrical on the two sides of the body.

History and Clinical Features.

Crocq (7) first used the word "acrocyanosis" to describe a condition in which the hands and feet had slowly become permanently blue, the discoloration ending gradually at the wrist and dorsum of the foot respectively. The colour was deeper on the volar surfaces, which were moist, than on the dorsa, which were dry and cold; it was accentuated towards the toes. Local pressure caused a white spot, which disappeared slowly. There was no œdema, ulceration, paresis, severe pain or contracture. It was readily distinguished from the local syncope of Raynaud's disease, and from Charcot's "blue œdema" with its paresis, contractures and severe pain. Crocq described two cases of acrocyanosis, both hysterics. One of them also suffered from arthritis followed by pleurisy, the other recovered from acrocyanosis when her hysteria was cured.

In two particulars Crocq's description needs amplification. As will be shown, the cyanosis is not permanent, except perhaps in the most severe cases, but it will appear to be so if the patients are examined only when the parts are cool. Secondly, œdema is constantly absent only from the milder cases.

The colour of the cyanosed skin is not uniform, and it usually contains bright red areas—so-called cinnabar red spots (10, 13); it is generally between X and XV on Lewis's scale (23), the colour approaching full cyanosis; above all it is exceptionally deep. The depth of colour depends partly on the position of the parts, being greater when they are dependent. The white spot which can be caused by local pressure, and was noted by Crocq, disappears spontaneously in a very characteristic way, the colour returning from the periphery only, and not also from below as in normal skin. Local œdema is fairly often present; it may merely cause the skin to feel a little tight—a condition seen typically in the fingers—or give rise to visible swelling, in which case pressure causes the usual pitting—a fact which has been denied (8, 18, 38). Chilblains are perhaps a little commoner than normal, but in their absence ulceration and gangrene do not occur, although in severe cases the nails become irregular and brittle, and in the most extreme examples examined (in mental defectives) the skin becomes dry and scaly. The syndrome appears to cause remarkably little disability, and mental patients do not complain of any subjective symptoms, but lesions of the skin in the affected areas readily become septic and heal slowly. In hot weather, and when the subjects are warm or active, the hands and feet may be distinguished from the normal by their clamminess, by a brownish-yellow tinge on the backs of the hands, or in some cases not at all.

This brownish-yellow colour, which has not previously been reported, ends just above the wrists and is most obvious in the summer. It is presumably due to the fact that since the hands are kept still and exposed, they become more tanned by the sun than those of normal subjects. It was only seen on the feet of one patient (A. P—, Appendix, Case 6), and she had not been wearing stockings.

Clamminess of the palms and soles was noted by Crocq and others since him (18, 38), but no further details were given. In this investigation numerous observations with a hand lens have shown that, when present, it was invariably due to liquid issuing from the sweat-ducts. Now Kuno (16) has shown that perspiration at low temperatures occurs more on the palms and soles than elsewhere, is increased by hyperæmia, and, failing to evaporate, collects on the surface. These are precisely the conditions we have in acrocyanosis. If, however, the circulation to the skin ceases, perspiration will fall to a minimum, and this explains the dryness of the parts in Raynaud's phenomenon. He thinks that the greater sweating on the palms and soles serves to keep the thick stratum corneum moist and pliable. It seems probable that in cases who stand about unoccupied this layer atrophies, and the perspiration, being more than sufficient, accumulates and makes the skin wet. The opposite extreme is familiar in the dry, horny palm of the labourer. It is, of course, conceivable that excessive sweating of the parts precedes the development of acrocyanosis—a possibility that will be discussed below (p. 414).

There was no evidence of severe sensory changes in this series. The mental condition of the cases investigated was such that subjective sensory observations could not be made.

Differential Diagnosis.

Acrocyanosis is frequently complicated by erythrocyanosis crurum puellaris, cutis marmorata, which may be extensive, and the pernio follicularis of Klingmüller and Dittrich (13). There may thus be a considerable amount of cyanosis in other parts, and the condition of the patient may bear a superficial resemblance to general cyanosis from a central cause; the pattern and distribution of the skin colour is, however, quite distinctive, and red areas can always be produced by local rubbing or other trauma. The complicating conditions mentioned at the head of this paragraph are themselves easily distinguished from acrocyanosis, as none of them affects the hands or feet.

Thrombo-angiitis obliterans is differentiated by its progressive character, the frequent presence of so-called trophic lesions, and the absence of pulsation in the arteries of the part.

The chief disorder likely to be confused with acrocyanosis is Raynaud's disease. But the former does not cause ulceration or gangrene, hence the small depressed scars, so often seen on the tips of the fingers in cases of

Raynaud's disease, are absent. Local trauma, such as pricking, rubbing or pinching a small area, causes local redness within the surrounding blue of acrocyanosis; but in Raynaud's disease restoration of colour can only occur by an orderly spread from the proximal end, so that at a given instant all parts distal to a cyanosed area must themselves be cyanosed, and the cinnabar red spots, so characteristic of acrocyanosis, are not seen.

The accurate use of the term "acrocyanosis" has not always been observed, e.g., Barker and Sladen (1) have described under this name cases which showed ulceration and gangrene, and appear more probably to have been examples of thrombo-angiitis obliterans. It is indeed uncertain that all the cases collected here from the literature are of the same type, originally described by Crocq, as those investigated below, but the similarity seems such as to justify that conclusion.

Induction of Attacks.

It has been found in this investigation that, if patients known to suffer from acrocyanosis are examined out of doors on an average winter's day, a proportion of them only will manifest the condition. On another such occasion it will be noticed that some of those previously affected are active and warm, with pale and not blue extremities, whilst others, who previously appeared normal, are now seen to be acrocyanotic. This is because the cyanosis of the extremities is partly dependent on their temperature, being most severe with a moderate degree of cold and gradually disappearing as the temperature rises. It explains the observation of Claude and Baruk (7) and Layani (18) that the degree of acrocyanosis varies with the amount of catatonia, for when the latter decreases the patient will be more active and therefore warmer. It also explains Crocq's reported cure of his second case (7), for she probably kept her hands warmer after mental recovery. Patients who do not show this syndrome merely because at the time of examination their extremities are warm may be suitably called cases of latent acrocyanosis—a description which will be used below. In such cases it will be necessary to cool the hands and feet in order to demonstrate the syndrome.

Cooling to the region of 0–10° C. is of no avail, for it makes the hands red. This redness was found by T. Lewis (27) to interfere with the induction of attacks of Raynaud's phenomenon, and it prevents the occurrence of attacks of acrocyanosis for reasons which he gives: dissociation of oxyhæmoglobin is slow at these temperatures, and excessive cold causes dilatation of the arterioles —a reaction discussed below.

Reactions of Normal Skin Vessels to Ice and Iced Water.

T. Lewis (26) showed that local hyperæmia occurred when the normal skin was cooled to the region 0°–10° C. It was believed that the H-substance (22) was liberated and gave rise to an axon reflex, but though local redness and

rise of temperature occurred, and there was a diffuse erythema around the cooled area, this could not be shown to be of reflex origin, since it might equally well have been caused by conduction of cold along the skin from the cooling agent.

If, however, the absence of such erythema around the cooled area could be demonstrated in cases in which the cutaneous sensory nerves had degenerated, it would be evident that the erythema noted above was due to an axon reflex. This was shown by the following observations :

(I) Mrs. H— was first seen in May, 1930, when she had a small abscess, midway down the inner side of the left leg, opened by a transverse incision. The abscess subsequently healed, but she showed sensory changes corresponding to division of the long saphenous nerve at that point.

On July 9, 1930, there was an area of anæsthesia to cotton-wool over the whole of the anterior, posterior and medial surfaces of the lower third of the left leg, and of analgesia to pin-prick 6·5 cm. broad on the medial surface of this area, and here a scratch did not cause any surrounding "flare". Sensation in the right leg was normal.

Both legs were immersed in water at 30° C. for $\frac{1}{4}$ hour, and were then withdrawn and gently dried; their temperatures, measured with a thermal junction, were found to be equal. A lead capsule, through which ice-cold water circulated, was then applied to each leg in turn. The temperature of the outflow was found to vary between 2·7° and 4·5° C. On the right leg a flare was seen extending for a total distance of 4·5 cm. from the edge of the capsule; on the left leg no flare was seen in the analgesic area.

