Graves's disease, Raynaud's disease, and some of the allied forms of vasomotor disorder (vasomotor ataxia) / by Solomon Solis Cohen.

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GRAVES'S DISEASE, RAYNAUD'S DISEASE, AND SOME OF THE ALLIED FORMS OF VASOMOTOR DISORDER (VASOMOTOR ATAXIA)*

BY SOLOMON SOLIS COHEN, M.D.

Professor of Clinical Medicine in Jefferson Medical College, etc., Philadelphia, Pa.

GENTLEMEN: I invite your attention to-day to one of the most obscure subjects in clinical medicine, as well as in pathology. The obscurity depends, as in most of our medical problems, upon the fact that physiology has not yet given us the data necessary for its elucidation. We have numerous clinical observations, many pathological studies, and not a few fragmentary physiological investigations bearing upon it; but we still wait for the final coordinating discovery that shall harmonize apparent contradictions and reduce present complexities to a simple and understandable basis. There is reason to believe that it will be found through the study of those somewhat mysterious products of cell chemistry, the internal secretions—perhaps in that special group of substances known as hormones or exciting agents, through which one organ stimulates or restrains the activity of others, detoxicates the blood, or regulates, in some large or limited way, the nutritive and metabolic processes.

You are aware that within recent years much work has been done upon the physiology and pathology of the "ductless glands;" that, in especial, failures and perversions of the function of the thyroid gland have been connected with definite disorders of nutrition—cretinism and myxœdema—and with a certain definite syndrome or symptom-complex known variously as "Graves's disease," "Basedow's disease," or, from its two most striking features, "exophthalmic goitre." You know also that myxœdema and certain milder grades of disorder which exhibit some of the features of that affection, being attributed to failure of thyroid

* A clinical lecture at the Philadelphia Hospital.

secretion, are termed in general "hypothyroidism;" while Graves's disease and certain disorders akin thereto, but not exhibiting its complete picture, are attributed to excessive thyroid activity and termed "hyperthyroidism." This is but a small corner of the vast domain of the pathology of the internal secretions, and indeed but a portion of the field of perverted thyroidism. Yet even this is too large a topic to be handled in a single clinical lecture. I shall show you three cases, two of Graves's disease and another of an allied disorder, and shall point out certain features therein which lead me to doubt the current doctrine of their original and exclusive dependence upon thyroid disturbance. That they are associated with thyroid disturbance and that many of the later symptoms are thus to be explained is indubitable, and in various papers published during the last fifteen years I have given attention to that fact; but to me the principal element in these very various symptom-complexes is the vascular disorder that they manifest; and I am tempted to seek their proximal explanation in a failure of the cardiovascular regulatory mechanism. That the cause and intimate nature of this underlying failure in vasomotor taxis is still to seek must be admitted. That some very close relation exists between the sympathetic, or, to use Gaskell's better term, the visceral, nervous system and the internal secretions, not alone of the thyroid gland, but also of the adrenal gland, the pituitary gland, and very probably the thymus gland and the parathyroid bodies, is evident. But in the present state of knowledge we are not justified in asserting that the thyroid disturbance is the starting point of the disorders under study, and especially we are not justified—and here I come to a highly practical question—in looking to surgery upon the thyroid gland as the only or the best method of treatment. When long-continued thyroid disorder has given rise to pronounced morbid changes in the gland, there may, indeed, be not only justification but urgent necessity for operative interference; either because of mechanical danger from pressure of the goitre upon the windpipe or upon the nerves and vessels, or because the excessive or perverted secretion of the diseased gland is giving rise to dangerous intoxication. This, however, is a late stage of the disorder, and, if I may reason from a moderately large personal experience, is one that ought not to

be allowed to develop. It can, I think, be prevented by the timely use of hygienic and medicinal measures—certainly it can so be prevented in more than the majority of cases. Mark, however, the significant word—*timely*.

I was once asked in a discussion to formulate the indications for surgery in Graves's disease; and ventured to reply that I knew but one—*a belated diagnosis*. Perhaps the statement is too sweeping, but at all events it summarizes my entire personal observation. I have seen no case, in which the disorder was recognized early, which progressed to a point necessitating or even suggesting surgical intervention; while I have seen many cases, far advanced, in which the diagnosis had not until then been made. I would not imply that this is always due to neglect or ignorance upon the part of medical men; on the contrary, the larger number of such patients had failed to consult physicians in time. In some instances, however, I must confess that the medical attendants had failed either to observe, or to realize, the significance of the phenomena distinctive of the disorder. This error is the more readily made in the incomplete cases, in those which lack one or more of the three cardinal symptoms—protrusion of the eyeballs, enlargement of the thyroid gland, acceleration of the cardiac rate. For we may have exophthalmic goitre not only without tachycardia, but without exophthalmos or without goitre, and sometimes without both.

If, therefore, the avoidance of surgery depends, as I have said, upon the timely use of appropriate non-surgical measures—and if this depends in turn upon the avoidance of a belated diagnosis—it follows that our principal concern is with the means of making a timely diagnosis. And just this is the importance of the conception of the disorder that I want to impress upon you; namely, that it is a variety of angioneurosis—a cardiovascular disturbance—an *ataxia* of the vasomotor system. And even if we grant—as I am not yet prepared to do—that this vasomotor instability in itself indicates thyroid intoxication, from excessive activity without hypertrophy of the gland, the lesson is no less important—the lesson, I mean, of the character of the symptoms significant for early diagnosis. For, so long as attention is concentrated upon the thyroid body, the frequent absence of goitre,

or even demonstrable thyroid enlargement, may lead one astray. On the other hand, when once we realize that the clue to a correct diagnosis is to be found in the vascular and neurotic phenomena, and become, in consequence, on the alert for their recognition, it is improbable that many cases will escape detection. Moreover, when we get into the habit of looking for certain signs which I shall point out, we find the cases to be much more common than the text-books might lead one to suppose. These early cases, the ones whose recognition is so important for the future welfare of the patient, are termed "incomplete" or "larval" cases—or, by the French, *formes frustres*. They are in the early stages frequently termed "indigestion," sometimes "nervous indigestion;" frequently "nervousness;" or perhaps "neurasthenia" or "hysteria"; not rarely "neuralgia," "malaria," "rheumatism," "biliousness."

Sometimes, indeed, the visceral symptoms are so pronounced that a not unjustifiable diagnosis of inflammation or degenerative lesion is made—for example, appendicitis, gastric ulcer, nephritis. Cases simulating pretty closely the symptomatology of gall-stone or kidney-stone may occur, and give the physician as well as the patient great anxiety. I have myself counselled exploration or operation in order to remove doubt in one case of simulated hepatic colic and two cases of simulated appendicitis; and I may add that the sections, while negating the diagnosis of inflammation or calculus, at least permanently relieved otherwise intractable symptoms. Sometimes actual organic lesion, of the same kind as the commonly simulated affections, *e. g.*, gastric ulcer, appendicitis, nephritis, may develop in an angioneurotic subject, and such cases are doubly difficult. Displacements of organs (visceral ptoses) are not uncommon, and while these conditions have their own special symptomatology, relieved by appropriate, perhaps even surgical, treatment, they do not constitute the entire case.

With this general preliminary survey, you will now be prepared, I think, to appreciate the importance and significance of the special clinical phenomena exhibited by our patients.

Case I.—Graves's Disease: *Exophthalmos; Tachycardia; Tremor; Dermography, Factitious Urticaria; Tricolored Nails. No Goitre.*

I shall ask a member of the class to take a look at this man [1] and tell me what is noteworthy in his appearance. Recapitulating the answers given we find that his pupils are dilated slightly and unequally, the left pupil more than the right. The irides respond to light but relax again in a moment, though not to the same extent as before; a similar tendency to exhaustion is shown in the response to accommodation. There is no paralysis of the face or of the limbs; but the fingers tremble when the hands are extended. The protruded tongue trembles. There is slight tremor of the eyelids when lightly closed.

Does the next member of the class notice anything more than we have been told in regard to the patient?

You must train yourselves to observe a patient closely. Sometimes a correct, though not complete, diagnosis can be made without asking a question. There are certain quacks who advertise their ability to do this—though whether their diagnoses are correct or not, nobody knows. And you are familiar with Mr. Sherlock Holmes's astonishing disclosures to his clients as to their vocations, their places of abode, their habits, their amusements, their states of married or single blessedness, etc., based upon observation of their faces, their hands, their clothing, their gait, and various tell-tale details of speech, manner, and the like. Now I do not wish my pupils to imitate the quacks—or even to emulate Mr. Sherlock Holmes. As a rule I do not believe in snapshot diagnosis; but I want to impress upon you the fact that in certain cases the physiognomy, or attitude of the patient, or something else which you can see at a glance, gives the clue to the case. Of course one must be careful not to form his opinion upon this sort of evidence only. We must go on in an orderly way and study the case thoroughly; and especially study those points which are against the opinion first suggested. A complete diagnosis involves a complete examination. This careful preliminary inspection, however, is an essential part of the complete examination.

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[1] In lieu of the history and symptomatology of the patient, exhibited to the class through the courtesy of a colleague who will himself report the case, the author has here substituted facts taken from the case notes of a patient observed in private practice; preserving, however, the colloquial form of the lecture as reported stenographically.

Now can you tell me something from glancing at the patient? Yes, the eyes are staring; that is to say, the palpebral fissure is widened and the eyeball protrudes slightly. Exophthalmos, not great, but distinct, is present.

Now I will ask the patient to hold his head steady and follow this pencil with his eyes as I move it up and down in front of him. What do you notice? As the patient looks down, the distance between the cornea and the upper lid increases; that is to say, the descent of the lid is not instantaneous, but it lags for an instant behind the descent of the eyeball. This is known as Von Graefe's sign. You will sometimes find it when there is no apparent exophthalmos.

I ask the patient to keep looking at my pencil and, holding it centrally, approach it towards his nose to test the convergence of his eyes. You observe that the eyes converge very well until the pencil almost touches the face, and then the power of convergence seems to give way suddenly and the eyeball, as shown by the position of the pupil, shoots towards the outer canthus—there is lack of power of convergence, sometimes called "Moebius's sign." As we continue to watch this man's eyes we notice that winking is infrequent. He winks once or twice and then stops for an appreciable time. That is known as Stellwag's sign. Stellwag's name is also attached to the permanent retraction of the upper lid which is sometimes observed. This retraction may be unilateral and such cases are not so uncommon as was at one time supposed.

We have already noticed the tremor of the hands, but we will now look at it a little more particularly. There are two motions, a coarse tremor and a fine tremor; the coarse tremor increases with attention and fatigue. The finer motion of the fingers can be seen only by those of us who are quite close to the patient. As it increases with time and concentration of attention we note that he winks more frequently; or if we tell him to close his eyelids lightly they become more distinctly tremulous. That tremulousness of the eyelids, which disappears if the eyes are tightly shut, is often an early sign, appearing long before exophthalmos or goitre can be detected. I shall ask the patient to wrinkle his forehead, wrinkle it upward. This he seems to be able to do. Sometimes the wrinkling of the forehead is very difficult or even

impossible. I have seen the sign of Moebius, which this patient exhibits, occur unilaterally.

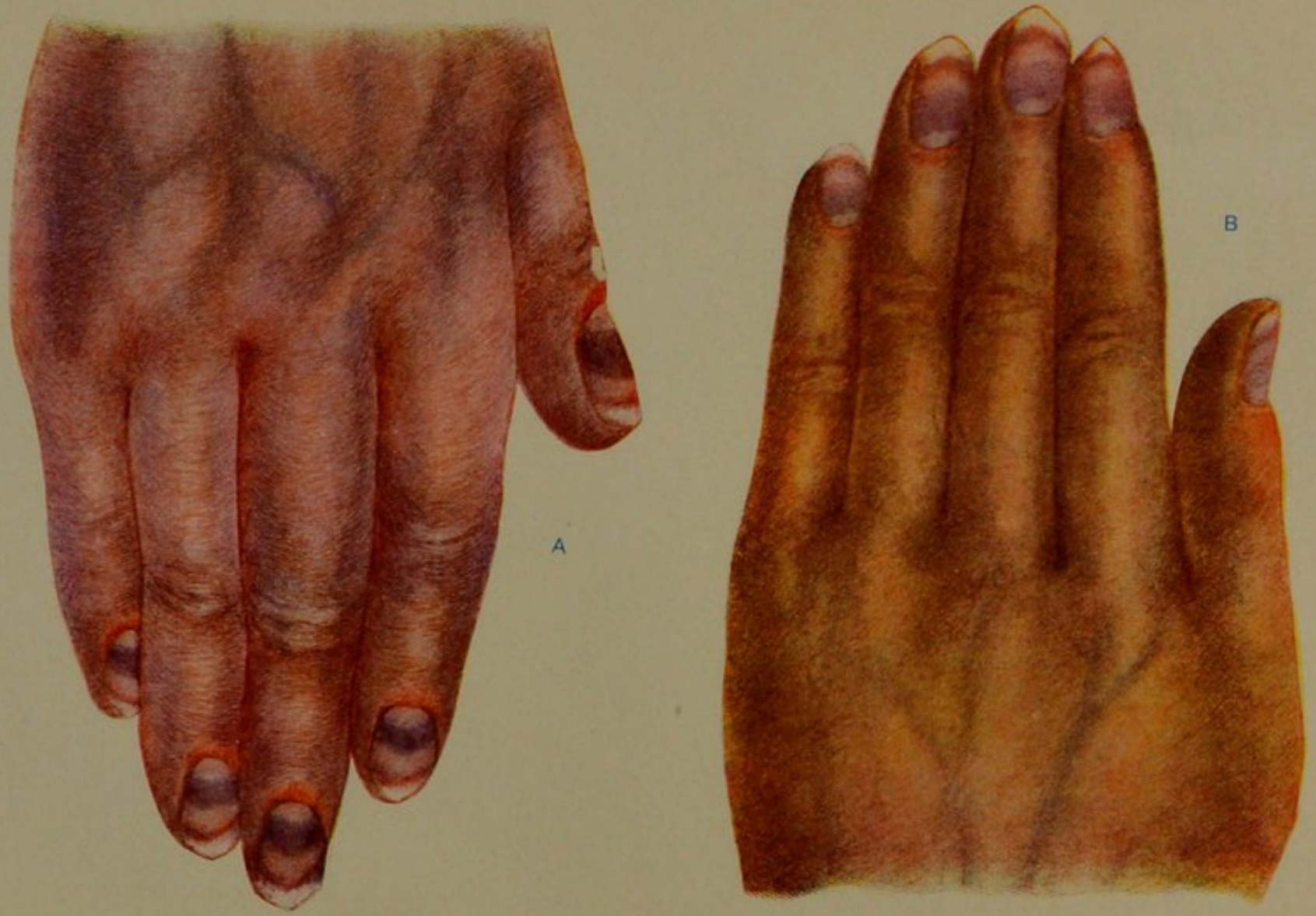
I now am going to try to develop another sign, to which I think I was the first to call attention, in so far as it relates to Graves's disease. It occurs in other conditions and has therefore only a confirmatory value. First, you observe that as the man's chest is exposed to the somewhat cool air there develops gooseflesh and that this passes off and recurs. If I touch him anywhere you can see that the gooseflesh increases, and especially if I draw my hand down along his spine you see that after an interval of some seconds a wave of gooseflesh, as it were, begins along the shoulders and travels down the chest. This is the so-called pilomotor reflex and in this particular patient it is very well developed. Now I am writing with a silver probe upon his skin; I use the slightest possible pressure. You see after a slight interval that the letters which I have traced upon the chest appear, first in white, and afterward in red lines. This phenomenon we term "dermographism"—skin writing. The details of its phenomena differ in different cases. The lines may be white only or red only or both red and white, as here. The red lines then become bordered on each side by broad white lines. Running the finger over these red markings we find that they are becoming somewhat elevated above the skin, and at the same time paler in color. In some cases the elevations are much more marked than these. They are veritable wheals, artificial hives, technically called "factitious urticaria." Sometimes the gooseflesh reflex is exhibited along the tracings of the probe, and only there. As this writing has faded out slightly I will apply over it a towel wrung out of hot water. It becomes brighter and more distinct. In some cases cold water will bring it out even better. The reactions to hot and cold water differ in different cases. In some cases both will make the dermography more distinct; in some cases one will diminish, the other increase it. In still other cases one or the other will cause a diffuse red flush in which the distinct outlines of the tracing are lost. These variations have certain minor diagnostic significance, but I cannot enter upon this to-day. I shall ask the class, however, to point out the general significance of the phenomenon. I am answered: "A vasomotor disturbance." That is correct. It shows

that transient paresis or stimulation of the peripheral capillary vessels is very easily brought about. Excessive pressure, as from the knout of Russian tyranny or the whip of a Delaware sheriff, produces red streaks and wheals upon a normal back. This redness indicates an excessive distention of the capillary vessels. Slight pressure produces a temporary dilatation, active or passive as may be, of the terminal vessels of the skin, and therefore redness follows the line of pressure.

This ready yielding of the peripheral vessels to slight pressure indicates a condition of low vasomotor tonus. This is the basic factor underlying this man's disorder. It is not a disease but a constitutional, frequently congenital, defect. Dermographism may be found in individuals who are in all other respects normal and who may not develop Graves's disease or other special syndromes of vasomotor origin during the whole of their lives; yet it is in itself a slight departure from normality. It cannot be obtained in every person, but only in a certain number—I have not attempted to keep statistics but should say approximately about 1 in 10. It is more common in some races of men than others, being notably frequent, as is the whole train of vasomotor symptoms, among Russian Jews—a circumstance probably to be attributed to the environment of anxiety and uncertainty in which they and their ancestors have so long lived. It is also more common among artists —musicians, actors, painters, sculptors, poets, orators —and others of mobile temperament. It is not the occupation which causes it, but the temperament which it signifies that leads to the choice of occupation. It is one of a number of signs of this temperament or this constitution, or this condition of vasomotor lability; which in itself, let me repeat, is not a disorder but which offers a basis upon which disorder or organic affection may develop. I shall return to this phase of our subject later. Let us look again at our patient.

Notice that his face is flushed, that his ears are red. The room is not unduly warm and none of us here in the ring with the patient are flushed. This apparently causeless blushing is frequently a marked symptom of vasomotor ataxia. Sometimes it is unilateral, though it may occur upon either side. Sometimes it is quite localized. It may be transient and then either fleeting

PLATE I.



A, hand showing paroxysmal acro-asphyxia with black band on nails; *B*, hand elevated showing change of color with gravitational emptying of congested vessels.

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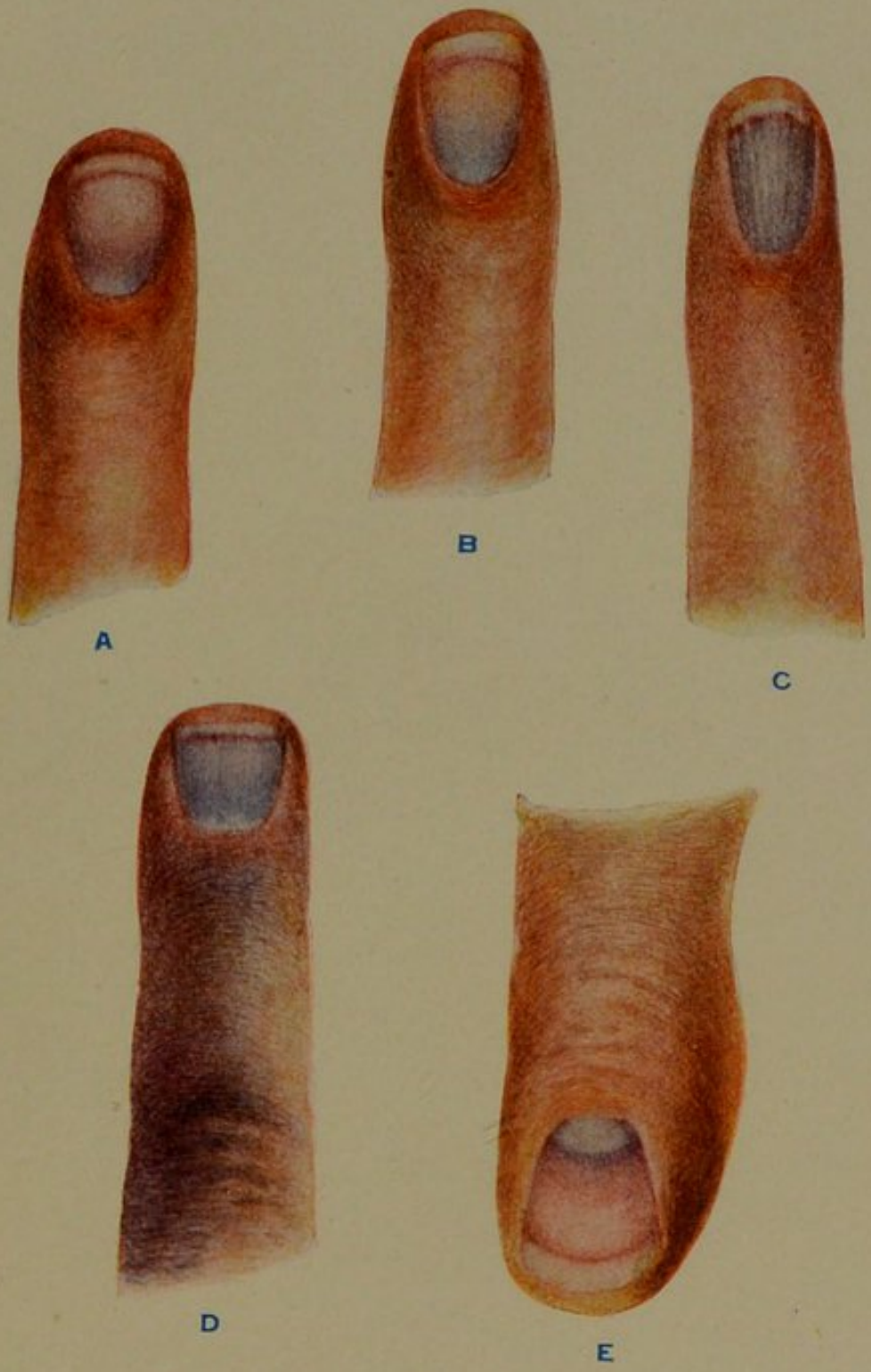
PLATE II.



Different types of color changes in fingers and nails in vasomotor ataxia. *A*, *B*, *C*, curved nails, thickened red skin; *A*, three color zones; *B*, two color zones; *C*, ridged blue nail; *D*, flat blue nail, purple finger; *E*, typical "red, white, and blue" nail. All show the terminal red line.

or quite persistent, of rare or of very frequent recurrence, or it may be permanent. In one of my patients the permanent blush, or erythema, as it might be called, was limited to an oval patch about two inches long just above the angle of the left jaw. Sometimes only the ears, or one ear "burns." Like all the other signs it differs much in degree and extent not only in different patients, but in the same patient at different times; and like all the other signs it differs from the normal, not in its character, but in its occurrence; that is to say, it results from causes which are not of the kind or degree to produce the same effect in normal persons.

What other symptom should we look for? