AN ESSAY ON THE MECHANISM OF ISOLATED CAPILLARY HAEMORRHAGES.

by

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S C H E M A.

INTRODUCTION.

Petechiae occur in a range of diseases almost as wide as Medicine itself. They are cardinal signs in all the purpuras, in many acute fevers, in a large variety of metabolic disorders, at some stage or other of most of the anaemias, in certain intoxications, in cardio-vascular disease, and in a proportion of the cases directly referable to the disturbance of endocrine balance. They may be associated with epilepsy, asthma and whooping cough. They may appear in persons apparently otherwise healthy. They may be produced experimentally, or quasi-experimentally, in a number of different and curious ways. And in the morass of dermatology they are visible at every turn. They are not, however, too common to be significant. They seldom occur unassociated with some underlying pathological condition; and, in the maladies of which they are the main feature, their incidence, character and distribution are important guides in diagnosis and prognosis.

It is remarkable that the mechanism of their production has not received more attention. This may be due to the fact that we have had to wait till recent years for a coherent description of the physiology of the capillaries and a realisation of their enormous importance as a separate and, in a sense, independent system. This essay is intended to demonstrate, in the light furnished by the researches of Krogh,

Hooker, Dale, Lewis and others, the more intimate factors which determine why one capillary or set of capillaries rather than another should give way and admit the passage of corpuscles through its walls.

The capillaries are simply constituted structures, reacting to a great variety of stimuli in a very limited number of ways; their behaviour in the human subject is easy to observe; and the breaking point, at which their physiological response is unable to meet the calls upon it and disintegration takes place, can be watched in a way that is possible for no other important organ of the body. These remarks apply to skin capillaries, and it is with skin capillaries that I shall mainly concern myself; but skin capillaries probably do not differ widely in their type of response from other capillary systems.

In considering the problems involved in capillary haemorrhage we are apt to be disappointed in more than one of the standard methods of investigation. Morbid anatomy, for instance, is likely to be of little assistance. Even the distant approach of death is signalled by such profound changes in the capillary system that long before the tissue reaches the microtome all direct evidence is obliterated by a sort of brouillard de guerre.

Statistical methods are hardly more helpful. In the simplest aspect of statistics, the incidence of petechiae, we

are confronted by the fact that they are seldom noticed by the patient himself, and the incidence of petechiae in any group of cases at any given time is of as much value to the observer as a similar statement of the incidence of epistaxis or any other vascular accident.

Animal experiments are set about with fallacies. Two such closely related animals as the cat and the rabbit show important differences in the types of some of their responses, and man, as regards his capillaries, is a creature apart in very many respects. The only weapons left us are vital experiments on man, observation and deduction. There is an excellent tendency in modern medicine to return to these methods, and, indeed, a large proportion of advances in knowledge have depended upon them alone. It would be wrong not to notice the valuable work done on the capillaries by morbid anatomists and experimenters on animals, but the three weapons of which I have spoken are most likely to be helpful in an enterprise like this.

The presentation of a prima facie case for these hypotheses is all I shall attempt in this essay. They cannot exhaust the possible factors in rhexis, for the ultimate factor in the production of even a pin-point haemorrhage may be the resultant of forces innumerable. My observations in their support are almost certainly lopsided. Emphasis will be laid on points not really important, on theories that are

vieux jeux, on notions that are in all probability purely fantastic. The excuse must be that the generally accepted etiological facts can stand on their own legs without the help of dialectic. It is the forgotten, the unnoted, the unpopular facts that require support; and even they are necessary if a conception of how petechiae are caused is ever to be reached.

Perhaps I should say also that this essay was completed before Lewis published in book form his classical work on THE BLOOD-VESSELS OF THE HUMAN SKIN. Most of this book had been published previously in the Journals. I find on reading it that it is unnecessary to alter this essay materially. Indeed the book contains a deal of matter for comfort.

THE APPEARANCES PRESENTED BY PETECHIAE.

Malcolm Morris has defined petechiae in the following terms: "Macules caused by the passage of blood, or of the colouring matter of blood, into limited areas of skin are termed vibices when linear, and petechiae when punctuate. If of large size they are styled ecchymoses."

With petechiae which are caused by the passage of haemoglobin or its derivatives through the vessel wall, this essay is not concerned. It is very doubtful whether any petechiae are primarily formed in this way. The bright red

macules known as Morton's spots, which are probably telangiectasia in which the corpuscular elements have become disorganised, are not intended when petechiae are referred to in these pages. I wish to deal only with petechiae formed by rhexis or by diapedesis. It is noteworthy, however, that patients not suffering from acute illness who show evidences of capillary rhexis often also are well supplied with telangiectases - perhaps congenital, for the patients say they have "always been there."

Petechiae due to rupture or partial solution of a capillary or capillaries are situated just below, and flattened out against the stratum lucidum. They are very evidently the result of bleeding and soaking into the rete Malpighii into which the damaged capillary loop has projected with its little process of cutis vera. The granular layer may be invaded by blood substance. The haemorrhages are of course associated with the skin papillae, and may or may not involve a hair follicle.

Such petechiae may be divided into two main types; the scarlet and the purple. The scarlet petechiae may be called the arterial type, and the purple the venous type.

The scarlet petechiae are pinpoint in size. They may be either multiple, where two or three or even four capillary loops have ruptured, but are aggregated into a very minute area, or single, when they may easily be overlooked if

a strong lens is not used. They may be irregular in outline, but have always a definite tendency towards a circular shape. They may persist for a fortnight or longer, but after a day or two usually tend to contract, leaving a zone of "bruising" (yellow in colour) round their peripheries. They become brown, like minute freckles, and finally disappear altogether.

Their distribution is mainly on the abdomen, the fatty parts of the chest and the subscapular region. They do not often appear on the limbs, but, when they do, the supinator surface of the forearm, the inner surface of the upper arm, the front of the thigh, and the buttocks are the favourite sites. The wrists and ankles occasionally show a rich crop, but spots hardly ever appear singly in these areas.

All petechiae of the "arterial" type occurring in the skin are surrounded, for a time at least, by a zone of pallor of from 0·1 to 0·5 mm. in diameter. Most patients showing petechiae show several of these pale patches without petechiae at their centres.

The "venous type" is much larger in size, and may extend to 2 or 3 mm. in diameter, or actually form a blot of such size as to deserve the description "ecchymosis." This type contains venous blood, usually, in the early stages, containing a fair number of corpuscles. It resembles the arterial type so closely in its situation that there is reason to suppose that, in a large proportion of cases, at least, it

is also a capillary haemorrhage. In many cases the spot takes a curious ring form with a white, ischaemic area (which later becomes yellow), in the centre. The spots are often close together, and may coalesce. They disappear more rapidly than the first type, but follow a similar series of stages. The distribution varies with the specific condition, but by far the largest number are seen round the joints, and on the extensor surfaces of the limbs. They differ, too, from the other type, in that they frequently appear on the face. The tip of the nose is no uncommon site. The general question of distribution will be discussed in Appendix A.

While both types of haemorrhage may appear in any condition associated with a purpuric eruption, not only as distinct types but in finely graded transitions, the second type is more often associated with general infective processes or grave vascular disease. The first appears in respiratory diseases and in a more "accidental" type of case. It is not incompatible with apparent health.

HYPOTHESES FOR DISCUSSION.

The factors causing the dissolution of a capillary may be intrinsic or extrinsic. The first group contains biophysical factors (anatomic and haemodynamic factors), biochemical factors, and neurodynamic factors; the second group such actions as those of heat, cold, light, gravity and trauma,

together with the action (for the purposes of this argument) of embolus. The ultimate tabulation of all these factors and their innumerable subdivisions and interweavings is no part of the task I have set myself in this thesis. I propose rather to advance a short series of hypotheses which I believe to comprise most of the important possible factors in capillary rhexis; to discuss their application to a short series of clinical cases; and to illustrate their validity, if possible, by quoting experiments and clinical observations.

I propose that:

1. Three possible anatomical factors in the rupture of a capillary are:
   a. Distance of the capillary from the main head of blood - i.e. in an artery.
   b. Position of the capillary in a loose reticulum; or in a reticulum subject to considerable chemical and physical alterations.
   c. Morbid condition of the capillary wall.
2. The other elements in the circulation may be direct factors in one of the following ways:
   a. In the event of sudden variations in venous pressure.
   b. In an event of prolonged venous hypertension.
   c. In the presence of a persistently high pulse pressure.
   d. In the presence of structural alterations due to disease in the arteries close to the capillary bed, or in the tissues surrounding these arteries.

3. Factors producing dilatation of the capillary may also produce rhexis in certain circumstances; and the time element is important in the decision as to whether rhexis or dilatation will result.

4. Rhexis occurs in some circumstances where the only plausible explanation is that the capillaries are innervated and that this innervation is a deciding factor.

5. The interplay of toxin-maintaining endocrines with metabolites, toxins, drugs or gases is an important factor in the production of rhexis; and, in rare instances, the sudden removal of a tonic substance may result in haemorrhage. Adrenalin may create a situation like this, by delaying its own access to a capillary attacked by a metabolite.

6. Abnormalities in the chemical, physical and cytological characters of the blood must play a part; but probably these factors are more secondary than has generally been supposed.

THE PHYSIOLOGY OF THE CAPILLARIES.

It is necessary to set out here the theories of capillary action I am prepared to accept as the basis for argument.

Malpighi discovered the capillaries in 1661. Stephen Hales, a clergyman, was the first to make detailed observations

on their physiology in 1733, when he made observations on the velocity of blood corpuscles in the capillary circulation. After a barren stretch of over a century, Vierordt continued and amplified these observations, using the entoptic method of examining the retinal capillaries. He estimated the mean velocity of a corpuscle in a capillary to be ·75 mm. per second. As this figure represented the axial, and therefore maximum velocity of the blood stream, he estimated that the true mean velocity was about ·5 mm. per second, or in the neighbourhood of 1/640 of the velocity in the aorta.

A fresh impulse was given to the study of the capillaries in 1873 by the discovery of Rouget's cells. Von Kreis of Leipzig, in 1875 devised the first method of obtaining pressure readings from the capillaries. Roy and Graham Brown, a little later, made further observations on capillary pressure, and established the important fact that the diameter of the capillaries is not proportional to arterial pressure. This view was amplified and qualified by Bayliss and Starling, who held that if in any area the resistance in the arterioles does not vary, a rise of both the arterial and the venous pressure, or the rise of one while the other remains constant, will produce a rise in the capillary pressure. If both pressures fall, or if one falls and the other remains constant, the capillary pressure falls also. Bayliss in his last pronouncement on the subject, summarised the situation

by saying that capillary pressure is more directly related to the pressure in the veins than to that in the arteries; and that accordingly the state of distension in the capillaries will depend rather upon the indirect effect of the arterial pressure on the general venous pressure.

Lord Lister was the first to observe, in 1858, that in ordinary circumstances a large proportion of collapsed, or resting capillaries occurs in any given field. Langley and Krogh confirmed this, but Lewis and Florey have found reason to doubt its universal application.

Rouget, in 1879, came to the conclusion, from observations on newt larvae that his cells contained a contractile element. Steinach and Kahn produced independent contraction of the capillaries of a cat in 1903 by subjecting them to electrical stimulation. They described a latent period of some seconds, followed by a contraction and then slow dilation. Cotton, Slade and Lewis produced independent evidence for contractility in 1917, and Vimtrup, in 1922, published his observations on the Rouget cells. Before Vimtrup's work it was generally assumed, according to Krogh, that contraction of the lumen of a capillary was not accompanied by a corresponding diminution of the outer diameter (as Stricker stated in 1876) and that accordingly the contraction of the lumen was probably brought about by a swelling of the protoplasm by osmotic or imbibition processes. Vimtrup and the Danish

School believe with Rouget that the contraction of a capillary is exogenous. The Rouget cells are branched structures placed at intervals on the outer surfaces of the capillary walls. They have oblong nuclei and envelop the capillary wall with fine thread-like structures. The long axis of the nucleus lies in the direction of the blood stream. Transition types of the same cell occur up to the arterioles, where they are shown to contain plain muscle cells. In all the cells a fibrillar form of protoplasm can be made out. Contraction of a capillary begins immediately beneath the Rouget cells, and just before the contraction the cell shows an increase of refractility. The depth and area of the cells varies almost directly as the degree of contraction or dilation of the capillary.

Kiyono, quoted by Aschoff, objects to these views of the Rouget cells. He claims them for adventitial cells - histioblasts, or early types of the histiocytes characteristic of the reticule-endothelial system. It seemsnot utterly impossible, especially in such novel grounds as Aschoff and Krogh are treading, that cells so curiously organised and so obviously transitional in type may have a double function, or even more functions, and be histiogenetic, amoeboid and contractile at different phases and in varying conditions. Vimtrup's theories are so fascinating that it is difficult to part from them, and I propose to accept them

in so far as they affect my argument.

Krogh's description of the happenings in capillary contraction is as follows:

"After a latent period of about fifteen seconds the "Rouget cell under observation will show an increase in "the refraction of light, and a few seconds later the "contraction proper will begin. The nucleus of the cell "is observed to sink a little into the capillary and on "the opposite wall several small indentations make their "appearance. Some of the ramifacations, as a rule, "become distinctly visible, when the capillary is already "somewhat contracted, and it can be observed that their "positions correspond to the indentations seen in the "endothelial wall. After two or three minutes' stimula- "tion a maximum, though usually incomplete, contraction "is generally obtained, but about this time a very curious "change takes place in the tissues, which lose their "normal transparence and become so opaque that no struc- "tural details can be observed. When the stimulation "has ceased the tissues regain their normal transparence "and the contracted Rouget cells relax in the course of a "few minutes."

Krogh regards this system of Rouget cells and their processes as a muscular coat for the capillaries peculiarly adapted to meet their special function of distributing

substances to the surrounding tissue.

That the capillaries are a separate unit in the vascular system as regards tonus or posture, was demonstrated by Roy and Graham Brown as far back as 1879. They observed independent variations in calibre in separate capillaries in response to pressure over a given field, and concluded that the degree of dilation of these vessels was regulated independently of the cerebro-spinal vasomotor centres, and that "individual capillaries contract or expand in accordance with the requirements of the tissues through which they pass." Recent work by Thomas Lewis and others has confirmed fully this dictum.

Various attempts have been made to prove a hormonal control of capillary tonus. Krogh has isolated what he calls an X substance from the normal circulating blood. He considers that in its absence capillary tone disappears, and has identified the substance with pituitrin. Dale and Richards have produced evidence in favour of adrenalin. The action of both hormones, and the work of Krogh and of Dale upon them will be discussed more fully in the appropriate place. It is sufficient to say that both have an undoubted effect in maintaining and increasing capillary tonus in health and in disease.

It is now necessary to discuss briefly the dilator action of the capillaries. This may be summed up by saying that the capillary has at least a triple response to any given

stimulus. It shows a direct mechanical or biochemical response. It shows an axon reflex, or branch response resulting from the stimulation of a neighbouring capillary innervated by the same axon. It shows a "spreading" response almost certainly due to an actual spinal reflex. Lewis sums up capillary response in slightly different terms. His triad of reactions is as follows: (i) active dilatation independent of the nervous system; (ii) reflex dilatation of the neighbouring system from a local axon reflex; (iii) local oedema from increased permeability.

When the "triple physiological response" of the capillaries is mentioned in writings on the subject, I imagine that Lewis's triad is generally intended. It seems to me to have some grave defects as a statement of the case. In the strict sense of the word "response," as it is used in the first two units of his triad, oedema is not a response at all but a possible manifestation of a response or of several responses. A feeling of warmth after a hot bath, the passage of urea through the walls of a glomerulus, have claims to be included in the triad if the word "response" is to have so generous an interpretation. A student might deny that Lewis has produced a triad at all, and yet be unblotted by the stigma of pedantry. What is perhaps more pertinent is Lewis's exclusion of the possibility of a spinal reflex. I shall try to argue this matter at some length in the clinical section of

this essay, but for the purposes of this short survey of the physiology of the capillaries I am prepared to accept Doi's experiments and conclusions. Doi found that stimulation of the posterior nerve roots caused dilatation of the capillaries even after the arterioles had been fully dilated by the action of acetyl choline. Similiar experiments had been carried out, perhaps with less precision, by Loven, Muller, Ebbecke, Bayliss and Krogh, and though these observers were at some variance, as to the exact mechanism of the reflex all were agreed that a reflex existed and that it was essentially a spinal reflex. On the whole it may safely be assumed that independent corractility, reaction to local requirements, sympathetic innervation, and reflex dilatation are proven facts. I propose to make this assumption.

It remains to consider the response of the capillaries to certain stimuli, the relationship of the capillaries to the general circulation, and to take some note of what is known of pressure, permeability and the phenomena of shock.

The capillaries in different sites vary in their response to heat and cold, and the capillary system of each individual has its own response to variations in degree of these stimuli. Broadly speaking, the behaviour of capillaries subjected to extreme cold exhibits three stages. The first is dependent on the increased viscosity of the blood, the contraction of the arterioles, and the slowing of the blood stream. It consists in an emptying of the capillary field

without demonstrable contraction of the individual vessels. The second stage is contraction, which may be brought about by reflex action (Wernoe) or as a purely local response (Breslauer). Probably both elements are present. The third stage is dilatation, following a series of more or less regular contractions. The response to heat is characterised by contraction of the arteries and dilatation of the capillaries, with opening up of new capillary elements and a varying degree of stases. At very high temperatures the arteries also dilate. (Krogh). The final result of prolonged exposure is paralysis (telangiectasis) and pigmentation. In no case has the contraction of the arteries been observed to persist.

The response to ultraviolet light is curious, and is not yet entirely understood. In some respects it resembles the response to heat. Finsen's experiments, and those of his pupils Jansen and Dreyer, showed that dilatation and stasis appeared after a long latent period - three hours in a normal subject, and considerably earlier in subjects on whom sympathectomy had been performed. After-effects, demonstrated by pigmentation and increased excitability, lasted for months after each experiment. Krogh suggests that the power of resistance of the small vessels to the internal pressure of the blood becomes very gradually lowered by some unknown process induced by the light. The behaviour of the arteries and arterioles, has not, so far as I know, been studied. Some experiments carried out in Stobhill Hospital by Dr. Mary Proudfoot and

myself showed that short exposures to ultraviolet light produce a characteristic pulse pressure curve which goes on varying for twenty-four hours before an equilibrium is reached. The effects observed in a series of thirty cases were a sharp rise of the systolic pressure within ten minutes with a corresponding drop in the diastolic pressure. This was followed by a steady fall in both the systolic and the diastolic pressure, with a tendency to approximation of the two curves (fall of pulse pressure) until the curves, in anything from twelve to twenty-four hours reached an equilibrium at a lower level than the initial or pre-exposure pressures. After this point the curves tended to rise towards normal. Control experiments with hot baths and electric packs produced rather similar curves, but the initial rise in pulse pressure was not so evident nor were the results so prolonged. These observations suggest that something analogous to arterial changes produced by heat occurs also in exposure to light, and lends support to Krogh's view of the nature of the specific action of light on the capillaries.

The action of inflammatory poisons on the capillaries may be typified by their response to iodine. One per cent iodine applied by Krogh to a frog's tongue produced violent contraction of the underlying muscles, and a strong, spreading dilatation of the peripheral capillaries. After section of the lingual nerve, no muscular contraction took place, the capillaries dilated "somewhat," but there was no spreading. In Ricker's experiments contraction, early dilatation and inflammatory changes proportional

to the strength of the dose were noted. Leucocytosis, stasis, oedema and small haemorrhages persisted for a day or two, and adrenalin did not contract either the arterioles or the capillaries. Powdered pumice stone produced hyperaemia, oedema, and later stasis. The deeper vessels were not affected. The later stages, up to five days, were of the mild inflammatory type.

Histamine may be taken as the prototype of special capillary poisons, though it may be mentioned in passing that the double salts of some heavy metals, and such alkaloids as emetine have, when introduced into the blood stream direct, a specific effect upon the capillary wall, and may actually produce haemorrhage.

Histamine-action is now generally believed to be identical with the action of (presumably) protein derivatives released into the circulation by tissue trauma, and in most writings on the subject the expression is used indifferently to express the action of these bodies. It typifies also products of partial digestion and bacterial action and tissue extractives generally carrying a depressor function - the "vasodilatins" of Popielski. Barger and Dale, in 1911, found histamine itself is present in these vasodilatins, in the mucosa of the small intestine, and in commercial peptone; and Abel and Kubota, in 1919, were able to extend its known distribution to many more animal tissues, organ extracts and enzymatic products both of animal and vegetable proteins. Whether or no histamine is a universal or an essential part of

these products, it has been clearly demonstrated that "shock" generally is identical in its manifestations with those produced experimentally by histamine.

The conclusions of Dale and Richards are all that I need quote on the question of histamine action, for these conclusions have not been seriously challenged. Briefly they are as follows:

Histamine, in doses of the order of ·01 - ·1 mg. to the kilogram, produces constriction of the arterioles and dilatation of the capillaries. It lowers the blood pressure and slows or abolishes the blood flow. The action on the capillaries may be modified by certain conditions. After recent section of all the nerves to a limb the dilator effect of histamine is not, at first, abolished, and may be intensified. When degeneration has become fully established, the dilator response is usually lost, but this does not apply when sympathectomy alone is practised (Burn). Loss of capillary tonus tends to inhibit a histamine response, but Burn's conclusions show that this is not the only factor.

The distance of the point of introduction from the observed capillary field is another factor which appears to apply to other capillary poisons than histamine. Dale and Richards found that introduction of histamine into the aorta, the vena cave, and the portal vein respectively caused an appreciable difference in the timing of the reaction.

An antagonism between adrenalin and histamine has

been fairly generally assumed. There is an increased output from the suprarenals of the cat when histamine is injected (Kelleway and Cowell). Removal of the suprarenals from a cat results in increased sensitivity to histamine, and in death from relatively small doses. (Dale). In histamine shock there is a concentration of the blood owing to loss of plasma. Adrenalin inhibits this.

Whether the capillaries form the principal battle ground for these antagonists is not to be considered as definitely proved, but it is usually held that adrenalin, while it does not prevent and may even assist the primary action of histamine is concerned in preserving tonus, even in extreme dilatation, and ultimately, by the increase of its concentration, in producing contraction to a normal calibre.

Lovatt Evans, reporting a conversation with Dale, says that Krogh and his collaborators have been able to show that the injection of pituitary extract into a cat suffering from experimental histamine shock will restore the blood pressure. Krogh's theory is, of course, that pituitrin is the "X" principle ressponsible for capillary tonus. He has identified a dialysate from blood which resembles pituitrin in many respects, and is capable of raising capillary tone. He has found that injections of pituitrin do, in fact, raise the tone of capillaries. He has found the melanophores of the frog responsive both to pituitrin and to his X dialysate. He has found loss of tone in the capillaries to follow removal of the frog's

pituitary body. He considers that the normal, circulating blood of the frog contains the equivalent of 1 : 100,000 to 1 : 1,000,000 of Parke-Davis pituitrin.

In the meantime that is all I have to say about histamine and hormonal action on the capillaries. I propose to raise the question later when I consider the part played by these substances in the actual production of petechiae.

SOME ANATOMICAL AND HAEMODYNAMIC CONSIDERATIONS.

The capillaries of the skin are to be regarded as a fine mesh-work of vessels, each from ·42 to 1·1 mm. in length, whose walls consist of a single layer of endothelial cells, and whose lumen diameter may vary from 0 to 9·54. They are arranged in groups of about twenty, and drain narrow short arteriole branches from the sub-papillary plexus. They supply the germinative layer of the epidermis, and are almost exclusively confined to the papillae. The arterioles from which they spring take no part in the general anastomoses, of the subpapillary plexus. In the area of these anastomoses, there are many direct arterial connections with the venules, and there is reason to suppose that direct exchange of gases and other chemical substances takes place through the thin walls of the veins, and, indeed, that the venules and not the capillaries are responsible for the respiratory and nutritional requirements of the subpapillary and extra-papillary areas. We may look upon the

capillary loops of the skin as forming the extreme distal twigs of the vascular tree.

The form and arrangement of these loops is of some importance. Normal capillaries observed in the fold of the nail by the direct illumination microscope take shape, in their visible extent, as loops or commas. The loops are crescent shaped objects, tapering at either horn into little whip-like processes. The maximum cross diameter of the loop is near the vertex, and the minimum is between the "processes," which may actually cross. The loop is thickest at the vertex, and the thicker process is that by which the blood enters. The tapering appearance is not entirely or even principally due to microscopic perspective. The capillaries are not, as the text book diagrams suggest, dropped vertically to the epidermis, but are disposed in more or less parallel layers making a fairly acute angle with the surface, and, in some instances, the loops are so bent as to lie parallel with the granular layer and to show cross section in a vertical section of the skin. Another reason for supposing that the tapering is not due to perspective is that the tapering is observed in a perfectly clear field, and that narrowing continues in some instances till the capillary is lost to sight in the deeper tissues, no blurring of the outline having occurred.

The capillary loops, in addition to lying for the most part "flat to the surface," tend to lie in the same

direction in any given field. This was true of five fields counted, apart from very slight radial variations. The actual figures were:

	Pointing distally from main blood stream.	Not so pointing.
Field I.	22	0
Field II.	54	5
Field III.	44	5
Field IV.	51	1
Field V.	14	2

The broader, or entering limb may be on either side of the loop, and, even during a single observation, a loop may fill up from either side alternately. The fact that blood may flow through the same capillary in either direction is pertinent to the question of rhexis. It was first pointed out to me by Dr. Marshall of the Glasgow Eye Infirmary, and I was able to verify his observation by slit lamp examinations of the conjunctiva. This reciprocal current may be explained in several ways. The tension of the neighbouring tissue may alter and reverse a stream which is virtually flowing in a circle. Very little may alter the angles of an anastomotic capillary joining two other limbs, and cause a gravitational disturbance in the direction of the flow. Whatever the explanation may be, the fact indicates that intra-capillary

pressure in any given capillary can have very little direct relationship with arterial pressure - a point already emphasised by Schade and supported by Clifford Allbutt.

When a capillary is dilated and atonic, as in telangiectasis, the appearance of the crescentic loops suggests that the greatest amount of dilation occurs at and tends to obliterate the arch of the loop. In a proportion of such loops the appearance is as if one had attempted to draw the loop with a J pen and had blotted the space between the "processes." In other words the lesser curvature of the loop seems to have fallen, without becoming convex, to a much greater extent proportionally than the greater curvature has risen. Indeed the outer perimeter of the loop has altered very little. The exit limb of the loop is represented by a very thin trickle of blood, or it may be collapsed and invisible.

The appearance I have described is so common that a few of such loops may be observed in any telangectiatic field. Even the more common appearance of the dilated and atonic skin capillary - like a comma very heavily marked - suggests that the main dilation occurs at the arch of the loop, and that the exit limb, once stasis has been established tends to collapse.

If it be accepted as true that the lesser curvature of the arch of a capillary is the first and principal part

of the wall to collapse on dilation, the phenomenon will be hard to explain on any known principle of haemodynamics. In a tortuous brachial artery, which resembles a capillary loop in so far as it contains the blood stream and shows arching, the head of blood obviously impinges with its maximum force on the apex of the greater curve. The artery may be actually moved quarter of an inch out of its alignment by each systole. In reality there is no analogy between the two cases. The velocity of the blood as it enters the peripheral circulation is constantly, if irregularly, diminishing. If Poiseuille's Law were valid for the capillaries, by the time the loop was reached the mean velocity would have reached a minimum. It may be assumed that the deeper capillaries of the network also are dilated, and if this is the case, transudation of plasma must have taken place through their walls. Florey describes the tendency of the fluid in any degree of stasis to draw away and leave a block of corpuscles. A probable view of the course of events is that first a general dilation of the peripheral capillaries takes place; that the corpuscles are forced slowly into the distal loop, less in the form of a stream entering a pipe than in the form of coins being poured into a purse. The arch in such circumstances (gravity being substituted for the vis a tergo of the blood stream) might become more distal in position, but any change

in its span would be in the direction of narrowing and not broadening, and the piling up of the coins would flatten the lesser curvature.

It is to be remembered in addition that the outer arch often rests against tough epidermal tissue, while the lesser loop surrounds rather more loosely packed cellular structures.

The collapse of the distal part of the loop is explicable on the (correct) assumption that this "aneurysm" of the capillary is momentary in its causes, its manifestations and its effects. Almost as soon as dilation takes place the blood stream stops so far as the loop is concerned; stasis and dialysis follow; and the distal "process," robbed of its function, empties and collapses.

The remaining point in connection with this appearance of the capillary loop, is the relatively large calibre of the crescent as compared with the limbs. The loop is, of course, an elastic structure, but, as it consists of a single layer of rather loosely connected cells, it is probable that the main onus of resistance to unusual pressure rests upon the reticulum in which the loop happens to be situated. That is to say that the capillary depends very largely for its integrity on the nature of its support. If, then, rupture is to take place, it should occur at that part of the capillary

which presents the widest, most attenuated wall, and in that part supported by loose areolar tissue. The loops I have described comply with these conditions.

The anatomic and haemodynamic relations of the capillary beds with the arterioles of the sub-papillary plexus must be of great importance in the consideration of rhexis. On the haemodynamic side, however, there is such a poverty of ascertained fact that it is almost impossible to draw any but the most speculative conclusions.

Clifford Albutt, in his book on Diseases of the Arteries admits as much. "Of capillary dynamics," he says, "we have but little knowledge, yet it is true that here lies the longest circulation time. If, as Broadbent was wont to argue, peripheral resistance lay in this field, it could scarcely be on hydraulic principles; indeed he himself attributed it to some clogging or sluggishness of tissue exchanges." After mentioning physical coefficients such as osmosis, diffusion, surface tension and absorption, Albutt goes on to say: "The enormous pressure which these energies - dialysis for example - can bring into play, reduce even gravity to a negligible quantity!"

Metiri se quemque suo modulo ac pede verum est. I do not propose to rush in where a Master of Medicine ventures so delicately. While the pulse wave may be expected to exercise

some influence on the capillaries, it is impossible to disentangle this influence from scores of other. The pulse wave itself depends on elasticity, gravity, thickness of wall and viscosity. Schade, who is quoted by Albutt, lays emphasis on the hydro-dynamic cushions on which the capillaries lie - infiltrated with blood which is incompressible but still tidal; varying momentarily in its colloidal, chemical, and static condition.

Bayliss and Starling considered that capillary pressure is more directly related to that in the veins than to that in the arteries. Bayliss believed, and Krogh agrees with him, that the state of distension of the capillaries will depend more on the indirect effect of the arterial pressure upon the venous pressure than on any direct correspondence. In the experiments of Roy and Graham Brown and of many others it was clearly shown that closely adjacent capillaries might require quite different pressure applied externally to obliterate them; and that, after a short pause, the relative pressures of the two capillaries might be reversed, the capillary which previously collapsed at the lower pressure now requiring a higher. This could hardly be if the capillary pressure depended on the pressure in an arteriole presumably supplying both of the vessels concerned.

The capillary state shows some easily recognisable

relation to the pulse pressure only in disease - in the condition of aortic regurgitation. Lewis (B.M.J. i.737.1924) thinks capillary pulsation a direct consequence of arteriolar dilatation, and that the macroscopic capillary pulse is due to the passing of the pulse from the arteries and through the capillaries to involve in greater or lesser degree the minute skin venules.

The vexed question of the capillary pulse may rest for the moment. If one may sum up the general situation in a highly unsatisfactory way, the prima facie probabilities suggest that arterial pressure must have some effect upon the capillary wall, for the blood is forced directly against it from the arteriole; but there is no evidence to show what that effect is. The character of the veins, their rapid distensibility, the ease with which they distend to their fullest capacity make them a more probable factor in vascular accidents than the more elastic and delicately balanced arteries. No small proportion of petechiae, especially those associated with vascular disease or with lesions of the aortic valve, are 'venous' in character. On the whole it seems reasonable to suppose that if blame is to be cast between the two a rise in venous pressure is more likely to result in rhexis than a rise in arterial pressure.

I had intended to illustrate and elaborate this point by some rather speculative reference to clinical cases, but Lewis and Harmer by a simple and beautiful expedient have brought down two of my birds with one stone. These observers found that, in persons subject in the nature of their illness to petechial haemorrhages, it was possible to produce petechiae at will be raising the venous pressure. They used in most of their experiments a Riva-Rocci armlet applied to an arm placed in such a position that the venous pressure of the limb approximated to atmospheric pressure. They applied a known pressure below that of arterial pressure for 3 minutes and were successful in producing petechiae (at 70 mm. Hg.) in ten cases of subacute infective endocarditis, five assorted anaemias, and two cases of purpura simplex. A similar number of healthy subjects showed no petechiae at 70 mm. Hg.

The petechiae corresponded in every respect to the bright red pinpoint type referred to in my opening description.

These observations provide a short cut to a conclusion and leave a large field unexplored and unexplained; but at least they prove two facts beyond cavil. Increased venous pressure is a factor in the production of petechiae, and disease or disorder of the walls of the smaller vessels is another factor. I have repeated Lewis's venous pressure test

on a number of cases, and will suggest, in the Appendix, a few subordinate conclusions. The main conclusions - that a high venous pressure and (from whatever reason) a low breaking strain may of themselves produce capillary haemorrhage - are not affected.

In cases where a low breaking strain of the capillaries can be accepted as an important factor in rhexis, it is reasonable to suppose that the conditions which bring about such changes in the capillary wall may also bring about that state of "paralytic dilatation", or refractory state of Lewis, typified in marbling, erythema ab igne, and telangiectasia. The clinical evidence for this supposition is to be found in the almost invariable association in the same person between body petechiae and some form or another of telangiectasis, and by the common distribution of petechiae on sites commonly selected for telangiectatic phenomena. William Becker, of Rochester, U.S.A., has quite recently made a very complete summary of the known facts in the aetiology of telangiectases, and one or two of the factors he has unearthed are equally germane to petechial haemorrhages. He finds telangiectasis classifiable under three aetiological heads - (a) neurogenous, (b) mechanical and (c) toxic. As I have discussed the "heurogenous" and toxic factors in rhexis elsewhere in this essay, we need be detained only by the mechanical propositions adduced by Dr. Becker. It is interesting to note, however, that he

visualises the peripheral vascular system as being "bombarded" intensively by a great number of different and combined agents before signs of defeat or of dissolution become manifest.

In Becker's report of 63 cases of all ages suffering from generalised telangiectases, no fewer than 31 are noted as having definite or presumptive arterial disease, and syphilis accounts for 18 cases. Becker's own investigations led him to suppose that intimal proliferation of the subpapillary arteries immediately proximal to the lesion was of very common occurence. He concludes that this, with its consequent perivascular infiltration, produces a definite mechanical obstruction to the circulation, but he refrains from speculating as to how this mechanical obstruction acts. While a number of possibilities suggest themselves, it will perhaps be sufficient to record the fact that the mere mechanical changes of arterial disease have been observed profoundly to influence the local capillaries, to dilate and paralyse them, and conceivably, in certain circumstances, so to alter their nutrition and tone that they will readily give way under strain.

NERVE ACTION IN THE PRODUCTION OF PETECHAIE.

At this point I wish to introduce a few cases from which I shall attempt to draw certain conclusions.

Case I. J.O'B., labourer, aet. 35, was admitted to Stobhill Hospital as a case of rheumatoid arthritis. During the War he suffered from a chronic cellulitis of the right arm following an injection of anti-tetanus serum. For three years before his admission to Stobhill he had suffered from a polyarthritis of the chronic infective type, and for the past two years from flatulent dyspepsia. He was well-nourished, and except for characteristic deformities of varying degree in most of his joints, he looked healthy. Except that his abdominal reflexes were unusually brisk, no other abnormality was noted. Nine days after admission he complained of epigastric pain, and vomited six times. He stated that a year before he had a similar attack, and described symptoms suggestive of duodenal ulcer. He was in hospital (Oakbank) at the time. The blood pressure was 126/112 mm Hg.

On the following day he showed a coffee-ground vomit. A ptosed right kidney was palpated. Before palpation three bright red pinpoint petechiae and two telangiectalic spots were seen 1½" below the xiphisternum. During palpation of the kidney eight fresh petechiae appeared. Seven were seen on the right side above the umbilicus - three

above the costal margin and four below. One appeared over the left iliac fossa.

Before palpation of the kidney the abdomen had been stroked gently to elicit reflexes. No tache followed. When, however, the kidney was palpated a few minutes later a bright tache appeared following the lines of stroking. The tache on the right side was particularly strong. The usual tache phenomena followed but were very intense. The white tache and the erythema beyond it lasted for more than 15 minutes - 5 minutes after the red tache had faded. The red tache was raised. A deep flush was seen over the palpated area. No tenderness was elicited. The pulse after the tests was 84, the charted pulse of four hours earlier being 66.

On a subsequent day the ptosis was reduced easily and the kidney "joggled" slightly. Two fresh spots appeared. These and some of the earlier spots, when they were marked with light ink circles showed broad areas of erythema surrounding and encroaching on the circles. The larger and brighter and more recent the spots the deeper and wider was the erythema. The tache phenomena were as before.

Three minutes after this manipulation of the kidney miii of 1/1000 adrenalin hydrochloride was given intravenously. Six pinpoint haemorrhages appeared. These were much deeper in colour and appeared on examination by a strong

magnifying glass to be situated in a deeper layer of the cutis than those seen on the previous day. The distribution was much the same as before, except that two spots appeared below the right scapula. These spots resembled more closely the "manipulation" spots than the "adrenalin" spots. Stroking of the skin resulted in two minutes in definite urticarial wheals surrounded by broad irregular erythema. Tremor and palpitation appeared early and persisted for fifteen minutes. The pulse rate and blood pressure were not elevated. Considerable numbers of "deep" spots continued to appear up to ten minutes after the injection.

Case II. G.M., 48, forms a companion case to the above. He was a labourer who had suffered for two years from flatulent dyspepsia and constipation. He was a bulky, pale man, and examination, including fractional analysis and skiagraphy, failed to reveal any lesion other than a floating kidney. The kidney was less mobile than in Case I., and lay transversely in the right lumbar region of the abdomen. The kidney was at first palpated without result till, at one point in the manipulation, the patient complained of pain. The pain was referred by the patient to the point of pressure, (i.e. the lower bole of the kidney) and was described as shooting backwards into the loin. At that moment five scattered pinpoint haemorrhages appeared on the right segment of the abdomen, ranging irregularly from the hypochondrium

to the iliac region. The dermatographic signs corresponded to those described in Case I.

On each successive occasion when the kidneys of these two men were palpated, a fresh crop of haemorrhages appeared. The site was variable, but usually on the right segment, and the number of spots was seldom more than four. A jogging upward movement produced haemorrhages when ordinary palpation failed.

The petechiae described in these two cases were of the type probably due to purely capillary haemorrhage. I refer to them elsewhere in this paper as the First Type. They were very superficial, in the epidermal layer, bright scarlet in colour and slightly irregular in outline though their outline tended to be circular. They persisted in one form or another as long as a fortnight, but after a day or two tended to contract leaving a zone of bruising brown and then yellow in colour round the periphery. The central part later became brown, like a very minute freckle, and finally disappeared altogether. They often occurred at the apex of a skin follicle but did not invariably so occur.

Cases of ptosis of the kidney are not particularly numerous in general hospital practice, but I have recently had the opportunity of seeing five other cases, all of the "neuropathic" type, all between twenty-five and forty. Four were women and one was a man. I could find nothing in their histories that appeared to me material, and I shall

not quote them here. In two of these cases, female, petechiae were elicited by palpating the kidney, and two others showed little bright telangiectatic spots, alleged to have been present "for a long time." The fifth, a female, showed tenderness but no capillary phenomena.

I should like to quote more fully a parenthetic case which, while the kidney was not palpable, exhibited signs which may be regarded as parallel to those seen in Cases I and II.

Case III, J.C., female, unmarried, Aet 52. Envelope Bander. She was admitted to Stobhill Hospital on 6th October, 1926, complaining of giddiness, palpitation, mild syncopal attacks, and hot, flushing sensations all over the body, these of two years' duration. She complained also of myalgia of twenty years' duration, and coarse tremor on excitement of eighteen years. Catamenia ceased ten years ago.

The patient was stout and florid; she talked quickly and intelligently but had difficulty in fixing her attention for any considerable time. The tongue was dirty, the teeth artificial, and the bowels were constipated.

The abdomen was prominent, and covered with a thick layer of loculated fat. Physical examination showed vague general tenderness, tympanites, and a loaded and ptosed colon. X-ray examination showed general ptosis of

the bowel, a spastic ileum, and a redundant ascending colon lying deep in the right iliac fossa. The stomach emptied normally.

The deep reflexes were all exaggerated but not pathologically so. The abdominal and epigastric and umbilical reflexes were absent. The pupillary reactions were normal and there was no nystagmus. The gait was shuffling. Rombergism was present, the patient tending to fall forwards. Intention tremor was marked.

Epicritic, protopathic and thermal sensibility were all disturbed in all areas of the trunk and limbs. The dulling of sensation was most distinct over the thighs and legs.

The fundus oculi was normal. Barany's caloric tests revealed no abnormality.

The heart showed a short systolic murmur in the mitral area. The sounds were muffled, rapid and varied in force. The blood pressure was 106/64. The blood count was normal.

The lungs showed evidence of a slight general bronchiolitis, and cough and sweating were complained of at night.

The Wasserman reaction was negative.

No genito-urinary abnormality could be detected.

When this patient's abdomen was palpated, she

complained of generalised tenderness, the maximum area varying from day to day. From one to four minutes later a deep pink flush appeared in quite irregular patches. The first patches usually appeared in the iliac region, and later patches were seen not only over the abdomen but on the back of the trunk and on the arms, legs and thorax. Repeated examinations failed to show any correspondence between the areas and sites of the patches and the areas palpated or the number and force of the stimuli. On the occasions on which the patient complained most of tenderness, however, the flush appeared more rapidly and was more pronounced.

A minute or two after their appearance, the pink areas became somewhat raised, and each patch became gradually covered by small pale papules. These papules varied in size, some becoming as large as lentils. The large papules were umbilicated. The erythema died away gradually as the papules attained full growth, and had completely vanished after ten minutes. The papules persisted for twenty-four hours, when they disappeared by irregular degrees.

On one or two subsequent occasions the papules appeared before the flush and in two areas, in the lower abdomen, the flush did not develop at all, though the papules developed according to type.

On one occasion twenty-three petechiae (pinpoint haemorrhages) were counted on the abdomen and flanks. The

skin had been clear on the previous day and no definite exciting agency could be discovered.

The common factor in these three cases may be expressed in the following terms. The stimulation of an abnormally placed viscus - the kidney in the first two cases, the colon in the third - was followed by gross circulatory disturbances in certain areas of the skin. In examining the possible chain of events linking these two phenomena, one cannot escape the consideration of a nervous reflex mechanism. I propose to consider first whether a reflex arc can be theoretically constructed between the viscus and the various skin areas involved; and the manner in which such an arc could conceivably produce petechiae. The reflex concerned, assuming its existence, must be either a spinal reflex or some species of axon reflex, and its action must be limited either to vasodilatation or to vasoconstriction. The first problem may be stated in this concrete form. Can a spinal reflex path exist through which stimulation of a ptosed kidney will produce vasodilatation of the minute vessels of the skin?

Stimulation, trauma and increased intracapsular tension of the kidney may be expressed remotely either as shock and general collapse - in the familiar effects of the boxer's kidney punch -, or as apparently local visceral pain, or as pain referred to the distribution of certain

sensory nerves supplying skin areas. The fact that this latter type of pain is brought about by cross integration in the cord can hardly be in dispute. If it is possible to identify this pain route with a vaso-dilator reflex path, half the journey will be accomplished. It will be necessary, however, to establish this part of the arc in some anatomical detail before attempting any such identification.

(Note: In Case IV, I was able to bring out a point which had escaped my attention in Cases I and II. This woman, a syphilitic of 46, suffering from perioophoritis, showed at one period eight petechiae on the abdominal wall. Six were on the side corresponding to her lesion, and two in the lower segment of the opposite side. Pinching the skin over each petechia elicited definite tenderness in each case. Although a general panniculitis was present, tenderness was quite obviously less in all other areas of the abdomen. Deep tenderness was present over the right ovary. This observation suggests a case for the identity of the two paths.)

According to Gaskell there is no evidence that the kidney, regarded as a cellular structure, is under the control of the nervous system at all. The blood vessels are supplied with sympathetic fibres, which can be traced to the renal ganglion and in turn through the solar plexus, the lower and

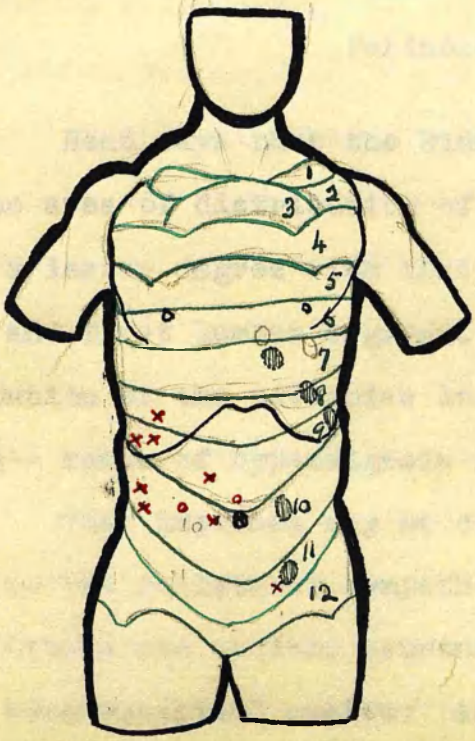
outer part of the semilunar ganglion, the aortic plexus and the lesser and smallest splanchnics. Apart from an extremely doubtful afferent supply of the capsule and pericapsular tissue, the nerve supply of the kidney appears to be purely vasomotor. The renal ganglion is represented by connector nerves in the roots of every segment from the fourth thoracic to the fourth lumbar. (Gaskell) This is the largest collateral representation of any viscus in the body, a fact that is explained by the essentially segmental evolution of the nephric organ. The white rami or central connections of the sympathetic system do, in this particular area of representation, contain afferent fibres; and their presence has been taken as proving that so far as the thoracic and upper lumbar portions of the sympathetic system are concerned, impulses of a sort can be conducted inwards.

Even if this afferent function of the sympathetic is not admitted, and the first part of the hypothetical "pain arc" is accordingly not established so far as the kidney is concerned, it must be remembered that in the cases referred to the kidney was not the only structure stimulated. James Mackenzie makes the observation - so simple and so obviously true that nobody seems to have thought of it before him - that no conclusion can be drawn as to the sensitiveness of an organ that has been stimulated through a structure itself sensitive. In Cases I and II a large variety of structures

(including a pocket of stretched peritoneum) was undoubtedly stimulated at the same time as the kidney. The suprarenal body itself may have been directly stimulated, although a ptosed kidney in its descent commonly leaves the suprarenal body behind. As direct stimulation of the suprarenals involves other considerations, I shall refer to it later. Yet, while a route between the kidney and the skin through the cerebro-spinal system is not an essential part of my argument, a quantity of clinical evidence goes to show that such a route exists. The following areas of referred pain and cutaneous hyperalgsia have been mapped out in cases of renal colic - where definite and demonstrable intracapsular increase of tension existed. In their segmental distribution they correspond with part at least of the afferent connector system referred to above.

Sensory Nerve.	Distribution.
Dorsal ix, x, xi, & xii.	Lower thoracic, abdominal and lumbar.
Ilichypogastric.	Suprapubic and anterior gluteal.
Ilioinguinal.	Upper inner part of thigh.
Genitecrural.	Scretum and upper anterior 3rd of thigh.
External cutaneous.	Anterolateral surface of the thigh to the knee, lower gluteal and tensor regions.
Obturator.	Lower inner third of the thigh and the knee joint.
Anterior crural.	Skin over rectus to the knee. Anteromedian aspects of thigh, leg and foot.

Diagram illustrating p. 45.



Petechia × Ola petechia o Head's tender spots

Small sciatic.	Inferior gluteal and pudendal regions, back of thigh, knee and ankle.
Pudic.	Perinoeal region.

Head says that the kidney is particularly associated with the area of distribution of the tenth dorsal segment, and to a lesser degree with that of the eleventh and twelfth dorsal and first lumbar segments. In the diagram ( ) the distribution of the petechiae in Case I. is shown in relation to Head's zones of hyperalgesia for these particular segments.

That impulses may be conducted through the autonomic fibres to the collateral sympathetic chain, through the connector fibres and excitor neurons to the appropriate segment of the cerebro-spinal system; and that these impulses may produce on the sensorium a pain-pattern corresponding to the distribution of a peripheral afferent nerve may be taken, for the moment, as proved. Although the sympathetic system is essentially an efferent system, between the first thoracic and second lumbar segments afferent fibres exist in the white rami and are responsible for what we recognise as visceral pain. There is also a growing mass of evidence which suggests that this route may, in certain circumstances, be prolonged by an antidromic flow of impulses along the appropriate sensory nerve, and that local vasomotor disturbances may result in its distribution.

Bayliss obtained vaso-dilatation in the hind limb of a dog by stimulating the roots of the sciatic plexus. He suggested the possibility of the dorsal root fibres dividing near their peripheral terminations, one branch supplying the sensory and organ, and the other acting as an efferent inhibitory end organ on the muscular coat of the arterioles. This explanation suggested both spinal reflex and a reflex similar to the axon reflex of Langley in response to stimuli. The sensory end organ might pass impulses direct to the efferent end organ. He showed the fibres responsible to be anatomically indistinguishable from ordinary sensory fibres, failing to degenerate when the roots were cut between the cord and the ganglion, but degenerating when the dorsal root ganglia were removed. They appeared to be identical with Head's protopathic fibres. Bayliss and, later, Krogh are nearer conviction than King Agrippa that at least some sensory nerves have a vaso-dilator action and that this action extends to the capillaries.

While these reserved conclusions are based mainly on animal experiments, there is a good deal of clinical evidence to bear them out. As it is necessary to trace such a reflex path if the nervous factor in the production of petechiae is to be shown valid, this clinical evidence must be examined shortly.

Perhaps the most familiar instance of capillary dilatation over the distribution of a sensory nerve is found in herpes zester. In this condition secondary degenerations can be traced from the posterior root ganglia to the peripheral distribution of the nerve, and also backwards into the posterior columns of the cord. (Muir) The primary lesion is in the ganglion. It has occurred in cases, such as spinal caries, when the direct infection of the ganglion was obvious. Pain or itching is invariably the first symptom, and local capillary dilatation follows more or less rapidly on its heels. The rate of recovery of the damaged skin is commensurate with the intensity and duration of the pain. That is, the indications of capillary paralysis and destruction are commensurate with the indications of involvement of sensory function.

With the facts of herpes before us we are driven almost irresistibly to the conclusion that, in certain morbid conditions of the efferent neuron, the functions of pain and vaso-dilatation are interchangeable. If this is accepted the possibility, at least, of a part of the reflex route in these cases of nephroptosis is established. One or two instances of like reactions occurring where the disorder of the neuron is not so obvious may give further corroboration.

The behaviour of structures associated with the ulnar nerve should serve as an apt illustration, particularly

as they include at least one syndrome in which the alpha and the omega find expression in vascular disturbance. This syndrome is angina pectoris.

The ulnar nerve and its branch, the internal cutaneous, take origin from the posterior and anterior cornua in the eighth cervical and first thoracic segments, the posterior or sensory component being closely associated in its thoracic origin with the afferent nerves from the heart. The anterior portion is also closely associated with the intermedio-lateral tract in its upper limit, and therefore with the higher rami communicantes of the sympathetic and the stellate ganglion. The cervical enlargement, in which all these structures are situated, is the integration centre for the sensorimotor reactions of the upper limb. If we accept the principle of the overflow of nervous stimuli from one part of a cord integration centre to an adjacent part, there can be no reason to cavil at this part of the route. It is an essential link even if we do not accept the theory of antidromic stimuli. Without it the clinical phenomena I shall presently describe would be inexplicable. With it one can explain these phenomena even if one accepts Lewis's most recent dictum in its narrowest sense - "that the tone of the minute vessels, terminal arterioles, capillaries and minute venules as a whole is influenced locally by the needs of the tissues which they supply."

In 1919 Dr. Ivy MacKenzie drew my attention to the appearance of a flush on the ulnar aspect of the hand in certain cases with anginoid symptoms and in certain groups of psychasthenics. He has since worked out the integrations of the ulnar nerve in connection with palsies, causalgias, and vasomotor phenomena fully, and, I believe, conclusively. At that time I made the observation that if a patient's hand were rubbed over the palm gently and evenly for a few moments, in a percentage of cases a bright ulnar flush appeared. It was strongly demarcated by the limits of the ulnar distributions and faded relatively slowly to the slight hyperaemia of the rest of the palm. I tried this ulnar reaction over a series of 82 patients attending the Ministry of Pensions Neurological Clinic, with the following results:

Ulnar Reaction in Pensions Patients.

	Positive.	Negative.	Doubtful.	Total.
Psychoneuroses.	44	1	8	53
Hysteroepilepsy.	10	1	2	13
Reflex Palsies. (Babinski)	6 (hand)	3 (leg)	6 (hand)	15
Graves' disease.	3	0	2	5
Aneurysm.	1	-	-	1
G.P.I.	1	-	-	1
?Trench Fever.	-	1	-	1
Transverse Myelitis.	-	1	-	1
Cerebral syphilis.	-	-	1	1
	63	5	15	82

All cases showing disturbance of the cardiac rhythm or of the digestive apparatus showed a positive reaction.

Later observations on Hospital patients has led me to the belief that most cases of carditis, most cases of aneurysm or mediastinal enlargement, most cases of active intrapulmonary disease, most children showing any visceral disturbance of a prolonged or severe nature, whether thoracic or abdominal, all exophthalmic goitres, all cases of angina pectoris, and a large proportion of neuropathic patients show either a static flush over the ulnar distribution in the hand, or an increased vasomotor excitability in that area. Cases of organic nervous disease, with the possible exception of victims of disseminated sclerosis and Syringomyelia, do not as a rule show the reaction. It is worth specifying here progressive muscular atrophy. In early cases, where trophic changes in the course of the ulnar nerve were present but were not fully established, I have not seen the reaction. In advanced cases it is also absent.

Where the static flush occurs in angina pectoris the erythema corresponds very closely with the area of conducted pain in the arm, and where the patient is not able to be definite about the site of his conducted pain, tenderness, or, in rare cases, anaesthesia may be elicited over the blushing areas.

Types of vasodilator phenomena partaking in their

nature of a reflex action and essentially resembling this ulnar reaction are probably more common than the literature appears to indicate; but they are not so susceptible of demonstration. One instance, however, arises:- the conjunctival suffusion so often seen in trigeminal neuralgia where the upper division is affected. This phenomenon resembles that seen in Bruce's experiments with mustard oil, and, like it, may be ascribed to an axon reflex. But the conjunctiva is sometimes so remote from the skin surfaces obviously affected that it is almost necessary to postulate a preganglionic and antidromic flow.

A spinal reflex is the most plausible explanation of these ulnar and other phenomena. If we reject this explanation, and attempt to reconcile them solely with the local "needs of the tissues," we are confronted with a problem involving the so-called trophic function of sensory nerves. It must, however, be admitted that dysfunction of a sensory nerve - a nerve charged with the appreciation of environment - may result in a great deal of abnormal behaviour on the part of tissues in immediate contact with environment and supplied by that nerve.

On the whole we shall be safer if we answer the question, "Can a spinal reflex path exist through which stimulation of a ptosed kidney will produce vaso-dilatation of the minute vessels of the skin?" by saying, "Yes. It can. In certain circumstances."

The nature of many of these circumstances is sufficiently clear. All the experimental evidence establishing the various parts of the "Pain route" was associated in its very essence with brutal maltreatment of the structures involved. The clinical evidence is based on cases in which James Mackenzie's increase in the excitability of the receptor fibril is a very mild assumption. In the ulnar cases, Ivy MacKenzie's suggestion of a state of irritability, or "tumult," in the integrative regions of the cord, with an increased liability to cross communications, quite satisfies the probabilities. The cases showing the ulnar reaction could all be loosely classified as suffering from "nervous instability." And a proportion of them gave a presumption of abnormal and repeated stimuli discharged along the afferent neurons of some viscus or other. Patients suffering from nephroptosis are notorious for exhibiting signs of so-called sympathetic disturbance. We should be saying nothing incredible if we stated the following as a possibility. That when certain dysfunctioning or displaced viscera (among them the kidney) are stimulated a spinal vaso-dilator reflex can occur; that this reflex is dependent for its existence on a morbid state of the structures concerned; and that its components are (1) the sympathetic supply of the viscus or afferent fibres associated with it, (2) the spinal ganglia and the rami communicantes of the dorsal segments, (3) the terminal

neurones of the afferent fibres in the rami, (4) the posterior cornua of the cord, (5) a short irradiation area, (6) the protopathic neurones of a sensory nerve, (7) the skin distribution of that nerve by an antidromic wave, (8) the smaller peripheral vessels.

If we assume this to be the case, the second problem arises. Can a nervous reflex mechanism which, in the circumstances considered, produces referred pain and vasodilatation, account also for a similarly distributed vasoconstriction?

The answer to this contains fewer assumptions and is less open to debate than the answer to the first problem. Several vasoconstrictor and pilomotor reflexes have been described and their mechanism is fairly well understood. These occur in health. The initial impulse is conveyed along the sensory nerve to the cells of the receptor neurone in the posterior root ganglion. From there it passes to the connector neurone in the lateral horn of the cord. Its fibres run out in the anterior root, forming the white ramus, and communicate with the excitor neurones in the sympathetic ganglion. From the ganglion its processes are distributed along with the appropriate spinal nerve to the reflex area.

Detailed investigation (by Leriche and Policard, Krogh, Harrop and Rehberg and others) appears to have proved at least a sympathetic vasoconstrictor innervation of the

capillaries beyond cavil. It will be noted that in all observations on capillary constriction under nervous stimuli the arterioles have been seen to contract first, to be followed by capillary constriction after an almost infinitesimal interval. The part played by the behaviour of the smaller arteries and veins remains to be discussed, but the possibility of a purely capillary reflex action does not fall to the ground because other reflex actions can and do participate in the production of the final result. Further, it may be stated here, that whether the capillaries prove ultimately to be as well supplied with a reciprocal innervation as the arteries themselves, or whether their claim to an innervation is finally dismissed, sudden alterations in the calibre of distal arterioles and veins must certainly play some part in altering, even violently, the calibre of the capillaries. If this is so, and reflex action of the nature I have described does occur in the arterioles and venules, then reflex dilatation and constriction of the capillaries is possible.

One difficulty in accepting this "vasoconstrictor arc" is provided by the fact that though experimental evidence is ample and the theoretical mechanism relatively simple, clear clinical evidence is remarkably scanty. Either the pallor (which is the outward and visible sign of vasoconstriction) is generalised, or the significance of pale localised patches has not been appreciated, or, as in the case

of Raynaud's disease the factors are so varied and complex as almost to defy analysis. The blanching of the hand which, in certain persons, follows a knock on the funnybone, may be an illustrative case, or less probably the cold feet of constipation. Again any part of the body is bruised or wounded, the erythema round the injured spot is always surrounded, for a longer or shorter period by a wider area of ischaemia. This is shown with very great clearness by patients who have been cupped over the loins. The bright area of erythema left by the cup is surrounded by a roughly circular cincture of white, into which it tends gradually to encroach. The pale area may persist for hours after the cup has been removed, and may have quite a sharply defined circumference. The great width of this white area and its suddenness and persistence, differentiate it from the familiar white tache which follows stroking of the skin. The "stroking" tache may be explained in its first appearance as a direct effect of stimulation, and in its second (beside the red tache) as the product of direct reaction or of an axon reflex. The "cupping" tache resembles much more closely a spreading type of reflex.

It can now be stated with some plausibility that given a state of excitability of the receptor neurones (Mackenzie); or a state in which the block of certain synapses has been weakened or removed (Langley), the stimulation of a

viscus may produce characteristic changes in the blood supply of the skin; and that these changes may be represented either by narrowing or by widening of the minute vessels; and that the paths by which these reactions are brought about may be identical with those co-operating in referred pain. It now remains to examine the relationship between such disturbances and the petechial haemorrhages seen in Cases I and II.

Three facts about these haemorrhages strike the attention first. They appeared suddenly. There was something fortuitous about their appearance, for their number and distribution varied considerably on different days. They were accompanied by changes in the mode of response of the capillaries to direct stimuli over wide tracts of the abdomen.

The suddenness of their appearance certainly suggests a reflex. In Case I, when the kidney was simply handled, no petechiae appeared. The moment it was "jogged" two or three flashed into view as if the kidney had been jogged and the skin pricked with a pin in the same movement. Other explanations, which will be reviewed in their turn, mostly involve a delay or latent period. For example, a change in arterial pressure could hardly have such instantaneous effect on the periphery. Again, the possible effect of a pressor substance in the blood would be liable to the same objection, even if the experiment performed with adrenalin on Case I had not shown, rather prettily, a different order of results. It will

be recalled that after adrenalin had been injected into the blood stream the spots which appeared were deeper in the tissues and that their incidence in time was spread over an interval of ten minutes, though the kidney was not touched during this interval. The meaning of these results I take to be that the adrenalin was capable of reinforcing an existing morbid reflex. The whole sequence of events in Case I and in other cases where the little haemorrhages were watched at the moment of their appearance suggested a literal connection between the disturbed viscus and the petechia.

I have described their appearance as fortuitous. If we consider that an area of 0·5 sq. mm. of skin may contain 20 capillary loops, and that the petechiae are scattered over something like 500 sq. cm., it is fair to draw the inference that the haemorrhages are an extreme expression of disturbance in the capillary bed over which they are situated. That is to say, a change occurs in the capillary wall that may progress to rupture.

One implication of this inference is that certain loops are less able to bear strain than others. This aspect is dealt with under the first and second propositions of my introduction. Some light may be thrown on a second implication - that a state of strain is brought into existence in the capillary bed - by the consideration of the third point of observation. The haemorrhages were accompanied by changes in the mode of response of the capillaries to direct stimuli

over wide tracts of the abdomen.

Whether the tests for the abdominal reflex will produce a tache in the normal individual depends upon who applies the test. A different strength of stroke is habitual to each individual. My own stroke does not produce a tache in any but vaso-neurotics. In the cases under review, no tache appeared till the kidney had been manipulated and until more than the usual five to eight minutes had elapsed. When the kidney was not manipulated no tache appeared under very much heavier pressure than had been applied in the first instance. When the tache did appear it was very intense and resembled the reaction found in hyper-adrenalism. Both in their vaso-dilator and in their vaso-constrictor reactions, in their direct and in their indirect responses, the capillaries showed great hyperexcitability. The ring of erythema round the ink markings was further evidence of this excitable state, and it is noteworthy that such rings were more strongly marked round the fresh haemorrhages. Round the Morton's spots, which were also marked with ink, erythema did not appear.

While these facts make it plain that the capillaries involved were in a state of hyperexcitability - a state in which the application of fresh local stimuli produced violent reactions - they leave us in the dark as to the exact nature of this "state" before the fresh stimuli were applied, and,

further back still, before the kidney was manipulated. They do suggest that a negative phase of excitability is present, in that the capillaries concerned do not respond to stimuli which would ordinarily produce a reaction. The abdomen in each case was pale when a tache was sought for, and the most likely description of the state of the capillaries would be one of hypertonus. This is more probable when we reflect that any rapid alteration in the state of the capillaries is followed by a period extending to hours, days and even weeks before the system recovers its normal function; and that the very existence of the reflex path I have tried to trace (if indeed it does exist) is dependent upon a long series of unusual stimuli - a condition fulfilled by the circumstances of nephroptosis. If this assumption of hypertonus is correct we are almost forced to the conclusion that in so far as the petechiae are produced by nervous action they must be produced by a sudden increase of vaso-constriction in arterioles, capillaries or venules already hypertonic, or to a dilatation of these vessels at a layer of the skin sufficiently deep to make them invisible. No flushing whatever was observed round or near the fresh petechiae until they were stimulated by the pen-point.

If Case III comes into the same category as Cases I and II, it is, at first sight, difficult to reconcile its appearances with those conclusions. This patient, after she

had been stimulated in an almost exactly similar fashion to that used in the first two cases, responded with apparently vasodilator phenomena. She also, following an exciting cause unknown but presumably of visceral origin, displayed petechiae. The response to abdominal palpation, it may be remembered, was a series of papulo-urticarial patches. This case will not, I think, discount the probability of the hypertonic theory if we take papillary oedema as the most important part of the picture.

Reputable dermatologists are so divided on the mechanism of urticaria, that the inexpert clinician may be forgiven for suspecting that there is more than one way in which urticaria may be brought about. The descriptions given by these gentlemen are so various and often so strangely informed that perhaps it would be better to neglect them altogether and consider this particular case on what merits it has. It is generally assumed, moreover, that intercellular oedema, when it results from alterations in capillary physiology, is essentially a result of dilatation. Krogh, in one place, commits himself to the statement that the permeability of a capillary is directly proportional to its degree of dilatation. Florey, in some recent studies on capillary stasis, has shown that this is incorrect. Indeed Krogh himself implies, in his remarks on oedema, that increase of capillary pressure (such as might well result from a general

hypertonus over a capillary bed) can itself produce a filtration oedema without any question of dilatation. I suggest that something of this nature occurred in Case III; that the rapid contraction of certain small vessels in the skin papillae actually squeezed plasma through their walls; and that the outward manifestation of this act was the appearance of papules. Such flooding of the papules might be expected to produce either a syncitial or an axon reflex action on the deeper and neighbouring vascules. This in effect did occur. The swelling of the papillae was not obvious till two or three minutes after the flush had appeared, but, judging from the slow progress of the swellings after they could be easily seen by the naked eye, the process must have begun very early, concievably in the very short interval before the erythema appeared. The fact that on some days and in some instances the papules appeared before the flush, and even without it altogether, lends colour to this explanation.

The neighbouring vaso-dilatation corresponds, of course, with the behaviour of the capillaries in many similar circumstances.

Now we can find some support for a statement proposing one of the ways in which petechiae may be produced. A viscera may be in such a state of disorder, that spinal reflex phenomena may be produced in certain areas od the skin, and its vessels. These phenomena, as they affect the capillaries, take the form of hyperexcitability. This excitability is

represented ordinarily by hypertonus; but when the viscus is unusually disturbed the already high capillary pressure may be greatly increased. The increase of capillary pressure may result directly in a local filtration oedema. In the case of a terminal capillary loop, where the wall is ill supported or has undergone some morbid change, such increase of pressure may be sufficient to cause rupture. The hypertonus of the capillaries may be such that ordinary direct stimuli may fail to produce the normal dilatation; but, as the contractile cells of the cutaneous capillaries relax after mechanical stimuli of a certain strength (Krogh P.253.), a powerful reflex stimulus may result in sudden relaxation, and an apparently exaggerated response over the previously unresponsive area. This "exhaustion relaxation" might result in a wholesale diapedesis through the wall of one or more exhausted capillary, or, in the presence of increased capillary pressure, in actual rhexis. In a third set of circumstances, the arrival of an antidromic impulse in an area supplied at high pressure by hypertonic capillaries may produce forcible dilatation, or even rupture in individual capillaries situated near the appropriate sensory nerve endings.

Any attempt to throw statistical light on the problem of "reflex" petechiae must, in the very nature of the problem be hopeless. Enough has been said to show that they may happen only in exceptional circumstances, and may easily escape notice. The patient never notices them. If a Delegate from the Medical Research Council attempted to gauge the incidence of

epistaxis in enteric by trusting to the evidence of his senses and the daily observation of several wards full of patients, he would be of but little profit to his masters. The two cases are not very different. If it can be shown first that they are probable and second that they actually occur, the purposes of this essay will be served.

The following case suggests their presence in pulmonary disorder, although in this class of case a number of other important factors may contribute to the rhexis. Case V. W.R., male, aet. 41. Chemical Worker., who was admitted to Stobhill Hospital on 14. 2. 27. He suffered from pulmonary fibrosis, general emphysema, and dry pleurisy. He had bronchitis, but little or no cough or spit. There was no dyspnoea. He had been in bed for some weeks before admission. He gave no history of any of such violent respiratory crisis as make the petechiae of asthma or of whooping cough so easily explicable. He complained of pain at the left lower axillary region when he took a deep breath. There was local tenderness over the upper pole of the spleen (which was not enlarged). Physical examination showed loud rhonchi, diminution of R.M. and some crepitation on the left side, with two patches of pleurisy: one at the eighth and ninth ribs just in front of the anterior axillary line; the other in a circular area of four inches diameter including the right scapular angle in its upper part. In the upper half of the latter area there were four fresh

petechiae and two Morton's spots. There was one Morton's spot in the lower half. The petechiae were grouped transversely and lay over the spot where friction was loudest and most superficial. There was only one other petechia on the back - over the second lumbar vertebra. I shall not attempt to explain its presence. On the left side in front a series of six petechiae beginning at the manubrium and looping round the nipple to the anterior axillary line at the level of the seventh rib, one petechia over the friction area and two over the third and sixth ribs on the right side were seen. There was a Morton's spot over the manubrium sterni. None of the petechiae was tender to pressure or pinching. The patient had not noticed their appearance, but they were obviously fresh, and disappeared altogether in a day or two.

All that need be said of the distribution of these haemorrhages is that while they cover most of the dorsal "pain" segments, those on the right side correspond remarkably closely with the underlying lesion, while those on the left follow a line remarkably like that of the pain complained of by patients suffering from extensive peribronchial fibrosis.

It may be noted, however, on its general basis, that pinpoint rashes tend to be symmetrical. (See Appendix). It is possible to trace here a nervous basis.

HORMONES, METABOLITES, TOXINS AND GASES.

The glands of internal secretion assumed to play a direct part in the capillary economy are the suprarenal bodies and the pituitary. To these may be added the thyreoid and the parathyreoids, but their mode of action has not been fully elaborated, and they are not known to exercise any influence on capillary haemorrhage. Of the metabolites histamine may be taken as the type. When other protein poisons act on the capillaries, their action may vary in degree but not in kind, and it is safe enough to assume that where histamine action has been studied, the action of other metabolites to which the capillaries happen at the moment or in the individual to be sensitive will conform to the action of histamine. For this reason the term "histamine action" will be used, at times, to express metabolite action.

The action of certain groups of toxins - practically all the organic toxins - must, for want of more detailed knowledge, fall into the metabolite group, in the sense, of course, that their action on the vessels is practically uniform. The inorganic poisons will be referred to in so far as they are common and applicable to the points under discussion.

As I have less to say about pituitrin than about adrenalin, I propose to refer to it first. In the capillary

connection there are certain features common to both, and some remarks I shall make upon the agency of adrenalin in the mechanism of petechiae may well be taken as applying to pituitrin equally.

I do not know whether it is a common observation that pituitrin is, in certain cases, a sovereign remedy for oedema. In a series of cases of anasarca (hydraemic nephritis), I have seen very obvious diminution of the dropsy follow the daily administration of 0·5 c.c. of Parke Davis 'Pituitrin' in seven cases out of ten. In one case - a man of 28 almost moribund, anasarcous and passing 12 Esbach of albumen, oedema completely disappeared after five doses, and did not reappear up to his death ten days later. With the object of lessening oedema, I gave pituitrin to Case V, with unexpected results which have a bearing on this argument.

Case V, A.T. Male. Aet 74. Sheriff's clerk. Admitted to Stobhill Hospital as a private patient on 10.12.25. His complaint was of breathlessness on exertion and swelling of the feet and ankles. The oedema was apparently orthostatic, and usually disappeared shortly after he went to bed. His arteries did not suggest calcification or thickening to the finger. He showed evidence of a fatty heart. He passed from time to time a trace of albumen, and a stray hyaline cast. The Specific Gravity of his urine was 1015, and there was no poly - or oliguria. His weight was 15 stone, his

blood pressure averaged 160/95, and his Wasserman reaction was negative.

His oedema became very noticeable after he had been on his feet for upwards of ten minutes and, at times, extended to the knees. His dyspnoea was negligible except when he attempted to climb stairs.

In the course of some general experiments on oedema he was given 0·5 c.c. of P.D. pituitrin daily for 14 days. During this period, although he was out of bed and walking about the grounds of the hospital for several hours a day, the oedema was very much slighter. A mild, generalised prurigo, of which he had complained for a year or so, almost disappeared. The bronchial blood pressure was not materially raised.

On the day following the stoppage of his pituitrin, the oedema was noticed to have increased. The prurigo exacerbated. He stated that it was much worse than it had been before the injections. The oedema was now limited to an area extending from just behind the malleoli forward, and from the dorsum of the foot to the roots of the toes which were not affected. Above it reached three inches up the shin. The whole effect was of a cushion laid on the dorsum of the foot. The swollen area was red and the patient complained of heat and tingling over it. It did not feel hot to the hand. Above the affected area multiple capillary

haemorrhages appeared bright red in colour, and varying from the pin point type to patches as broad as a millet seed. Some were confluent. The larger patches were regularly circular. Four days later the haemorrhages still persisted, though some were fading. There were no fresh haemorrhages. The oedematous area was covered with a pale coffee coloured pigment. The flush was not obvious. A week later the haemorrhages had disappeared or been replaced by pigment. The pigment was still present over the oedematous area, which was not now so sharply defined at the edges. In three more weeks the patient's condition was as on admission, except that patches of the pigment remained and are evidently permanent.

This fortuitous experiment, while it raises issues too vast for the compass of this essay, is too vague to present us with any very definite conclusions. One or two legitimate inferences may, however, be drawn from it.

Note: I have only been able to trace one direct reference to experiments on the action of pituitrin on oedema formation. This is the article of SACKS in Heart XI. 353. 1924, where he is able to prove a diminution in the accumulation of experimentally produced oedema under dosage with infundin.

Whether or no the pars posterior and its commercial extracts contain the X substance of Krogh, there can be little doubt that the pituitary body, directly or indirectly, is concerned in the maintenance of capillary tone. Whether this influence is brought to bear through the general effect on the blood-vascular system, or whether the problematical action of the pituitary (anterior part) on calcium metabolism is concerned need not detain us at the moment. Krogh himself (p. 166) is non-commital. It may be worth while to introduce here one of a series of auto-experiments performed by myself.

Tight ligatures were applied to the middle fingers of each hand, until both were equally blue. A solution (·0012 c.c.) of P.D. pituitrin was injected into the base of the left finger, and both fingers were plunged into hot water. No change in the colour of the fingers occurred.

The ligatures were removed and the fingers again immersed. The left recovered at once. The right remained cyanotic for 1½ minutes. On its recovery the fingers were taken out of the water.

2". Right completely recovered. Left now flushed relatively to fingers of same hand. Flush took place from bed of the nail upwards.

3" Right normal. Left still flushed except for ischaemic area forming a semicircle distal to puncture and

extending to radius of $\frac{1}{2}$ inch.

15" Flush over left fading, but bed of nail still bright red. Ischaemic area if anything more marked. No difference observed in capillaries of microscopic fields in nail-beds of the two fingers, but the view obtained was not very good. Through a Zeiss No.4 eyepiece, the left capillaries appeared dilated and more numerous. The ischaemic area seemed to be very deep.

30". No change.

45". Nail-bed flush now no greater than in other fingers. Ischaemic area as before. Ligature marks are still present on left finger, but have quite disappeared from right.

Two hours later the blanched area of skin was still present, but was fading centripetally.

I shall discuss these observations in connection with some others made on adrenalin action. The only virtue claimed for the experiment is that it was performed on the human subject, and the only conclusion I wish to draw from it before returning to the case under review is that pituitrin can, in certain circumstances, produce not only arteriole constriction, but capillary constriction. There is no evidence that the local application of a small dilution of pituitrin can maintain local arteriole contraction for upwards of two hours.

Revenir a nos moutons, the behaviour of Case V is explicable on these grounds: 1. That the addition to the blood stream of a small dilution of a physiological substance so altered the condition of the capillaries of the foot that they were able to drain the intracapillary spaces of fluid they had previously admitted to them. 2.That the disappearance of the flushing corresponded with a return of capillary tone, and that this return was further evidenced by the absence of reaccumulation of fluid. 3. That the discontinuance of the supply of this added substance caused so sudden a loss of tone that numbers of the capillaries actually ruptured, a possible added factor being exhaustion brought about by the artificial maintenance of tone in diseased vessels. 4. That those superficial capillaries which did not rupture betrayed a well-known characteristic of paretic capillaries in the deposition of pigment.

It will be noted that I have assumed that the reappearance of capillary tone will tend to reduce oedema. This is an assumption for which there is no scientific proof, but on its face value it looks reasonable. The type of oedema present in this case was patently orthostatic, that is it was dependent to some extent on the state of resistance to mechanical permeation of the capillary walls. Such an oedema is intercellular. It is dependent upon the excess of the filtration pressure over the osmetic pressure in the blood.

While a change of calibre with a decrease of permeability consequent on the change will prevent further filtration, it is difficult to see how it can bring about a positive instead of a negative balance between the two pressures. It is possible that the lymphatic drain is rendered more effective by the improvement in its blood supply. An infinity of factors, chemical and physical, are concerned in the absorption of oedema. They have not yet been placed even on an arguable basis, and my assumption must remain for the present an assumption.

The experiment upon Case 1 (p.34) will serve as an introduction to my remarks on adrenalin. It will be remembered that this patient suffered from a floating kidney and that manipulation of this organ produced a series of petechiae. Three minims of 1/1000 adrenalin introduced into his median basilic were followed by six deep capillary haemorrhages, great increase of vasomotor excitability (as regards the skin capillaries) and shivering and palpitation. The fact that a ptosed kidney, in its descent, does not take its suprarenals with it made it improbable, but not impossible, that direct stimulation of the suprarenal bodies had anything to do with the production of the first crop of petechiae. The undoubted appearance of a crop of petechiae of a slightly different character after the adrenalin injection once again brought adrenalin action into the field.

Following this experiment, I attempted to produce

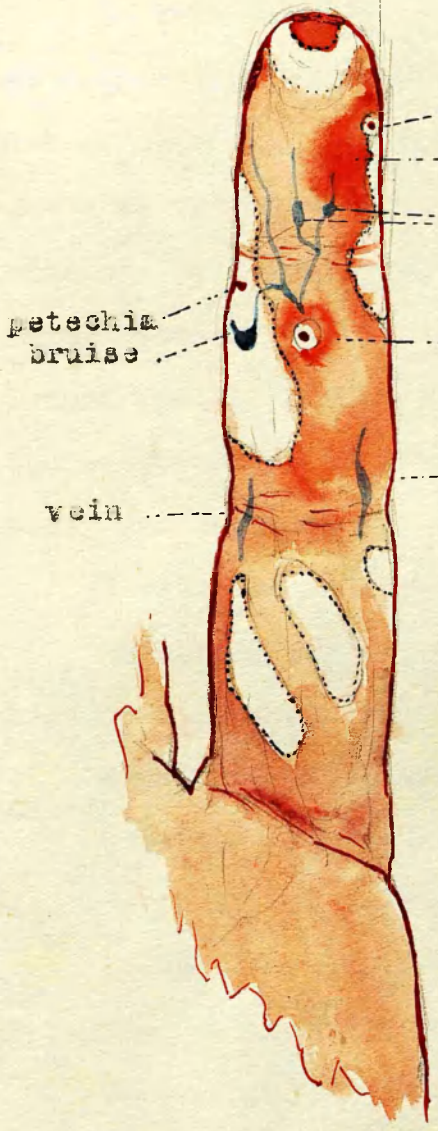
petechiae on myself in the presence of adrenalin action, and in time succeeded in doing so.

The breath was held for 10 seconds and a tourniquet put on the left little finger 5 minims of 1/4000 adrenalin was injected above the first joint on the inner aspect. Slight irregular blanching appeared. No petechiae could be seem. The outer aspect of the distal phalanx was then crushed with a Spencer Wells forceps. A white band $\frac{1}{4}$" long appeared at the crushed area, surrounded by irregular erythema. One petechia appeared at the margin of the white area. The tourniquet was removed. The white patch over the crush intensified and remained dead white for seven minutes, when it faded and was replaced by a slight erythema round a pink slightly raised band. There was no bruising near the crush. There was a general capillary dilatation throughout the finger, and a search with a strong lens revealed the presence of two more petechiae, slightly distal to the point of injection.

A drawing was made of the residua twenty minutes after the injection. The appearances in this drawing came gradually up to 20 minutes and disappeared slowly, being gone in an hour. The bruise above the terminal joint appeared half an hour after the injection, and appeared to be due to diapedesis through the wall of a vein. The white patches appeared as soon as the mechanical congestion caused by the tourniquet was relieved.

The back of the finger showed nothing but a deep

Diagram illustrating p. 73 et seq.



Dotted lines surround blanched areas.

flushing of the ulnar surface, and some blanching of the radial surface. There were no marks of the tourniquet, either in front or behind.

In this experiment petechiae were produced in circumstances suggesting the interplay of histamine-like bodies (product of crushing) and adrenalin. It is true that the balances were weighted by the induction of capillary stasis by bandaging, by "breath-holding" and by the injection of a relatively enormous amount of adrenalin. But the chances are so enormous against rhexis taking place in such a small area, that the introduction of other assisting factors should hardly destroy the interest of the result.

I take the main points to be these:

Injection of adrenalin was not followed either by petechiae or by patchy ischaemia.

Diffusion of adrenalin to some extent took place.

Crushing was followed by local ischaemia, marginal hyperaemia and, at one point, rhexis.

On the removal of the band and further diffusion of the adrenalin, gross vascular changes took place.

These consisted in local dilatation of veins, diapedesis through the vein walls, localised blanching (contraction of arterioles and emptying of capillaries into veins), and rhexis of capillaries in two cases.

The congestion of the rete from dilated and engorged capillaries was only inhibited in circumscribed areas.

A network of dilated veins joined the crushed area to the injection area.

As these findings correspond pretty closely with Dale's classical observations on histamine-adrenalin inter-reaction, it is difficult to avoid concluding that the petechiae observed here are somehow involved in the process. I think there is a possible explanation of how they occur, both in the auto-experiment and in Case I.

In Case I, the earliest step in the progression of events must be taken as due to the nervous element. In this case the event would be dilatation and stasis in the capillaries of the reflex field. The liberation of a certain dose of histamine, if it did take place, would probably happen a short interval before adrenalin was mobilised. This would result in still further dilatation of the capillaries relatively to the other skin vessels, the impounding of blood in the capillary field, and the accumulation of asphyxial products. The arrival of adrenalin at the terminal twigs of the vascular tree would coincide with circumstances at first unfavourable for adrenalin action of a local nature (i.e. not via the sympathetic system). The carry forward of the adrenalin by the blood stream would cease, and further advance would require to be by permeation, of what amounted to a block of corpuscles in a concentrated fluid medium. Permeation would be assisted by the contraction of the terminal arterioles through adrenalin action. Very

slight variations in the alkalinity of its medium influence adrenalin action profoundly, and the fall in PH in the capillary field due to the accumulation of asphyxial products would result in increased efficiency of that action wherever and whenever the adrenal made contact with the capillary walls. In the circumstances such contact would be uneven. The restoration of tone at the arterial end of the capillary loops would increase the pressure at the venous end. No material fall in venous pressure could be expected in such a short sequence of events in time. The arterioles and capillaries emptying them would be squeezed like a sponge. The "venous" capillaries would be subjected to relatively great strain, and the weaker members would break. I cannot see any escape from the conclusion that the adrenalin itself is capable of producing haemorrhage. If this description of the events is valid, patients who suffer from a consistently high venous pressure should be particularly liable to haemorrhages of this nature, and, as a matter of fact they are so.. Cases of aortic incompetence, whose varying blood pressure makes a continuous call upon the suprarenals, are peculiarly liable to sudden petechial haemorrhages, and these are almost always of the venous type.

Further corroboration of the part played by adrenalin in these bleedings is to be found in the fact that many of them occur into a blanched area. A case seen in the Victoria Infirmary showed this quite dramatically.

Case VI. Mrs. A.B. 47. Subacute endocarditis of a year's duration three-valve incompetence. In terminal phase developed hypostatic pneumonia, and widely distributed "venous" purpura. P.M. showed multiple ecchymoses in lungs, liver, spleen and heart wall. The ileum showed at one level a series of four bands of hyperaemia about 5 cm. broad, intersected by bands of ischaemia of a similar breadth. Bleeding pinpoints were very numerous, both into the lumen and into the adventitia of the ischaemic bands, but none could be found in the hyperaemic.

BLOOD CONDITIONS AND PETECHIAL HAEMORRHAGE.

Petechiae appear in almost every morbid condition of the blood. A plumber must take cognisance of the chemistry, the contents, and even the types of living cells in the fluid contained in his pipes, and it would be absurd to suppose that the character of the blood cannot influence capillary rupture. It is very difficult, however, to come at a consensus of opinion as to what properties in the blood produce isolated bleedings in such a condition as myelogenous leukaemia, for instance. It is easy to visualise diepedesis in certain blood conditions - cases in which the plasma cells may be actually amodrid and lead their fellows out like sheep through a fence. It is easy to picture starved capillaries containing attenuated blood failing, here and there, to hold

that blood within their walls. But the step from the mind's eye to the microscope and the test tube is a long step. Certainly bio-chemistry does not help us much here; and the only eytological point upon which everybody is agreed is that certain cases of purpura of whatever sort show a diminution of platelets.

As I have no original observations to offer on this aspect, I may be allowed to quote Letheby Tidy who summed up the situation neatly in an article in the British Medical Journal of April 7th, 1928 (after this essay had been written). He says in effect that platelets may be absent from the circulation without the occurence of haemorrhages; that an attack of purpura haemorrhagia may pass spontaneously while platelets are still absent; and that platelets have been experimentally reduced to very low figures, no haemorrhages have occurred.

He concludes that increased permeability or defect of the capillary wall is the essential cause of the haemorrhages in the haemorrhagic diethesis. This is one of my hypotheses.

EMBOLISM CONSIDERED AS A FACTOR.

In writings on purpura this phrase, or its substance, occurs with some regularity: "The haemorrhages are probably due to emboli in the terminal vessels." The probability or

improbability of this explanation may concern us for a few paragraphs.

Stephen Mackenzie relates that capillary emboli have been found in sarcoma, in leucocythaemia and in pyaemia. He admits that they may have a direct causal influence. But, he says, numerically such cases are very infrequent, and afford no explanation of the majority of cases of purpura in which they are absent.

The source of the hypothetical embolism is made clear in most of these writings. They appear to be visualised as clumps of bacteria floating in the blood stream. The rarity of such "clumps," even in fulminating pyaemias, need not be stressed here. They have simply not been seen, let alone demonstrated satisfactorily in the peripheral vessels. It is therefore probable that if they do occur they are minute and rare. In the types of purpura where there is clear evidence of bacterial infection, the petechiae are very numerous. It is not to be supposed that more than a small percentage of "clumps" will produce petechiae. If "clumps" are rare and petechiae numerous, the conclusion is that "clumps" do not produce all the petechiae. Even in pyaemia, when large portions of foreign matter may be presumed to float free in the plasma, the number of infarctions is usually remarkably small, and petechiae are not more common than in cases where no such bodies are presumed.

Carey Coombs, in a recent book, goes so far as to say that the petechiae found in certain cases of rheumatism are, in fact, infarctions. If he and the other writers are correct in supposing petechiae to be embolic in origin, they must be infarctions. But are they so?

An infarction occurs when an end artery is blocked - that is, an artery to an area where the circulation cannot be satisfactorily restored by collaterals. Robert Muir describes the events as (a) interference with the nutrition of the part and necrosis, and (b) certain circulatory disturbances - congestion and haemorrhage. The term infarction, he says, is applied to the altered area which has its blood cut off. Neither of these events is recognisable in purpura affecting the skin, and one would expect to find both if the embolic theory were valid. Congestion and haemorrhage - and the two are inseparable in infarction - do not occur together in petechiae. The unmistakable skin infarction shows like a tiny bruise with a surrounding zone of congestion. This zone expresses an attempt to establish a collateral circulation and is invariable. Scarcely less variable is the zone of blanching round a petechia.

The actual haemorrhage in infarction may be due to rupture of an arteriole from vis a tergo, or to reflux from the veins. A third possibility is illustrated in cases of embolism of the superior mesenteric artery, where the

collaterals allow blood to flow into and distend the arteries, but where the pressure may be insufficient to produce a satisfactory current of blood through them. The capillary walls, deprived of nutritional or tonus-maintaining elements in a proper sufficiency, give way. The first type of haemorrhage is very different from a petechia. The rupture of the minutest arteriole produces a characteristic haemorrhage. It is wedge shaped. It forces itself through the tissues to irregular lengths. Its appearance is well typified in the flame-shaped haemorhages of the retina. The common petechia has a neatness and regularity of spread that suggests that the blood has "soaked" through the tissues centrifugally as soon as its containing wall has given way, and that the element of force is almost, if not quite, absent.

The possibility of infarction being due to reflux from the veins has been discussed by Conheim and dismissed by Litten. That such a reflux actually occurs in cases of purpura is suggested by the nature of the blood contained in some purpuric spots, and will be supported, I think, by some considerations I advance on the haemodynamics of capillary haemorrhage. But these considerations depend on quite different conditions from those commonly found in infarction, and if the reflux is due to extra-capillary causes and results from a forcible flowing back of the blood into the capillary system, the appearances presented will resemble, in kind at

least, those of arterial haemorrhage. Given the necessary conditions - for example increased pressure on the capillary wall from the back flow - a group of capillaries will be likely to give, and a bruise result.

The third mode of production of infarction is more pertinent as it presupposes changes in the capillary wall itself. While the instance quoted refers to the stoppage of a relatively large vessel and is not necessarily applicable to the skin, it yet illustrates a striking incident in many if not most of petechial haemorrhages: that they occur in an area of ischaemia. Most of the processes of my argument touch at some point or another this very salient fact, and it must be admitted that in a sense capillary haemorrhages are here the result of embolism. As I hope to show, however, that several other agents may produce the same set of conditions, and that after the agent is, so to speak, established and active, a prolonged series of rather complicated events must occur before the actual haemorrhage takes place, I may be allowed to class this type of embolism as a remote, or at least not one of the intimate factors, in capillary rhexis.

The characteristic manifestation of bacterial emboli is not far to seek, and it is quite different from purpura. Abscesses are not uncommon, but perhaps the most characteristic occurrences from the point of view of this

essay are those little tender areas of induration described by Poynton as Osler's nodes, and familiar to everyone who has observed many cases of malignant endocarditis.

DISEASES OF WHICH PETECHIAE ARE A FEATURE.

It is not improbable that petechiae occur in health, or in what is generally understood by that condition. In a series of 240 recruits for the Territorial Army, I have looked for petechiae about the arms and trunk - not, it is true, with a lens. The cases in which petechiae were present were those in which there was evidence of cardio-vascular or respiratory disease, or of pronounced oral sepsis. None was found in "healthy" recruits. I exclude, of course, petechiae caused by body parasites.

It is not within my present scope to trace the factors mentioned in the hypotheses through the various diseases of which petechiae are a feature. It may, however, be a useful sort of summary, if I cast these diseases into groups and show for each group which factor my argument makes dominant. The simple mention of many of these groups gives a show of probability to much of my thesis.

Most petechial or "purpuric" diseases are covered by the following grouping:-

Class I. The Purpura group (including all so-called idiopathic purpuras)

Class II. Cardio-vascular disease.

Class III. Acute Infections.

Class IV. Blood diseases.

Class V Organic or inorganic intoxications.

Class VI. Metabolic diseases.

Class VII. Convulsive diseases.

Class VIII. Diseases principally of the nervous system.

Class IX. Diseases depending on senile or congenital vasomotor defect.

Class X. Chronic wasting diseases.

Class XI. Suprarenal disease.

It will be readily admitted that in Classes ii, iv, v, vi, ix, & x the attenuation of the capillary wall is a ruling factor. Malnutrition, morbidity and stress occur in varying proportions in each class.

In Class xi (and possibly in Class vi) a tonic substance is deficient, and some such explanation as is contained in the fifth Hypothesis and the section on Hormones becomes valid.

To Classes ii, vii & viii this explanation may also apply.

Classes ii & iii may derive some explanation from the second Hypothesis.

Class iii is probably explained in part by the third Hypothesis in conjunction with Lewis's theory of "flare." It must be borne in mind that a varying but intense bombardment

of the periphery by metabolites must occur in all acute infections. These metabolites may be derived from the destruction of white cells, fixed tissues, or even the invading organisms themselves. Their presence suggests the application of the fifth Hypothesis. The haemorrhages in Class viii are usually such as can be explained on the lines laid down in the section on Nervous Influences (Hypothesis 4.).

The specific factor in Class v must, of course, vary with the intoxicating agent. Snake venom, the most characteristic of the organic poisons, has an action closely resembling that of histamine or choline. Its production of purpura actually takes all of the Hypotheses to explain it. A short reference to inorganic poisons will be found under the section on Hormones, Metabolites, Toxins and Gases.

Class vii shows almost invariably a sudden high venous pressure (Hypothesis 2a) and a sudden call on adrenalin (Section on Hormones).

There remain the purpuras proper. There is a modern tendency to ascribe these cases in increasing numbers to the action of various strains of haemolytic streptococci. This etiology would place many cases described as purpura simplex, Henoch's purpura and Schonlein's purpura at once in the category of Acute Infections. (Class iii).

Purpuras occurring in the course of a chronic low infection - as certain types of so-called purpura rheumatica -

may conceivably be a phase of the same process that ultimately produces panniculitis, nodules and fibrositis. The haemorrhage undoubtedly occurs "in a reticulum subject to considerable physical alterations" (Hypothesis 1.b); and in the neighbourhood of arteries, whose surrounding tissues are undergoing structural alterations (Hypothesis 2.d). But in this, as in all other purpura of obscure origin, many of the other hypotheses may be called upon. I am only able to suggest that the factors, which are so obvious in many less obscure diseases, may apply here also.

A P P E N D I X.

Von Dusch's Disease is, however, of Interes

I attach a chart and diagram showing the

twelve cases of purpura seen in th

ing the past two or three years.

APPENDIX A.

Distribution of petechiae on the body surface.

The distribution of petechial rashes is very various. Adamson [*] has drawn attention to the liability of certain areas of physiological mottling to become the sites of rashes. The darker (or "atonic") areas are evidently less resistant than others. Lewis believes that the distribution of a rash must depend on the distribution, potency, time of contact and diffusibility of the poison causing the rash and on the reactivity of the vessels and nerves concerned. I have suggested other factors which may determine the focal distribution. What may be called the "gross" distribution is another matter and raises far larger questions than can be dealt with here. A tendency for these rashes to correspond with the pigmented areas of Addison's Disease is, however, of interest.

I attach a chart and diagram showing the"gross" distribution in twelve cases of purpura seen in the Victoria Infirmary during the past two or three years.

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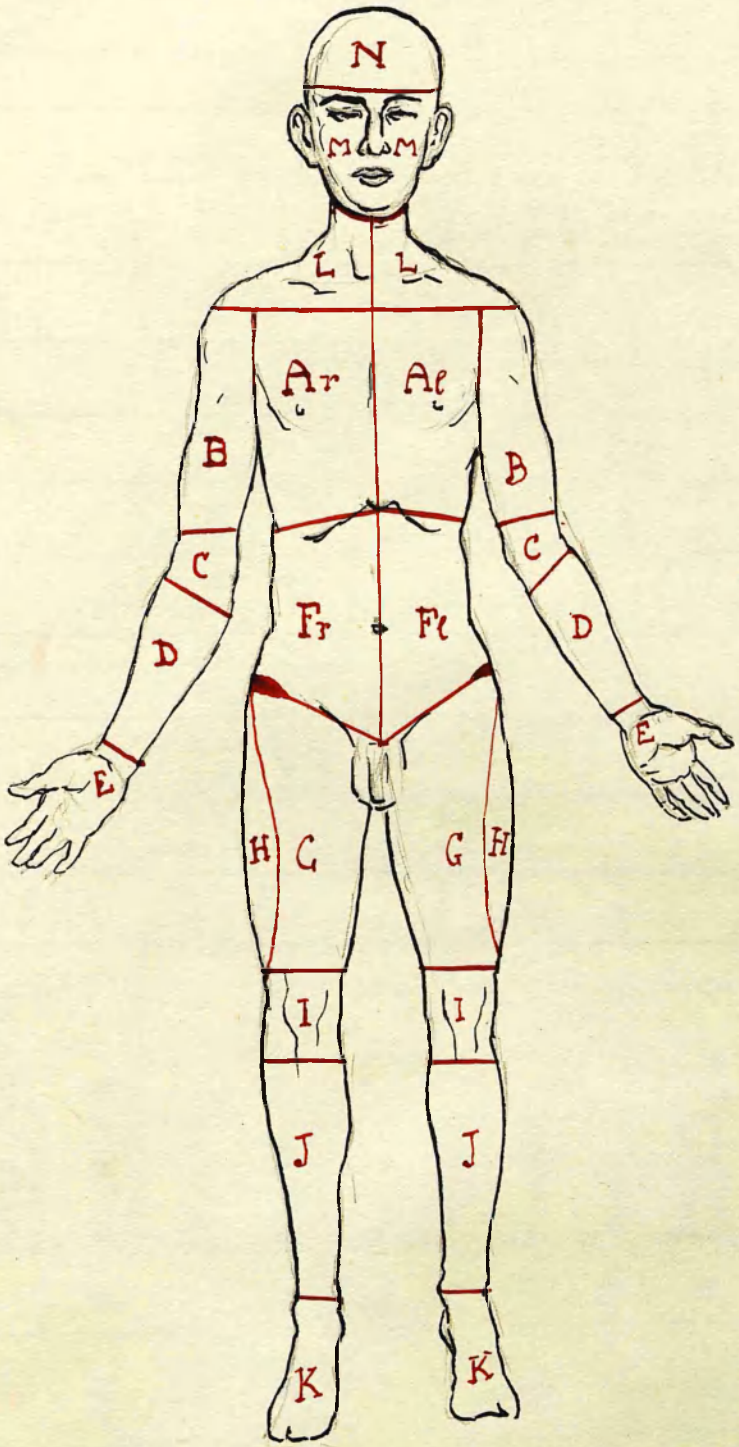
[*] Modern views on the significance of skin eruptions. LANCET I. 1041. (1912)

DIAGRAM ILLUSTRATING DISTRIBUTION TABLE.



APPENDIX A.

Case.	Age.	Sex.	Diagnosis.	A	B	C	D	E	F	G	H	I	J	K	L	M	Remarks
I.	7	F	Ac. Rheumatism c̄ Angio neurotic Oedema.									f ++ b ++	++ +	f+			
II.	38	F	Purpura c̄ Chr. Nephritis.			fl +					bl +		bl +				
III.	8	F	Purpura.	f ++ b +	++ ++	++ ++	++ ++	++ ++	++ ++	++ ++	++ ++	++ ++	++ ++	++ ++			
IV.	5½	F	Henoch's Purpura.			br ++ bl ++	fr ++ fl ++										
V.	2	F	Purpura		f + b +		+ +										
VI.	9	M	Purpura	f ++ b ++	++ ++		++ ++	+	++ ++		++ ++	++ ++	++ ++				
VII.	55	F	Purpura									fr ++ b o	fr ++ fl ++				Buccal m.m. +
VIII.	34	M	Purpura	b ++			f ++ b ++		b ++	f ++ b ++	++ ++	++ ++	++ ++	f ++			
IX.	35	M	Purpura rheumatica			b ++				f ++ b +	f ++	++	f ++ b ++	++ ++			
X.	24	M	Erythema iris								f + b +		+ +				
XI.	12	M	Purpura	b ++	b ++				b ++				f ++	f ++ b ++			
XII.	36	F	Chronic rheumatism.			f ++	fl ++ bl ++										

Explanatory Note: + means scanty
++ " numerous
f " front
b " back
r means right
l means left
Where the lesions are bilateral r and l are omitted.
The letters at the top of the columns indicate areas on the attached chart.

APPENDIX B.

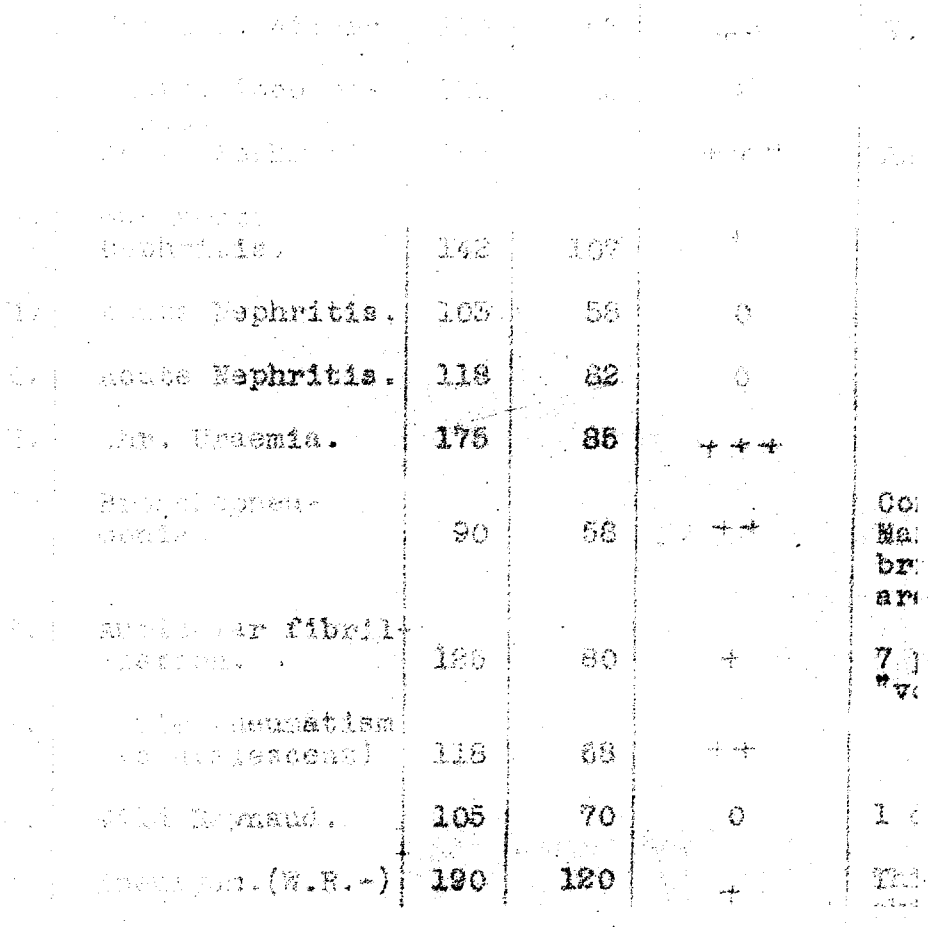
Lewis & Harmer's "Breaking Strain" Test.

Part of the test devised by Sir T. Lewis and Miss Harmer for determining the breaking strain of capillaries is as follows: The manometric cuff is applied to the upper arm and the pressure is slowly raised to 60 mm Hg. The maximum venous pressure in the forearm is reached in about 40 seconds. The pressure in the cuff is sustained for 3 minutes. In a proportion of cases this operation is followed by the appearance of capillary haemorrhages in the skin of the forearm. Spots may appear at intervals up to five minutes after the pressure has been removed.

In most "healthy" persons no petechiae appear unless the pressure is sustained for much longer periods than three minutes. Patients showing cardio-vascular disease, chronic wasting disease or anaemia usually show large numbers of petechiae. The type arbitrarily classed as of an "unstable vaso-motor system," seldom respond in this way. Probably, if their capillary bed were not capable of withstanding sudden and serious changes in venous and arterial pressure, they would hardly survive infancy! It is an interesting point in view of the recent orientation towards vascular hypotheses in the octiology of nephritis, that cases showing renal disorders tend to respond with large crops of petechiae.

The illustrative series I give here was taken at random in ordinary hospital practice. I have included only cases in which an exactly similar procedure was used.

4 - 9 petechiae are indicated by a single + ; 10 - 19 by + + ; 20 - 30 by + + + ; above 30 by + + + +.



		142	102	+
	Nephritis.	105	58	0
	Nephritis.	118	62	0
	Uraemia.	175	85	+ + +
		90	58	+ +
		120	80	+
		118	68	+ +
		105	70	0
		190	120	+

APPENDIX B.

Case.	Age & Sex.	Condition.	S.B.P.	D.B.P.	Petechiae.	Remarks.
1.	27 M.	Chronic Glomerular Nephritis.	165	122	+++	7 years' duration.
2.	23 M.	Generalised tuberculosis	160	110	+	
3.	36 M.	Chr. Glomerular Nephritis	145	178	+++	7 years' duration Arterio sclerosis
4.	55 M.	Aortic incompetence.	135	45	++++	
5.	35 F.	Post puerperal anaemia.	120	50	+	Albuminuria; some oedema.
6.	52 M.	Cardiac failure.	153	63	++	W.R.+
7.	58 M.	Mitral incompetence.	138	85	+	
8.	72 F.	Acute Nephritis.	185	95	+++	Anasarca. Died.
9.	46 M.	Sub acute Nephritis.	142	107	+	
10.	13 M.	Acute Nephritis.	103	58	0	
11.	8 M.	Acute Nephritis.	118	82	0	
12.	54 M.	Chr. Uraemia.	175	85	+++	
13.	11 F.	Bronchopneumonia.	90	58	++	Convalescent. Marbling with brilliant flare areas.
14.	42 F.	Auricular fibrillation.	125	80	+	7 petechiae of "venous" type.
15.	16½ F.	Acute rheumatism (convalescent)	118	68	++	
16.	29 M.	Mild Raynaud.	105	70	0	1 doubtful spot.
17.	54 M.	Aneurysm.(W.R.-)	190	120	+	Thick, brawny skin.
18.	23 M.	Pneumothorax.	112	72	+	Non-tubercular.
19.	43 M.	Subdural haemorrhage.	104	66	+++	B.P. reading after test was 78/58.

Case.	Age & Sex.	Condition.	S.B.P.	D.B.P.	Petechiae.	Remarks.
20.	10 M.	Chr. Glomenular Nephritis.	105	78	++	
21.	19 F.	? Hysteria.	130	98	+++	Patient had periodic suppression of urine and panniculitis.
22.	31 F.	Meniere's Disease.	110	70	0	
23.	28 F.	Chronic Fibrositis	105	58	0	
24.	40 M.	Healthy	120	85	+	
25.	62 M.	Mediastinitis: anaemia (secondary)	90	68	++++	Condition believed to be tubercular.

[illegible] an apparently stable equilibr[illegible]
[illegible]. This equilibrium may persist for 24 hou[illegible]
[illegible] always at a lower level than the ori[illegible]
[illegible]ing. In 50% of a series, not only w[illegible]
[illegible] problem, always a lower level, but [illegible]
[illegible] Then by after 24 hours the curve [illegible]
[illegible] to its original level.

APPENDIX C.

Ultra violet Light and the Blood Pressure.

The immediate event is a rise of the systolic blood pressure of from 5 to 18%, a fall of the diastolic pressure of from 9 to 25% with a consequent rise of the pulse pressure, which may vary from 25 to 162%. The maximum rise of the systolic pressure occurs not less than five and not more than ten minutes after exposure. The diastolic fall begins immediately, but does not reach its maximum for a period varying from ten minutes to an hour.

The immediate event is followed, in a very few minutes, by a steady fall of both the systolic and the diastolic pressures. This continues until, usually at the end of about four hours, an apparently stable equilibrium is reached. This equilibrium may persist for 24 hours upwards, and is nearly always at a lower level than the original blood pressure reading. In 50% of a series, not only the systolic and diastolic pressures showed a lower level, but the pulse pressure also. Usually after 24 hours the curve tends to rise slowly to its original level.

The experiments were carried out in the early afternoon. The lamp used was a mercury vapour lamp. The sphygmomanometer was a Tycos, and the same instrument was used throughout. The patients were sitting, with the eyes

protected, at 6 feet from the lamp. The chest from the manubrium to the xiphisternum was uncovered, and a full exposure of five minutes was given. Four blood pressure readings were taken, by the auscultatory method in the light room. The remainder were taken in the ward. The patients did not go to bed till the four hour reading had been taken. It was found by preliminary observations that no material variation was missed if readings were taken just before irradiation, five minutes after, and 10, 20, 40, and 60 minutes, four hours and 24 hours after.

Remarks.

It will be noted that while there is a large variation in the intensity of the reactions - a variation which seems to have some relation to the initial diastolic pressure - they fail to give the complete picture in only five out of the twenty-two cases.

Cases vii, xi, and xiii show no initial rise of systolic pressure. Cases vii and xvii show no fall of the systolic pressure relatively to the initial reading. Case xii, again, shows remarkably little change in his pulse pressure throughout the experiment. Case vii, an arterio-sclerotic, had been taking Potassium Iodide and Tincture of Belladonna for many months. Case xi had panniculitis and was taking gr xxx of Potassium Iodide daily. Case xiii, a sufferer from the Parkinsonian syndrome of encephalitis lethargica,

was taking 160 minims of Tincture of Belladonna daily. This patient also kept a constant pulse pressure, and the "paretic" appearance of his curve might serve as a pointer if one wished to speculate on the mechanism of these light reactions. Of the two cases (vii & xvii) who showed no systolic fall, one was a pigmented Portuguese, with an idiosyncracy for iodides. The other was an emaciated asthenic woman.

To sum up the happenings in this group:

The systolic blood pressure in the brachial artery rose first and then fell in 90% of the cases.

The diastolic pressure fell in all the cases.

The pulse pressure rose more than 20% in all the cases but one.

The pulse pressure later fell below the initial level in half the cases.

The diastolic drop was more than 10% in 95% of the cases.

The explanation of these phenomena is beyond the scope of this paper. The superficial explanation - that the curve is due to alterations in the peripheral (capillary) resistance, will not hold water. Even if the dilatation of the capillary bed was known to affect the blood pressure, the periodicity of the events does not correspond with the observed behaviour of capillaries under light stimulus. An action of freed metabolites on the circulation as a whole seems a possible way of accounting for the facts. In this connection we checked our observations by submitting patients for ten minutes to a temperature of 105 Fahr. The electric pack and the hot bath were used, and, of course, the entire surface area was exposed. The curves obtained were very like those given in the light experiments. The points of difference were: 1. Little or no initial systolic rise. 2. Very slight alteration in pulse pressure. 3. Earlier rise of the curve towards the original level.

Blood counts showed only the normal discrepancy between the peripheral and the venous counts, and were abandoned early in the series.

These observations were made at Stobhill Hospital in 1925-26 by Dr. Mary Proudfoot and myself.

Case.	Diagnosis.	Before radiation. S.D.P.	D.B.P.	P.P.	Maximum percentage Rise & Fall after radiation. S.B.P. Rise.	Time. (minutes)	S.B.P. Fall.	Time.	D.B.P. Rise.	D.B.P. Fall.	Time.	P.P. Rise.	Time.	Equilibrium stage. 4 hrs. after. S.B.P.	D.B.P.	P.P.	24 hrs. after. S.D.P.	D.B.P.	P.P.
I.	M.28 Asthenia.	124	100	24	3·20	5"	18·75	60"	Nil.	16·00	4hrs.	41·66	10"	100	84	16	108	92	16
II.	M.29 Chronic phthisis.	150	134	16	12·00	10"	16·00	60"	Nil.	25·54	60"	162·50	10"	126	110	16	134	110	24
III.	M.18 Chronic dyspepsia.	120	100	20	18·33	20"	8·33	60"	Nil.	10·00	20'	160·00	20'	110	96	14	118	96	22
IV.	M.41 Sciatica.	126	96	30	9·52	10"	12·69	4hrs.	Nil.	16·66	60	60·00	10'	110	84	26	118	94	24
V.	M.38 Chronic phthisis.	120	90	30	6·66	5"	15·00	60"	Nil.	8·88	20	33·33	5'	102	86	16	110	86	24
VI.	M.61 High blood pressure.	196	150	46	2·04	10"	18·37	60'	Nil.	13·33	60'	30·04	10'	166	130	36	170	130	40
VII.	M.67 Chronic bronchitis.	130	100	30	0·00	5"	23·07	4hrs.	Nil.	20·00	20'	33·33	5'	100	82	18	118	92	26
VIII.	M.58 Pulmonary anthracosis.	120	90	30	8·33	10"	00·00	20'	Nil.	11·11	20'	60·00	10'	120	84	36	120	84	36
IX.	M.29 Fibrositis.	130	98	32	15·38	5"	9·23	60'	Nil.	16·32	20'	56·25	10	124	90	34	124	90	34
X.	M.33 Pulmonary Fibrosis.	120	88	32	1·66	10"	8·33	20'	Nil.	13·63	20'	37·50	10	120	80	40	120	80	40
XI.	M.29 Fibrositis.	110	90	20	no rise	-	10·90	60'	Nil.	15·55	20'	20·00	10	100	80	20	104	90	14
XII.	M.18 Ac. rheumatism. (convalescent)	120	96	24	3·33	10"	10·00	60'	Nil.	14·79	40	66·66	10	110	84	26	118	88	30
XIII.	M.15 Post encephalitis.	110	80	30	no rise	-	9·09	20'	Nil.	7·50	10	6·66	5'	100	80	20	100	80	20
XIV.	M.26 Tonsillitis and fibrositis.	126	100	26	1·58	10"	12·69	40'	Nil.	20·00	40	46·15	10'	120	80	40	120	80	40
XV.	42 Tonsillitis.	108	94	14	3·37	10"	7·47	40'	Nil.	12·76	60'	57·14	10'	102	90	12	106	90	16
XVI.	M.25 Chronic appendicitis.	120	90	30	13·33	10"	3·33	40	Nil.	15·55	10	100·00	10'	118	84	34	118	88	30
XVII.	F.49 Chr. endocarditis.	110	78	32	9·09	10"	0·00	40'	Nil.	15·38	20	68·75	20'	114	72	42	114	76	38

XVIII/

Case.	Diagnosis.	Before radiation. S.D.P.	D.B.P.	P.P.	Maximum percentage Rise & Fall after radiation. S.B.P. Rise.	Time.	S.B.P. Fall.	Time.	D.B.P. Rise.	D.B.P. Fall.	Time.	P.P. Rise.	Time.	Equilibrium stage. 4 hrs. after. S.B.P.	D.B.P.	P.P.	24 hrs. after. S.D.P.	D.B.P.	P.P.
						(minutes)													
XVIII.	F.33 Dental Caries.	98	70	28	4·08	10"	4·08	60'	Nil.	14·28	40	35·71	20	94	66	28	94	66	28
XIX.	F.41 Exostosis.	126	86	40	4·76	10"	7·93	40'	Nil.	11·62	10	86·66	10	118	80	38	118	80	38
XX.	F.28 N.A.D. (healthy)	100	82	18	6·00	10"	2·00	60'	Nil.	17.07	40	100·00	20	100	78	22	100	80	20
XXI.	F.22 (healthy)	120	80	40	1·66	5"	10·00	40	Nil.	15·00	20	25·00	10	100	76	24	100	80	20
XXII.	F.29 N.A.D.	108	86	22	7·41	10"	12·96	40	Nil.	18·60	10	109·09	10	100	78	22	100	80	24

CHART A. Case II. Typical curve showing rapid rise of S.P. and fall of D.P.

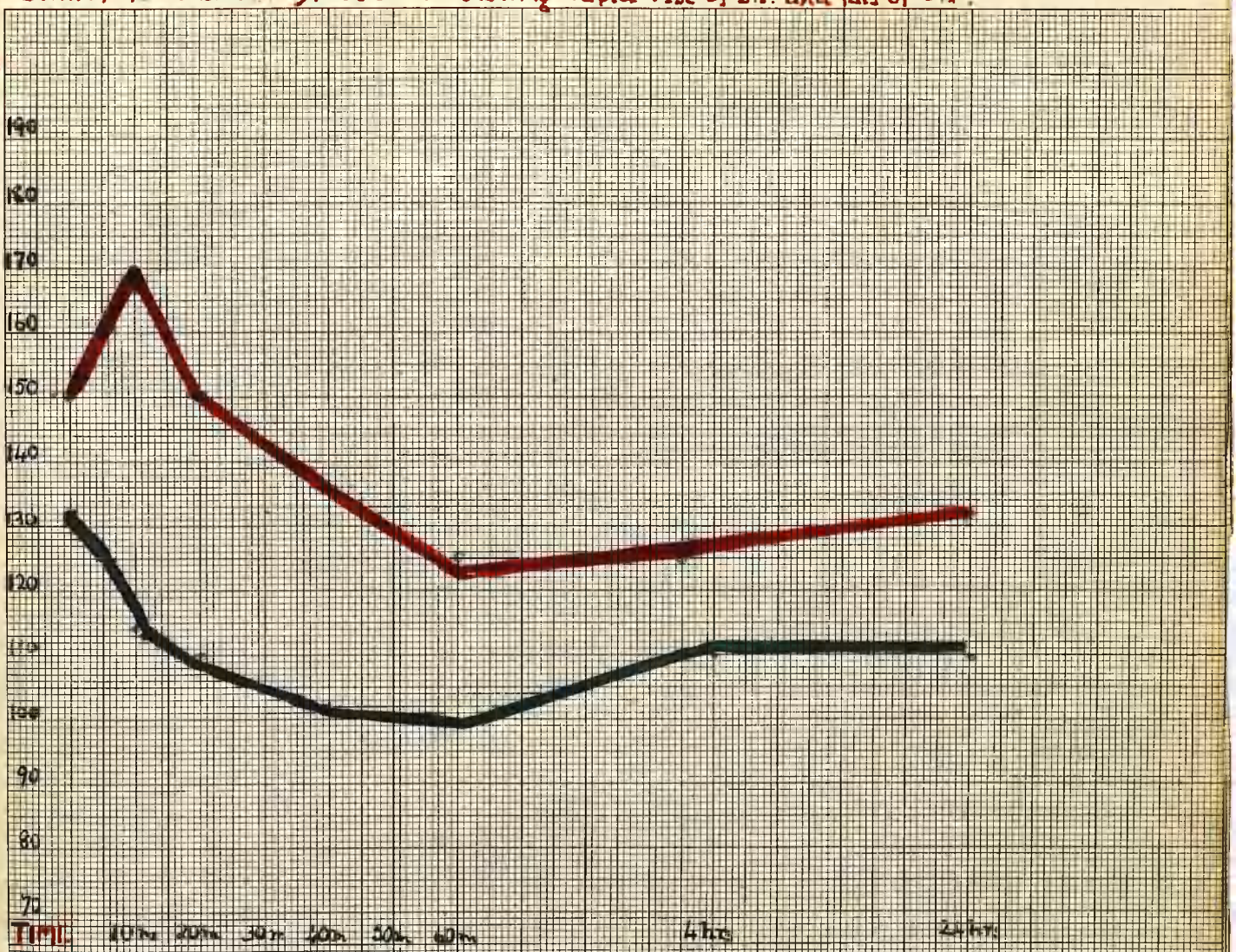


CHART B. Case of hyperplesis showing rapid fall of S.B.

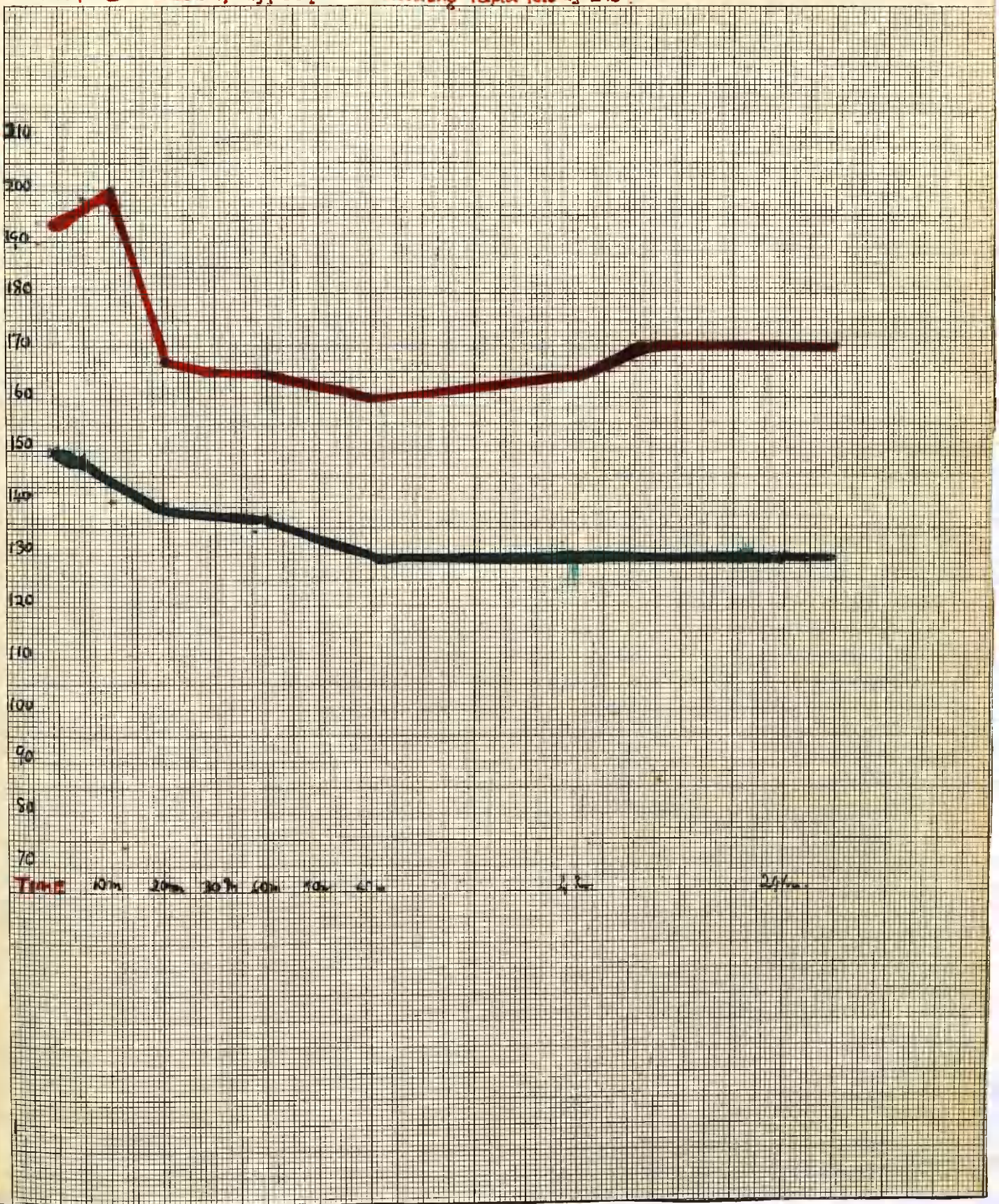
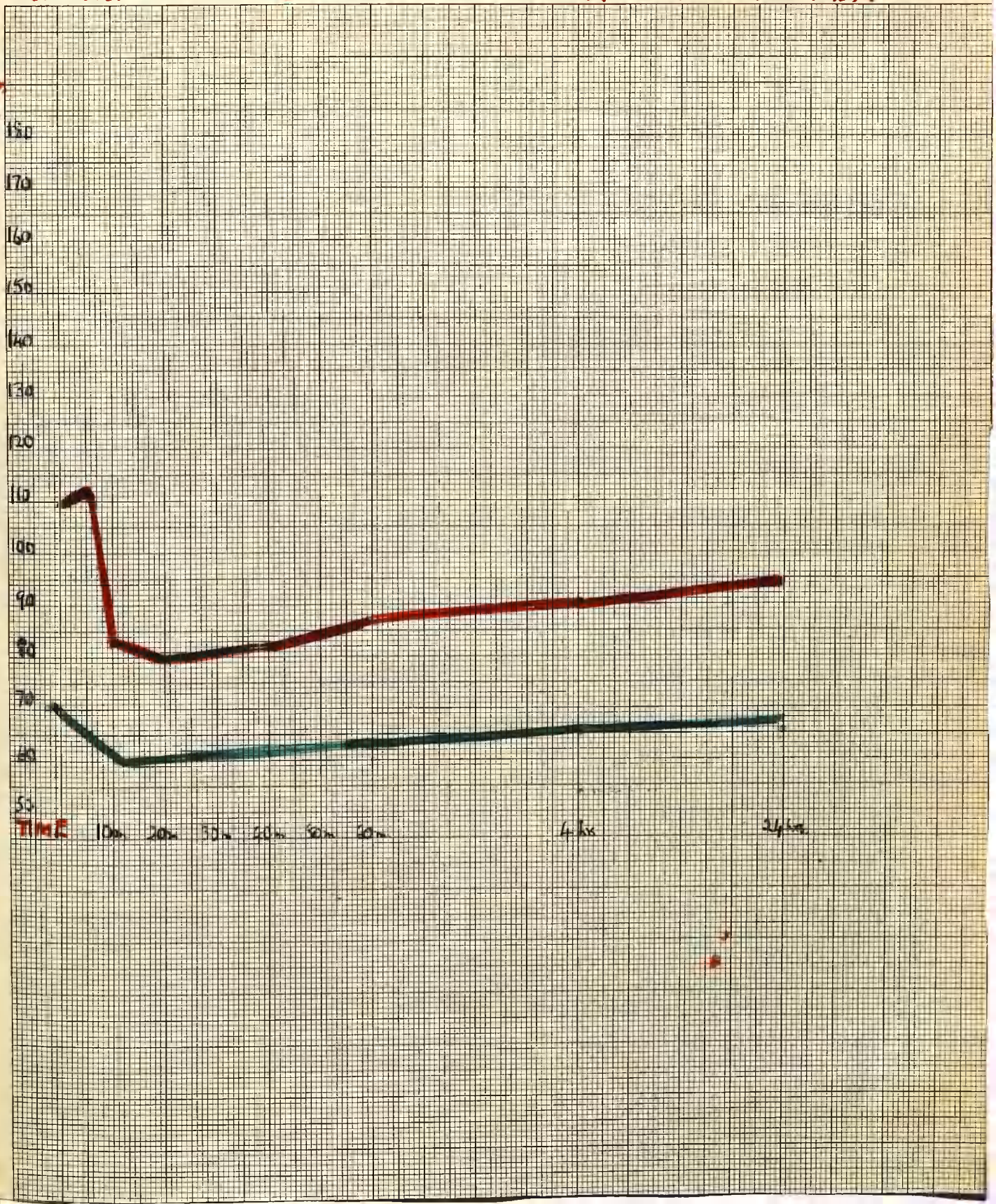


CHART C. Curve of patient exposed to heat. (105° F. Electric Pack).



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