(II) A similar observation, using a small block of melting ice as the cooling agent, was made on December 31, 1931, on a patient, J. Y—, who had had the left tenth thoracic intercostal nerve blocked with alcohol on November 14 previous, for relief from the pain of an attack of herpes zoster.

Thus the two elements, local redness and flare, of T. Lewis's "triple response" (22) are seen when the normal skin is cooled to the neighbourhood of 0–10° C. The third element, œdema, is observed when the skin is more strongly cooled, as was found by T. Lewis and Love (29). These observations support the view that the H-substance is liberated by cooling of the human skin below 10° C.

It will now be evident that strong cooling of the skin, far from inducing attacks of acrocyanosis in latent cases, will, by releasing the vasodilator H-substance, actually prevent their development. A striking confirmation of this is that on exceptionally cold days, subjects of this malady are found to have bright red, and not blue, hands.

ÆTIOLOGY.

Numerous suggestions have been made, but the logic of many of them is exceedingly difficult to follow. As is usual in obscure conditions, almost cryptic causes have been involved.

Delater and Hugel (8) described acrocyanosis amongst various other

erythrocyanotic changes in the limbs, all of which they consider to be due to an endocrine-neuro-vegetative disorder. Layani (18), who has written a monograph on this syndrome, thinks it is due to pluriglandular endocrine dysfunction acting through an abnormally labile autonomic system. Villaret (38) believes the cause to be endocrine, especially ovarian, except in such cases as catatonia, Parkinsonianism and hemiplegia. Kreis (15) does not consider it to be a true clinical entity, but to be due to a taint with hereditary syphilis. He states that, though there is probably a connection with the female reproductive organs, this will not allow us to seek the origin in an ovarian deficiency, since "Ce recours est équivalent à l'explication d'un phénomène inconnu par une nouvelle inconnue".

Most other authors, however, favour exposure to cold as the cause. Heidenfeld (11) and Moeller (32) have described cases of the allied condition erythrocyanosis crurum, which they believe to be due to the insufficient warmth in the modern clothing of young women. Klingmüller and Dittrich (13) include various cutaneous cyanotic conditions in the term "perniosis", and consider them all to be consequences of cold and fall in external temperature. Haxthausen (10) follows these two workers, and points out that the situation of these maladies on the face and hands, and in females the lower limbs, is consonant with such a cause, and also that the lesions have a certain similarity to the acute effects of cold. Nevertheless, he thinks there is another factor also concerned, and that acrocyanosis in particular "is the expression of a more diffuse, but not very intensive action of cold upon the skin, or rather that it is that form of perniosis in which the effect upon the vessels of the predisposing factors is particularly evident in comparison with that of the exciting factor—the cold".

In the course of these investigations it has been found that acrocyanosis occurs with striking frequency in catatonic dementia præcox. The observation is not a new one. Layani (18, 19) has called acrocyanosis in catatonics "cyanose de décliveté',' which is perhaps best translated as "gravitational cyanosis". Villaret (38) includes it among his "symptomatic acrocyanoses".

It was decided to investigate acrocyanosis in the patients occupying two subacute-chronic wards, one male and one female, in the Napsbury Mental Hospital of the Middlesex County Council. They were selected as a representative sample of mental hospital population in this country. Fifty-five patients of each sex were investigated. They wore ordinary loosely fitting clothes, with boots when out of doors, woollen hose, and no gloves. The observations on the women took from June to August, 1931, and on the men, from the latter month to January, 1932. In each case if an attack was not in progress, the hands and feet were cooled by immersion in water at 20° C. until an attack occurred or for $\frac{1}{4}$ hour. Actually only a small number of those affected were seen in a spontaneous attack, and in the absence of artificial cooling to a suitable temperature they would have escaped notice altogether.

The cases were classified by their psychiatric diagnoses, by whether they habitually stood about or were normally active, and by the degree of acrocyanosis obtained.

Diagnosis.	Habits.	No acrocyanosis.	Mild acrocyanosis.	Marked acrocyanosis.
Dementia præcox	Still, 45	14	5	26
	Active, 22	15	1	6
Mania	Still, 0	..	..	..
	Active, 8	6	1	1
Melancholia	Still, 6	3	1	2
	Active, 2	2	..	..
Delusional	Still, 3	2	1	..
	Active, 11	8	2	1
Epileptic	Still, 0	..	..	..
	Active, 7	5	1	1
Mental defect	Still, 2	1	..	1
	Active, 4	4	..	..
Totals	Still, 56 (100%)	20 (36%)	7 (12%)	29 (52%)
	Active, 54 (100%)	40 (75%)	5 (9%)	9 (16%)

There were 55 cases of each sex; altogether 26 men and 24 women had acrocyanosis.

It will be seen from the table that acrocyanosis is two-and-a-half times as common in those who habitually stand or sit about and allow themselves to be chilled as in the normally active. No other factor was found to bear any constant relation to it, although in each case the blood-pressure, full mental and physical state and, frequently, the blood Wassermann reaction were examined. There was no evidence of endocrine dysfunction.

In order to obtain still more reliable evidence, 49 of these patients were re-examined at the end of nearly four years; the results point to the same conclusion. It was found that 13 (26%) showed decreased activity, leading to greater cooling of the extremities, and in all of these the degree of acrocyanosis was found to be increased. Six (12%) showed the contrary changes of increased activity and warmth with decrease of acrocyanosis. Two (4%) inactive cases had developed acrocyanosis without change in their habits. The remaining 28 (58%) showed no change in either way. These 49 cases were selected only because they were the most readily available, and it is striking that the results, without exception, indicate continued cooling of the parts as the cause of acrocyanosis.

It is possible that, in some cases, cooling may arise indirectly from mental stress and so cause acrocyanosis, for Kuno has shown (16) that sweating on the palms and soles is principally caused, not by heat, but by emotion. This will, of course, cool the part. It has been demonstrated above that acrocyanosis results from continued local cooling. In the following case emotion may thus indirectly have caused a mild acrocyanosis:

J. H—, a schoolgirl, aged 13½, was referred to the North-Western Child Guidance Clinic in March, 1935, on account of emotional difficulties. She was precociously developed, but presented no other physical abnormalities.

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She stated that she usually suffered from broken chilblains on the fingers and toes in the winter, and that for about three years her hands had been noticed to go unduly blue when cold. Her mother confirmed this.

When examined on April 18, 1935, at a room temperature of 17° C. her hands were slightly bluish and warm except for the fingers. The palms were moist, and beads of sweat were seen at the orifices of some of the ducts on the fingers. After 15 minutes' immersion in water at 20° C. the right hand was colour XII–XIII, the left XIV on Lewis's scale (22), i.e., they were cyanosed. Both were pale, could be paled further temporarily by elevation or light pressure, and trauma caused local reddening.

The circulation in the feet was found to be normal. The blood-pressure was 107/71.

Incidence.

Most of the cases of acrocyanosis in this investigation were between 20 and 45 years of age. This is a little below the average age in mental hospitals, probably because as age advances catatonia decreases and the patients keep warmer. The youngest was an epileptic idiot aged 4 years and 9 months (a fairly severe acrocyanotic), and the oldest a paraphrenic aged 67 (a mild case of acrocyanosis), but it is not suggested that these represent limits.

Layani (18) and the French authors state that acrocyanosis is commoner among females. The table given above (p. 414) does not support this contention, for of 110 comparable cases consisting of 55 of each sex, 26 men and 24 women were affected. It may be, however, that in non-psychiatric practice women are more likely to seek advice for a condition that is unsightly rather than disabling.

It will be noticed from the same table that the syndrome is not confined to any type of mental disease, although it is particularly common in dementia præcox and rare in mania. It is apparently rather exceptional in the general population, though known in dermatological practice. Nevertheless it is important, for 50 patients out of 110, chosen as an average sample of mental hospital population, showed demonstrable acrocyanosis, only 18 of them being mild cases. Therefore, since the number of persons suffering from mental disorder, notified as under care in England and Wales on January 1, 1934, was over 150,000 (2), the condition must affect some thousands.

Mechanism.

It is customary to dismiss the question of mechanism of acrocyanosis, chilblains and the like, by attributing them to a "poor circulation". This vague phrase, which has been a veil for much ignorance, is best avoided, "poor peripheral circulation" being preferable if some such expression be necessary.

Boas (3) found the capillary blood-pressure to be lowered in acrocyanosis, and the capillaries thickened with a slow stream, which was accelerated in hot water. Delater and Hugel (8) state that there is spasm or endothelial

proliferation of the last arterial branches in acrocyanosis, but they do not give their evidence. In the allied condition of perniosis they found distension of the capillaries and of the veins of the subpapillary plexus, and also peristaltic inco-ordination, which they consider to be the primary factor involved. Nielsen (33) reports stagnation of the blood in the minute vessels in erythrocyanosis crurum, as also does Dittrich (9) in the various conditions he includes in the group of perniosis. The last author describes various histological changes in the vessels of the deeper layers, including thickening of the muscular and intimal coats, and thrombosis. His work is of a painstaking nature, but suffers from the confusion consequent on describing such obviously different conditions as acrocyanosis, erythrocyanosis crurum puellaris and chilblains under the single heading of "perniosis". According to Villaret (38), acrocyanosis results from venous hypertension due to a primary fault in the veins and venules. Claude and Baruk (6) report capillaro-venous atony but give no precise data. May, Bréant and Layani (31) examined the cardiac output in a number of acrocyanotics and found it to be normal, from which they concluded that there was no primary cardiac fault nor any obstruction to the circulation. Layani (19), in a separate paper, finds no arterial or venous spasm, but he thinks that acrocyanotics have a hypo-excitable sympathetic system, and that in the "cyanose de décliveté" there is a primary atony of the capillaries. In his book on this disease, however, Layani (18), having divided acrocyanosis into various types, considers "cyanose de décliveté" to be caused by the joint effects of gravity and vasomotor paralysis due to a supposed lesion of the cortico-striate nucleus. He is much concerned with endocrine and vasomotor considerations, and it is difficult to follow his arguments. A recent speculation is due to Paterson (34). He finds the respiration of schizophrenics to be shallower and quicker than that of normal subjects. When catatonia increases, the respiratory rate is said to fall below normal. He suggests that "failure of oxidation" may occur with cyanosed extremities. This is absurd, for cyanosis from such a cause, which would appear when there were about 5 grm. of reduced hæmoglobin per 100 c.c. of blood (Langdon-Brown (17)), would be general in type. Local cyanosis, like local inflammation, is always due to local causes.

In normal subjects local cutaneous cyanosis can readily be obtained by venous obstruction, as when a sphygmomanometer armlet, applied round a limb, is inflated to a pressure between systolic and diastolic. But in the case of normal cool skin, cyanosis is due to arterial or arteriolar constriction, which slows the blood-stream through the skin, resulting in dilatation of the capillaries, including the subpapillary venous plexus, owing probably to the effects of cold and an insufficient blood-supply. Such an area of skin readily becomes paler if raised above the level of the base of the heart, showing that there is no venous obstruction. T. Lewis and Landis (28) showed that this phenomenon could be demonstrated in a case of acrocyanosis. They also showed that

light pressure on the acrocyanotic skin caused a white spot, which disappeared in a few seconds leaving no trace, showing that the blood had merely been displaced temporarily to adjacent parts of the skin. Thirdly, since local trauma produced a red area within the surrounding cyanosis, they concluded that there was an arteriolar obstruction. At the suggestion of the former of these authors all the cases reported here have been subjected to these three tests, and in each case these results have been confirmed.

The slowly disappearing white area caused by local light pressure was first noticed by Crocq (7), and its method of closing inwards from the periphery like an iris diaphragm is well known (18). The time for this closing to complete itself in the cases investigated here varied with the size of the spot, the level of the part in relation to the base of the heart, the degree of œdema and various other factors, and took from a fraction of a second to about a minute. The returning colour does not always appear to come exclusively from the periphery ; a minute amount may come from the deeper parts, for the circulation to the skin has not entirely ceased in acrocyanosis, as is said to be the case in Raynaud's phenomenon (27), and a superficial prick or cut will cause bleeding.

The red area which follows local trauma in acrocyanosis is presumably due, as in normal skin, to a release of the H-substance which relaxes the arterioles. Lewis and Landis (28) noticed that the tint of the redness was very deep ; probably this is because the cutaneous capillaries and venules are already widely dilated and so readily fill with fresh blood. It has been observed in the cases investigated here that the area of redness produced always greatly exceeds the area traumatized, and also that if the circulation to an acrocyanotic finger be occluded for 7 minutes by a rubber band, and then released, the reactionary hyperæmia, instead of ending at the mark made by the band, as in the normal finger, extends from one to two centimetres proximal to it. These two phenomena are presumably due to the ready diffusion of the released H-substance through the dilated minute superficial vessels to reach other arterioles. Allied to the above are the so-called cinnabar red spots, believed by Klingmüller and Dittrich (13) and Dittrich (9) to result from local arterial paralysis from summation of cold effects ; they are simply areas of local arteriolar relaxation, probably sometimes due to local reactive hyperæmia as suggested by Haxthausen (10) or to any other cause of local inflammation, sometimes to trauma, but in all cases dependent on local release of the H-substance.

All these matters are readily explained by the hypothesis of T. Lewis and Landis (28) that in acrocyanosis there is an arteriolar obstruction. Release of the latter will be shown by the skin becoming bright red, and later normally pale as the capillaries and venules of the subpapillary venous plexus recover their tone. In the most severe cases, which occurred in mental defectives, relaxation is said never to occur, the feet remaining deep blue throughout the year, but even here local redness in response to trauma was obtained, though

after a delay of a few minutes. In the ordinary severe case pallor is present only during a period of hot weather or rest in bed. The effect of shorter and local warming is to cause incomplete release, as shown by the following observations:

Observation 1.

P. P— (Appendix, Case 1), December 8, 1933, p.m. Room temperature 7° C. The subject stood and immersed his hands and wrists in a bowl of water at the level of his lower abdomen.

The temperature of the water was kept at 39–41° C.

The hands were deep purple and cold, there were a few small ulcers, probably chilblains, with no surrounding erythema. The forearms were cold, marbled and blue.

Hr.	min.	sec.	
		0	Both hands immersed.
	5	0	Colour of both a little deeper.
	9	0	Distal phalanges of left hand bright red.
	13	30	Right hand has paled a little.
	40	0	Both hands deep blue, except around the ulcers, where there is now a slight erythema. Colour of forearms unchanged. Hands withdrawn and dried gently; subject returned to ward.
3	25	0	Both hands deep blue, though a little paler than usual.

Observation 2.

Same case, January 1, 1934, p.m. Room temperature 7° C.

The hands were cold, and deep blue except for the digits, which were deep red. The forearms were cold, marbled and blue. The procedure was as above except that the water was kept at 44–46° C.

Hr.	min.	sec.	
		0	Both hands immersed.
	3	30	Metacarpal regions red, knuckles still blue.
	5	30	When the blood is gently pressed out of the blue patches it returns at once, but is redder, and then recovers its original blue colour.
	13	0	No blueness left except on ulnar borders of hands.
	14	30	The skin superficial to the principal veins on both forearms is warmer.
	15	30	The skin is pink for 7 cm. proximal to the water line.
	16	0	Both hands remain red.
	20	30	The redness has spread up the radial sides of the forearms along the veins nearly to the elbows.
	24	0	The colour of the hands is still deeper and a little bluer than normal.
	40	0	No further change; both hands withdrawn and dried gently.
	41	0	Colour unchanged. Subject returned to ward.
1	34	30	Dorsa of fingers, knuckles and ulnar borders of hands red. Dorsa of metacarpals a little fuller in colour than normal. Thumbs and palms normal. The hands are still warm.

January 2, 1934: Hands fully cyanotic.

Observation 3.

G. S. M—, single, butter blender, admitted on November 27, 1932, aged 24; dementia præcox; shows waxy flexibility, automatic obedience, depression; stands about indifferent to his surroundings, rarely speaks and is impulsively violent. Marked acrocyanosis of his hands was noticed on January 20, 1933, and frequently since then. His blood was fully investigated, as in the appendix, and showed no abnormality.

December 12, 1933, p.m. Room temperature 9·8° C.

A less severe case than the above; he had kept his hands in his coat pockets all day; they were light mauve and slightly œdematous. The temperature of the water was kept at 38–42° C.

The procedure was as above.

Hr.	min.	sec.	
		0	Both hands immersed.
	2	30	Both hands reddening a little.
	4	30	Redness increasing.
	6	30	Left hand bright red.
	7	30	Fingers of right hand reddening more.
	10	30	Both hands paler. Forearms blue to water line, where they abruptly become bright red.
	13	0	Both hands bluer.
	18	0	Fingers of both hands going pink.
	23	0	Both hands redder; ulnar borders have remained bluish.
	35	30	Both hands bluish.
	41	30	Both hands mottled purple.
	42	0	Both hands reddening.
	43	0	Forearms still as at 10 min. 30 sec.
	43	30	Both hands going blue.
	46	0	Both hands reddening.
	46	30	Both hands withdrawn and gently dried; they at once went a uniform deep pink.
	49	0	Both still warm, going blue.
	51	15	Both bluish.
	52	30	Both going pink. Subject returned to ward.
2	30	0	Hands pale, but a little bluer than those of a normal subject.

In this observation the hands did not go permanently pink; their colour fluctuated simultaneously, recalling the phenomenon of "hunting" when the fingers are cooled in crushed ice (26).

T. Lewis and Landis (28) found by constructing colour-temperature charts and from the volume pulsation of the finger at various temperatures that the vessels could expand to near the normal, and so concluded that there was no structural change. These arguments are not conclusive. Recurrent spasmodic disorders of tubular structures are accompanied by muscular hypertrophy; e.g., congenital hypertrophic pyloric stenosis, and the hypertrophy of the intestinal, ureteric, or bladder-wall above a chronic partial or intermittent obstruction from any cause.

The cases of acrocyanosis observed here have stood or sat about, indifferent

to the temperature of the parts, for long periods in almost any weather. They have been under constant supervision, and so have not been allowed to become extremely cold. Their extremities have in this way often been cooled to a moderate extent, at each fall in temperature the cutaneous arterioles have

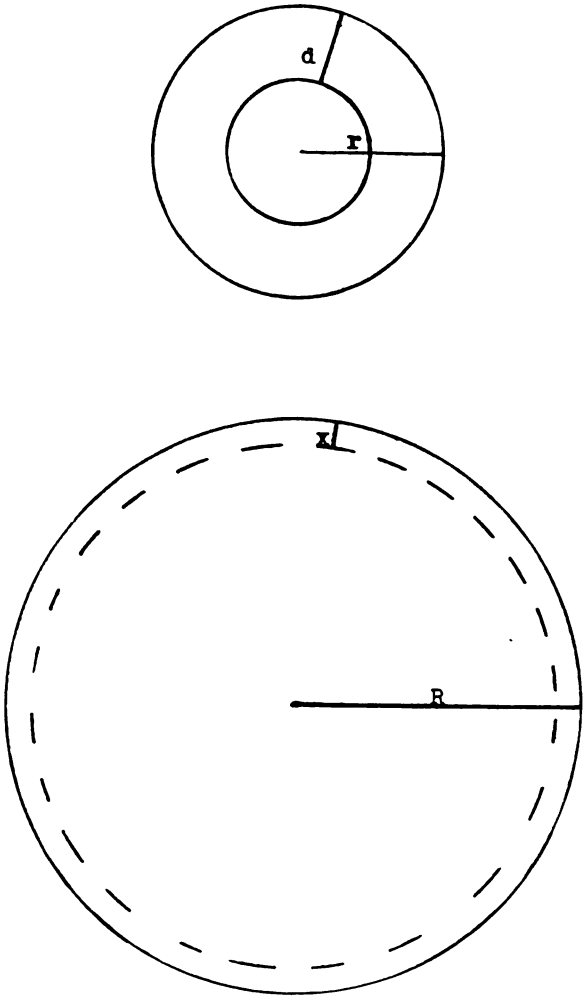

FIG. 1.

made the appropriate physiological response of contraction. Consequently hypertrophy of the muscle of the media of these vessels is to be expected. This involves some thickening of the vessel wall. Being elastic in nature, however, it will be negligible when the vessel is relaxed, as can be seen from the diagram (Fig. 1) and the following simple mathematical considerations.

Let the radius of the lumen of a normal arteriole when contracted be r. then let the muscular part of the vessel hypertrophy so that its wall becomes elastically thickened by an amount d. The radius of the lumen is now reduced to $r - d$.

Then the area of cross-section of the thickening is—

$$\pi r^2 - \pi(r - d)^2.$$

Let the vessel now expand and its new radius be R, which is big compared with r.

If the thickening in the wall is now x,

$$\pi R^2 - (\pi R - x)^2 = \pi r^2 - \pi(r - d)^2,$$

since the area of cross-section of the thickening of the vessel wall must be constant, i.e.,

$$x^2 - 2Rx + 2rd - d^2 = 0.$$
$$\therefore x = R \pm \sqrt{R^2 - 2rd + d^2}.$$

But since r and d are small compared with R, their second order terms are negligible compared with R^2.

$$\therefore x = 2R \text{ or } 0.$$

But the solution $x = 2R$ is inadmissible and is obtained because—

$$(r - d)^2 \equiv (d - r)^2.$$
$$\therefore x = 0.$$

i.e., when the arteriole is considerably expanded the thickening of the wall is negligible.

N.B.—In the above the density of the thickening in the vessel-wall is assumed constant, though in fact it will decrease on relaxation. But the error introduced will not be great enough to alter the result.

The above simple piece of reasoning is necessary for the proper understanding of affections involving spasm or thickening of the walls of the smaller blood-vessels. Ignorance of it has led to the "reactive hyperæmia test", long known (1), and recently described in exact terms by Pickering (35), being applied to differentiate obstructive from spasmodic affections of the peripheral vessels. His method is briefly as follows: The subject is kept warm in a room at or above 20° C., the limbs being heated by immersion for 10 minutes in water at 35° C., or by blankets and hot-water bottles. The limb is emptied of blood by elevation and its circulation abruptly stopped by inflating a sphygmomanometer cuff round the proximal segment of the limb to above systolic pressure. A bright red flush should reach the tips of the digits in less than 5 seconds, become maximal in less than 15, and fade quickly. The conditions laid down have been carefully followed. It was, however, found that warming of the limb by immersion in warm water was unsatisfactory, probably because

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the heat did not penetrate to the deeper tissues. Œdema of the part may also interfere with the validity of the test.

The following results were given by typical cases of acrocyanosis. The times are the number of seconds taken by the flush of reactive hyperæmia to reach the areas stated :

Case.	Pulp of fingers.		Pulp of toes.	
	Left.	Right.	Left.	Right.
1. App., p. 431	2·0	2·2	3·8	2·2
R. R—, p. 423	1·8	2·0	4·4	3·8
2. App., p. 431	..	..	1·4	..
4. App., p. 433	..	3·2	..	..
Case.	**Dorsum of hand.**		**Dorsum of foot.**	
R. R—, p. 423	2·0	3·8	4·4	3·8
4. App., p. 433	1·6	1·6	3·2	2·2
2. App., p. 431	2·8	..	..	..
J. C. C— (acrocyanosis and arteriosclerosis)	..	1·2	2·4	..

They are all within the normal 5 seconds limit. Probably the test holds good in the case of structural diseases of the arteries, where such anatomical changes are rigid, but it is not valid in elastic thickenings of the smaller vessels. The skin from the dorsum of the hand and foot of these cases was sectioned, and in each instance showed much thickening of the media of the arterioles (pp. 422–427). Pickering (loc. cit.) states that in acrocyanosis the test is normal, but erroneously considers this to be due to the spasmodic, as opposed to structural, nature of the disease.

Pathology.

I. Histology.

(1) H. W. B—, a married labourer admitted on December 12, 1930, aged 22 ; an epileptic imbecile. Physical examination showed no signs of disease ; the Wassermann reaction was negative. On November 7, 1931, he was found to have mild acrocyanosis of the hands and feet ; the systolic blood-pressure was 127.

He died in status epilepticus, and at the post-mortem on September 9, 1932, approximately 32 hours after death, a piece of skin was removed from the back of the right hand.

Sections show :

The veins of the subpapillary plexus are dilated. There is an increased amount of fibrous tissue in the cutis vera, where there is also slight hypertrophy of the medial coat in arterioles of about 40μ diameter. In the subcutis this hypertrophy is marked in arterioles of diameter 150μ and upwards. The largest arteriole seen just below the cutis has a greatly thickened medial coat and attains the abnormally large diameter of 400μ (Fig. 2).

(2) R. R—, a single man, admitted on March 19, 1926, aged 24 ; dementia præcox ; continuously hallucinated, impulsive, shows waxy flexibility, stands about a great deal, indifferent to his surroundings. Physically he shows no sign of disease. Examination on January 19, 1932, revealed marked acrocyanosis of the hands and feet ; this was frequently observed before and since then ; blood-pressure 113/78. On January 9, 1934, biopsies were made, using

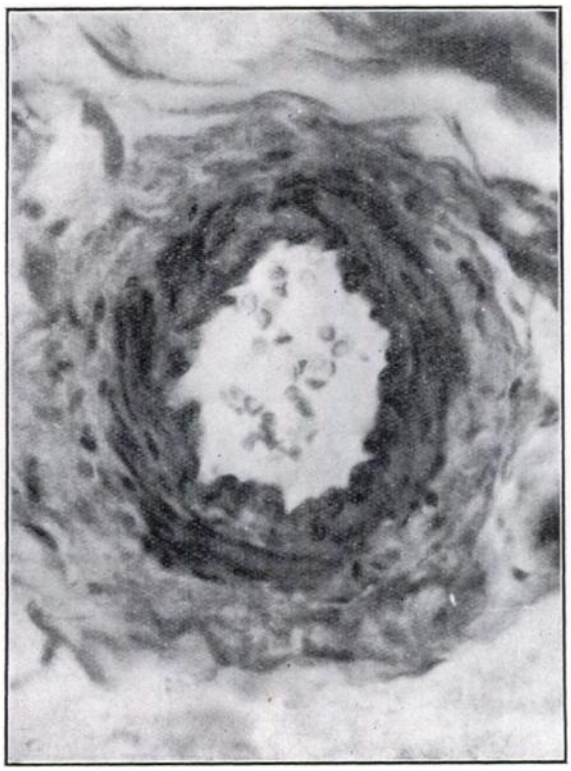

FIG. 2.—Cutaneous arteriole in acrocyanosis, showing thickening of wall. Case H. W. B—. × 400.

1% novocaine with adrenaline as a local anæsthesic, a few minutes being allowed for the fluid to absorb before removing the tissue.

Sections of skin of back of the left hand between the fourth and fifth metacarpals :

There is slight increase of fibrous tissue in the cutis vera ; the medial coat of arterioles of about 60μ diameter is considerably thickened.

Sections of skin of back of left foot 4 cm. proximal to the fourth interdigital cleft :

There is œdema of the cutis vera and subcutis ; just within the former there is thickening of arterioles of about 100μ diameter, the vessel wall being

three times the average thickness, and the number of nuclei in the muscle being greatly increased, showing that proliferation has taken place (Fig. 3).

(3) S. M. O— (Appendix, Case 2).

(*a*) Skin from back of left hand, just proximal to knuckle of little finger, removed on July 26, 1935, using 0·75% cocaine hydrochloride with 1/100,000 adrenaline as a local anæsthetic.

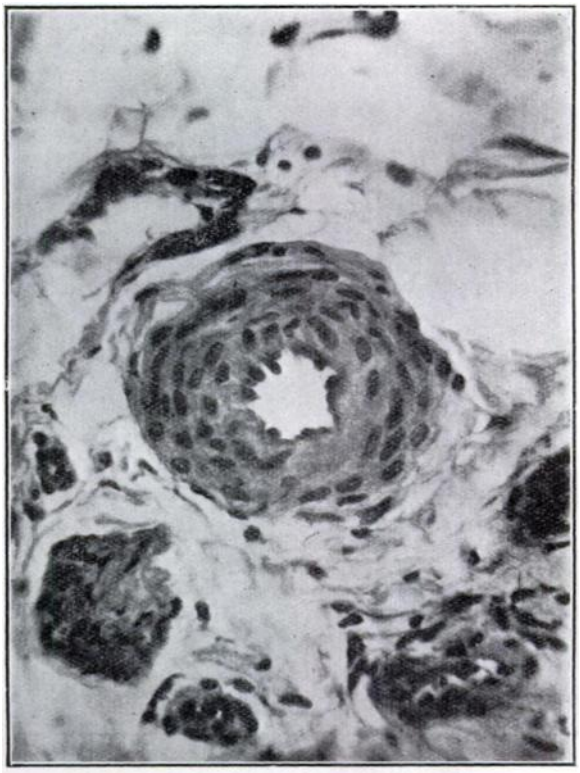

FIG. 3.—Cutaneous arteriole in acrocyanosis, showing thickening of wall. Case R. R—. × 400.

Section shows slight dilatation of the vessels of the subpapillary venous plexus, increase in the fibrous tissue and hypertrophy of the media of arterioles of about 30μ diameter with corresponding thickening of the venules in the cutis vera. The subcutaneous tissue is not shown.

(*b*) Skin from dorso-lateral border of left foot about 2 cm. proximal to fifth metatarso-phalangeal joint, removed as in (*a*).

One section shows increase of fibrous tissue in the cutis vera with hypertrophy of the medial coat of arterioles of 20 and 40μ diameter. The same change is seen in an arteriole of 30μ in the subcutis.

Another section shows medial hypertrophy in an arteriole of 250μ diameter in the subcutis.

(*c*) Skin from dorso-lateral border of right foot about level of fourth interdigital cleft, removed on October 25, 1935, using 1% novocaine only as a local anæsthetic.

Section shows the subcutis, which is œdematous, and contains arterioles of 70 and 250μ diameter, the medial coat of which is thickened.

(*d*) Skin from dorso-ulnar border of right hand 1 cm. proximal to knuckle of little finger, removed as in (*c*).

Section shows dilatation of the veinlets of the subpapillary plexus, œdema and fibrosis of the cutis and hypertrophy of the media of arterioles of 300 to 500μ in the subcutis; these represent vessels which, lying just under the cutis, are very much bigger than those normally found.

(*e*) Skin from corresponding part of left hand, removed as in (*c*) except that adrenaline was added to the local anæsthetic.

One section shows fibrosis and œdema of the cutis and thickened media of arterioles of 30 to 40μ diameter.

Another section shows dilatation of the veinlets of the sub-papillary plexus, fibrosis and œdema of the cutis. In the subcutis there is œdema and medial hypertrophy in arterioles of 60, 200 and 700μ diameter, this last being enormously greater than any arteriole normally found in such a place.

(4) T. A. C— (Appendix, Case 4).

(*a*) Skin from back of left hand 2 cm. proximal to space between knuckles of middle and ring fingers, removed on July 30, 1935, using the same method as in (3*a*) above, and allowing ½ hour after the injection before making the incision.

Sections show dilatation of the subpapillary venous plexus, increase of fibrous tissue and some thickening of the medial coats of arterioles of about 50μ diameter in the cutis vera.

(*b*) Skin from dorso-ulnar border of right hand at level of fifth metacarpo-phalangeal joint, removed on October 11, 1935, using 1% novocaine only as a local anæsthetic.

Sections show that in the cutis vera there is fibrosis and œdema, and that the sub-papillary venous plexus is dilated; the medial coats of arterioles of 50 to 100μ diameter are thickened.

(*c*) Skin from lateral border of right foot 5 cm. proximal to the tip of the little toe, removed as in (*b*).

Sections show, in the cutis vera, considerable dilatation of the subpapillary venous plexus, œdema, fibrosis, and also thickening of the medial coats of arterioles, including some of 70, 90, 120 and 300μ diameter, this last being a vessel enormously greater than that normally found in such a situation. There is œdema of the subcutis with thickening of the media of arterioles of about 70μ diameter.

(*d*) Skin from part of left foot corresponding to (*c*) removed in the same way except that adrenaline was added to the local anæsthetic.

Sections show, in the cutis vera, dilatation of the subpapillary venous plexus, œdema, fibrosis, and also thickening of the medial coat of arterioles of about 100μ diameter. Other sections show œdema and fibrosis of the cutis vera and thickening of the medial coat of an arteriole of 50μ diameter; at the base of the cutis a similar change is to be seen in arterioles up to 150

and 200μ diameter. In the subcutis is an arteriole of 300μ diameter, with thickening of the medial coat (Figs. 4 and 5).

Similar results were given by the examination of sections from 8 other cases of acrocyanosis; all were compared with the normal, and the degree of change was found to correspond with the severity of the disease. Sections

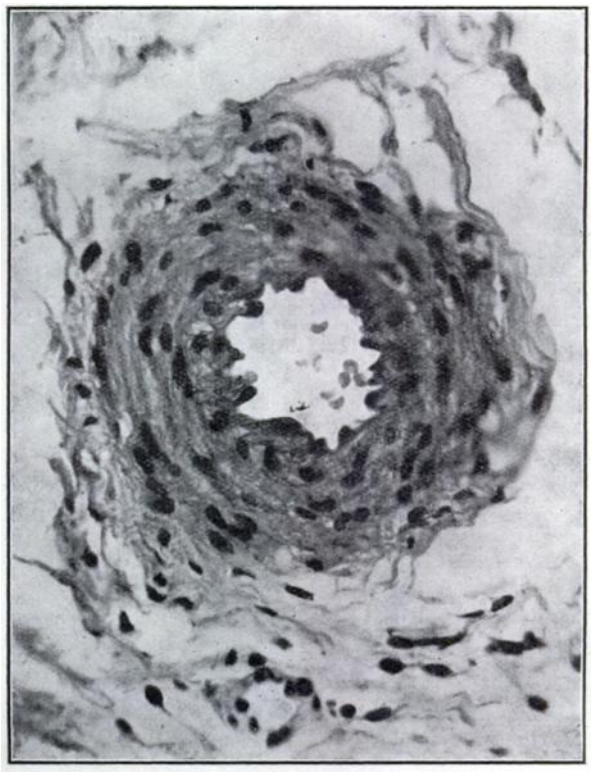

FIG. 4.—Cutaneous arteriole in acrocyanosis, showing thickening of wall. Case 4. × 400.

were stained with hæmatoxylin and eosin, and also with Weigert's elastin and van Gieson's stains in order to differentiate the medial coat. The essential change appears to be that the muscle tissue in the medial coat of all arterioles in the skin of from 30 to 700μ diameter is strikingly increased. This had been predicted by the considerations on p. 421 above, which also show that any such change must be great to be detectable unless the vessel is contracted.

It might be argued that in some of these cases normal arterioles merely in a state of spasm, perhaps from adrenaline, have been seen. The same changes, however, were seen in post-mortem specimens, e.g., (1), and in (3) and (4)

corresponding portions of skin were examined (*c* and *d*), and adrenaline caused no appreciable difference. It was further found that in comparison with normal arterioles which might have been supposed to contract to such a size, with a wall three times the normal thickness, the number of nuclei in the medial coat was more than doubled, showing that a proliferation and not merely a hypertrophy had occurred. Again, in some cases the thickening was so great that the adjoining parts of the cutis and subcutis contained arterioles much larger than are normally to be found there.

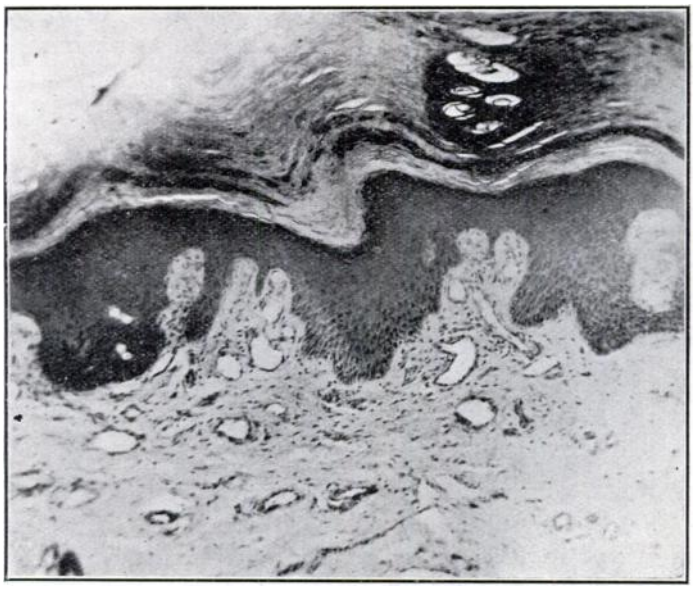

FIG. 5.—Dilatation of the subpapillary venous plexus and capillaries. Case 4. × 75.

The other histological changes—dilatation of the subpapillary venous plexus, fibrosis and œdema of the cutis vera and œdema of the subcutis are probably secondary to the local circulatory changes.

II. Hæmatology.

Layani (18) states that acrocyanotics show various blood disorders, especially prolongation of the coagulation time, up to an hour or more, change in the mode of coagulation caused by failure to retract properly on sedimentation, and lowering of the platelet count. These matters, and a number of others, have been investigated in some well-marked cases of acrocyanosis. In no case was any abnormality found; the results in 6 of these patients are given below in the Appendix.

Prognosis and Treatment.

Acrocyanosis is a chronic disease; some cases do, however, improve as shown above on p. 414. These cases have kept themselves warm for a period of months. The mechanism of cure is easily understood from a consideration of the histological changes in the arterioles, for if the parts are kept warm the arterioles will remain in a relaxed state, and so the muscle of the medial coat will gradually atrophy back to its normal size. The prognosis is, therefore, poor in the absence of a favourable change of habit.

Treatment consists in keeping the patient as a whole, and especially the extremities, warm for months. In cases with œdema or ulceration, bed is necessary.

Related Disorders.

Erythrocyanosis crurum puellaris is now a well-known condition, and is considered to be due to the insufficient protection against cold given by modern female fashions of clothing. It is rare in men with their warmer nether garments. With the related *pernio follicularis* it was common in the female cases of acrocyanosis reported here. Klingmüller and Dittrich (13) have suggested that pernio follicularis is simply goose skin which has become permanent as a result of its frequent repetition. In this connection it was noticed that the dorsa of the hands and feet, though covered with hair, are never affected with goose skin or pernio follicularis. It is suggested that erythrocyanosis crurum puellaris is similarly a consequence of arteriolar narrowing, which causes capillary dilatation, owing to impaired nutrition of the walls of these vessels, because of their diminished blood-supply. The narrowing of the arterioles is a consequence of their frequent contractions in response to moderate cold, with resultant muscular hypertrophy as in acrocyanosis.

Erythrocyanosis crurum puellaris is often accompanied by local œdema. This œdema was noticed to be of a peculiar character; it may be present in the legs only, or legs and feet, leaving the ankles free; it is unusually firm, though it pits on continued pressure, and it shows little or no tendency to sink downwards. By means of its presence, accompanied by the "nutmeg grater" feeling due to pernio follicularis, erythrocyanosis can often be diagnosed between attacks, e.g., in the summer, when the skin is warm and of normal colour. It is presumably caused by transudation of fluid through the walls of the minute cutaneous vessels, which are rendered permeable as a result of their impaired nutrition, and is thus quite different from the œdema of congestive heart failure which is produced within the serous cavities and then gravitates downwards to the most dependent parts (Bolton (4) (5)). It is significant that of the 110 cases systematically examined above, 38% of the women, but only 7% of the men, had œdema of the lower limbs.

Cutis marmorata is probably a mild form of erythrocyanosis seen in the trunk and upper limbs. Of two cases who showed it in the former area, one was an advanced case of syringomyelia with loss of temperature sense in this situation, and the other was in the habit of standing about in the open air regardless of the weather. The mottling disappeared if the patient lay down, showing that there was no obstruction on the venous side.

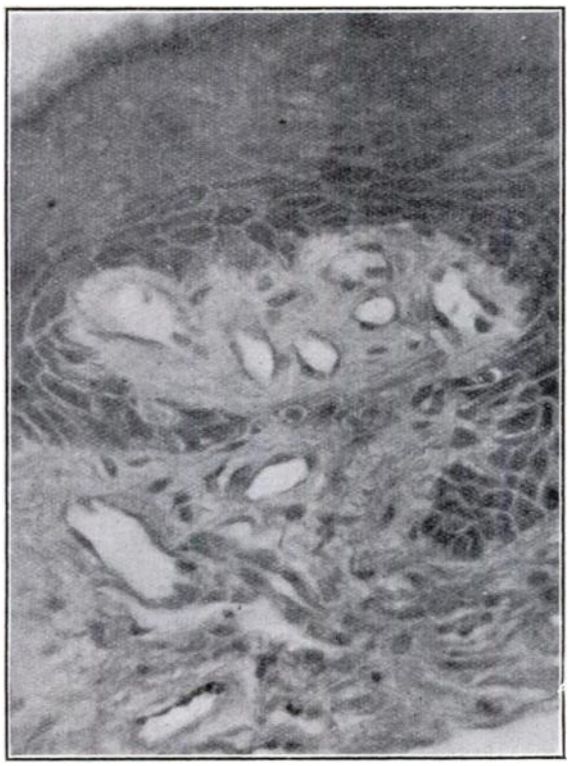

FIG. 6.—Newly-formed capillaries in the subpapillary region from a case of acrocyanosis. × 400.

Diffuse blueness of the face, especially the nose, lips, chin and cheeks, and sometimes the ears, was seen in 48% of 50 patients with acrocyanosis and only 10% of 60 without it. This blueness was of a similar shade and intensity to that of acrocyanosis. It is to be expected that exposed parts of skin should suffer from similar maladies, so that it is probable that the mechanism is the same.

The relationship of *chilblains* to acrocyanosis is doubtful, except that cold is an ætiological factor in both diseases. They were occasionally associated.

This may merely be due to the chilling of the extremities which had been allowed to take place.

In *Raynaud's disease* there may possibly be a structural change in the affected arteries, perhaps a hypertrophy of the muscularis of the tunica media as in acrocyanosis. There is, however, one great difference between these two diseases: in acrocyanosis the circulation is only slowed during an attack, in Raynaud's disease it is stopped. This could be accounted for if in the latter the tunica intima were thickened. T. Lewis has envisaged this possibility, and states that "such anatomical evidence as we possess, though admittedly meagre, points to the presence of intimal thickening" (25), though this matter is still uncertain.

The *heart* and *great vessels* are *small* in many cases of dementia præcox, as noted by N. D. C. Lewis (20, 21)—a phenomenon frequently observed in this hospital. It is probably the physiological consequence of an exceptionally inactive life, and is thus like acrocyanosis a secondary condition. In this connection it is interesting to note that during an attack of acrocyanosis the radial pulse is small and there is a little difficulty in recording the blood-pressure, owing to the feebleness of the beats on auscultation or palpation, presumably because the rate of blood-flow through the extremities is lessened.

Discussion.

It has been pointed out above that local cooling is the essential ætiological factor in acrocyanosis, but it may be doubted if this alone would always cause the disease. General cooling of the body will cause failure of the extremities to react to excessive cold by the normal defensive mechanism of arterial and arteriolar dilatation (T. Lewis (24)). In these cases there was an indifference to cold, so that the whole body, as well as the extremities, was allowed to cool. Moreover, in dementia præcox, the condition typically associated with acrocyanosis, there is such apathy to bodily discomfort that the tips of the fingers are often charred from carelessness in smoking cigarettes. It is significant that, though cases of chronic encephalitis lethargica, under similar conditions to the others, have been observed here for some years, not one of them has developed acrocyanosis. Probably this is because, in spite of their motor disability, sensation has remained intact, and so they have not allowed themselves to become chilled. On the other hand, in the neuritic form of progressive muscular atrophy, in which sensation is impaired, coldness and cyanosis of the affected parts often occur.

Normal people whose extremities are exposed to cold commonly adopt some means of keeping the rest of the body warm, and thus preserve their local heating mechanism; e.g., officers on the bridge, sailors on deck and sentries do not stand still in cold weather, but march smartly to and fro; the Scots make up for their bare knees by wearing a warm kilt or plaid—in the

absence of which the Boy Scouts' dress must be considered unphysiological for cold climates—and women commonly wear a warm wrap or fur to compensate for their scantily clad limbs.

The ætiology and morbid anatomy of acrocyanosis, demonstrated above, show that continued exercise of a muscle will cause it to hypertrophy, even in the media of the cutaneous arterioles of the exposed parts. Probably the same is true of other arterioles, and this may have some bearing on the development of arteriolar sclerosis and high blood-pressure. Again, attacks of spasmodic asthma are said to consist largely of spasm of the bronchial musculature, if this be so it follows that frequent repetition of attacks will lead to hypertrophy of this muscle tissue and to consequent chronicity of the disease. To cure this a prolonged period of complete freedom from attacks would seem to be necessary.

Appendix.

Cases whose blood was specially investigated. The men were patients at the Napsbury Mental Hospital and the women at the Shenley Mental Hospital.

Case 1.—P. P—, a single man of no occupation, admitted in November, 1930, aged 25; dementia præcox superadded to congenital mental defect. The history was that he had lived with his mother, who had been deserted by her husband. She developed ideas of persecution and later her son showed these same delusions. He lay in bed neglected at home. He can just read and perform simple calculations; speaks in a whisper. He is of puerile appearance, stands about always, totally indifferent to his surroundings, faulty in habits, does no work. Wassermann reaction negative. Since admission to this hospital he has been noticed to have marked acrocyanosis of both hands and feet. He has made no mental or physical change. Blood-pressure, 113/74.

January 18, 1935.

Hæmoglobin, 96%; red blood-cells, 4,930,000; colour index, 1·0; white blood-cells, 5,000.

Schilling hæmogram.—Basophils, 1%; eosinophils, 2%; myelocytes, *nil*; metamyelocytes, *nil*; banded neutrophils, 2%; multilobed neutrophils, 52%; monocytes, 2%; large lymphocytes, 8%; small lymphocytes, 33%.

Platelet count.—158,000 per c.mm.

Bleeding time (*Duke*).—2 minutes.

Coagulation time (*Dale and Laidlaw*).—2 minutes 26 seconds.

Calcium time.—Normal.

Prothrombin time (*Howells*).—Normal.

Fragility of the reds.—Hæmolysis commences at 0·6% and is complete at 0·5%.

Sedimentation rate.—Normal.

Case 2.—S. M. O—, a single man, formerly a clerk in the Admiralty, admitted February 19, 1934, aged 38; dementia præcox. There is a history of a previous attack in 1917, and he had been at home with his parents since 1921,

having spent the last 6 years in bed. His appearance is like that of a mental defective; he is indifferent to his surroundings and unoccupied. Wassermann reaction negative. He always stands about, and has acrocyanosis of the hands and feet and a purple face. He develops chilblains on his hands in the winter. The feet are often œdematous. Blood-pressure, 112/90.

Fig. 7 shows his hands on March 12, 1935. Histological reports are given on p. 424.

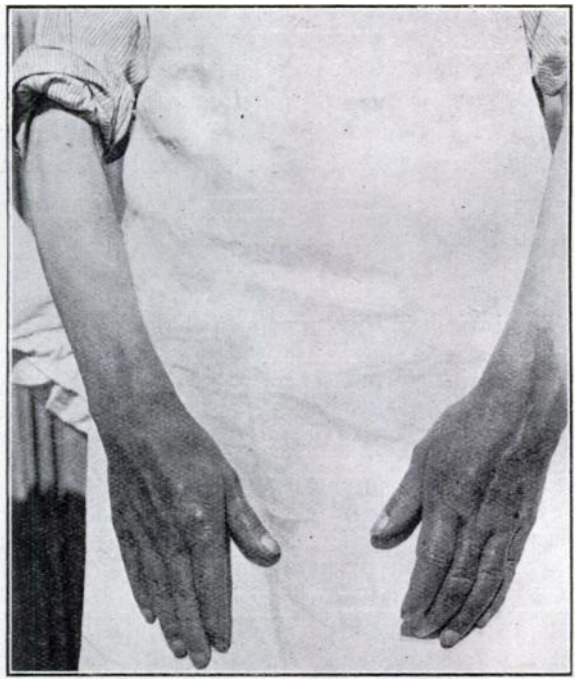

FIG. 7.—Acrocyanosis, the hands are dark blue, the colour fading gradually up the forearms. Appendix, Case 2.

January 18, 1935.

Hæmoglobin, 98%; red blood-cells, 4,860,000; colour index, 1·0; white blood-cells, 6,200.

Schilling hæmogram.—Basophils, 1%; eosinophils, 3%; myelocytes, *nil*; metamyelocytes, *nil*; banded neutrophils, 4%; multilobed neutrophils, 52%; monocytes, 7%; large lymphocytes, 9%; small lymphocytes, 24%.

Platelet count.—350,000 per c.mm.

Bleeding time (*Duke*).—4 minutes 30 seconds.

Coagulation time (*Dale and Laidlaw*).—2 minutes, 25 seconds.

Calcium time.—Normal.

Prothrombin time (*Howells*).—Normal.

Fragility of the reds.—Slight hæmolysis commences at 0·55% and is complete at 0·4%.

Sedimentation rate.—Normal.

CASE 3.—C. W. C—, a married labourer, admitted on May 18, 1934, aged 32; dementia præcox; hallucinated, suspicious, grandiose. He rapidly demented and became depressed and unemployable, indifferent to his surroundings, immobile except for automatic shaking movements of the head and upper limbs. Wassermann reaction negative. In January, 1935, he was noticed to have fairly severe acrocyanosis of both hands and feet, with œdema of all these parts and chilblains on the hands. He had by this time become quite catatonic, and then gradually developed a generally flexed attitude. Blood-pressure, 140/108.

January 21, 1935.

Hæmoglobin, 95%; red blood-cells, 4,530,000; colour index, 1·05; white blood-cells, 5,200.

Schilling hæmogram.—Basophils, *nil*; eosinophils, 1%; myelocytes, *nil*; metamyelocytes, *nil*; banded neutrophils, 1%; multilobed neutrophils, 31%; monocytes, 5%; large lymphocytes, 34%; small lymphocytes, 28%.

Platelet count.—389,000 per c.mm.

Bleeding time (*Duke*).—5 minutes, 30 seconds.

Coagulation time (*Dale and Laidlaw*).—2 minutes 45 seconds.

Calcium time.—Normal.

Prothrombin time (*Howells*).—Normal.

Fragility of the reds.—Slight hæmolysis in 0·5%, complete hæmolysis in 0·4%.

Sedimentation rate.—Normal.

CASE 4.—T. A. C—, a single bank clerk, admitted on April 6, 1934, aged 25; dementia præcox, catatonic, has a delusion that he is controlled by telepathy, is faulty in habits and continually masturbates. Wassermann reaction negative. Since September, 1934, his face has been blue and he has had acrocyanosis of the hands and feet. He has had slight firm œdema of the lower limbs, and blistering, probably a cold injury, of the backs of the fingers. He keeps his hands stretched out in a curious attitude; both are often œdematous, the right more so. As is usual the blood-pressure is difficult to take when the hands are acrocyanotic, owing to the small quantity of blood passing through the brachial artery. In September, 1934, it was 90/72. On March 8, 1935, the left arm gave a reading of 103/88, and the right one of 119/88; both hands were blue, the left being more so, but there was œdema of the right hand only. Local pressure caused a white spot on the back of each hand; this disappeared from the left hand in 46 and from the right hand in 5 seconds. This patient has shown no further change, he rarely speaks, but is aware of all that goes on around him.

Histological reports are given on p. 425.

January 7, 1935.

Hæmoglobin, 94%; red blood-cells, 4,880,000; colour index, 1·0; white blood-cells, 9,600.

Schilling hæmogram.—Basophils, 1%; eosinophils, 2%; myelocytes, *nil*; metamyelocytes, *nil*; banded neutrophils, 3%; multilobed neutrophils, 66%; monocytes, 4%; large lymphocytes, 9%; small lymphocytes, 15%.

Platelet count.—225,000 per c.mm.

Bleeding time (*Duke*).—4 minutes.

Coagulation time (*Dale and Laidlaw*).—2 minutes 45 seconds.
Calcium time.—Normal.
Howell's prothrombin time.—Normal.
Fragility of the reds.—Hæmolysis commences at 0·45% and is complete at 0·35%.
Sedimentation rate.—Normal.

CASE 5.—G. B—, a married woman, admitted on July 25, 1923, aged 31; dementia præcox, hallucinated, impulsive, suicidal, resistive to attention, usually walks backwards. She nearly always sits or stands about motionless and indifferent to her surroundings. Since 1925 she has needed occasional rest in bed for œdema of the feet; œdema of the hands was noted in 1926. In February, 1924, the extremities were noted to be cyanosed.

August 19, 1935: Face reddish; hands cool, appear normal, but the backs are yellowish, and after 12 minutes in water at 20° C. were in a typical acrocyanotic attack. Feet are cool and deep blue, showing severe acrocyanosis; the right big toe-nail has come off spontaneously; the left is atrophied and brittle; the feet and ankles are slightly swollen. There is slight pernio follicularis and firm œdema of the legs. Blood-pressure, 102/62.

January 29, 1935.

Hæmoglobin, 90%; red blood-cells, 6,060,000; colour index, 0·7; white blood-cells, 4,000.

Schilling hæmogram.—Basophils, 2%; eosinophils, 1%; myelocytes, *nil*; metamyelocytes, *nil*; banded neutrophils, 2·5%; polymorphonuclears, 66%; large lymphocytes, *nil*; small lymphocytes, 24·5%; large mononuclears, 4%. No abnormal reds or whites.

Platelet count.—340,000 per c.mm.

Coagulation time.—1st: 2 minutes 43 seconds. 2nd: 2 minutes 37 seconds.

Bleeding time.—4 minutes.

Volume index.—1·66 c.c.

Sedimentation rate.—

Mins.	c.c.	Mins.	c.c.
0	4·5	30	4·3
5	4·5	45	4·1
10	4·4	60	3·9
15	4·4		

CASE 6.—A. P—, a widow, cook, admitted on September 4, 1931, aged 58; demented, restless, resistive, rarely speaks, collects and eats rubbish, faulty in habits.

August 19, 1935: Face a little reddish, palms of hands reddish, backs brownish; after cooling in water at 20° C., as well as could be managed in the face of her resistance, they went into a borderline attack. She has not been wearing stockings, and the backs of the feet are exceedingly brown where not covered by the shoes; the legs are also sunburnt, and she has varicose veins. The feet were otherwise of normal colour when first seen; on cooling in air at 17·8° C. for 20 minutes they went into a mild attack of acrocyanosis. Blood-pressure, 126/79.

February 1, 1935.

Hæmoglobin, 114%; red blood-cells, 6,000,000; colour index, 0·9; white blood-cells, 3,400.

Schilling hæmogram.—Basophils, *nil*; eosinophils, 2·2%; myelocytes, *nil*; metamyelocytes, *nil*; banded neutrophils, 3%; polymorphonuclears 56%; large lymphocytes, 12%; small lymphocytes, 24%; large mononuclears, 3%. No abnormal reds or whites.

Platelet count.—620,000 per c.mm.

Coagulation time.—2 minutes 7 seconds.

Bleeding time.—4 minutes 30 seconds.

Volume index.—2·2 c.c.

Sedimentation rate.—

Mins.	c.c.	Mins.	c.c.
0	5·4	30	4·1
5	5·4	45	3·65
10	5·2	60	3·4
15	4·9		

Summary and Chief Conclusions.

1. Acrocyanosis is a true clinical entity; it may affect the hands or feet or both. Its features are described.

2. It causes little disability except in extreme cases.

3. It may be latent, and a method of provoking attacks is described.

4. The mechanism of the reaction of normal skin to cooling by ice or iced water is shown to depend on an axon reflex.

5. The ætiology of acrocyanosis is frequent moderate cooling of the affected parts in conjunction with chilling of the body as a whole.

6. The age-limits are wide; most of the cases in this investigation were between 20 and 45 years of age. There is no special sexual incidence. The disease is common in mental defectives and in the insane, being especially so in dementia præcox. There are thousands of cases in institutions in this country.

7. Its mechanism is a partial obstruction to the arterial blood-supply of the skin of the affected parts; the implications of this are discussed mathematically.

8. There is no evidence of venous obstruction, and it is shown that in any similar case, anatomical changes in the arterioles can only be excluded by direct observation.

9. The obstruction is shown to be due to an increase in the muscle tissue of the middle coat of the arterioles of the cutis vera and subcutaneous tissue of the affected parts. It is not a mere matter of arteriolar spasm. Fibrosis and œdema also occur locally but are probably only secondary. There is no evidence of any pathological changes in the blood, nervous system or endocrine glands.

10. The changes in the arterioles are the physiological consequences of the causes mentioned in conclusion 5.

11. In severe cases recovery from attacks may only occur after days of warmth. Treatment to be of permanent value involves practically continuous warmth for months.

12. The relationship of acrocyanosis to various other circulatory conditions and the bearing of this work on other diseases is discussed.

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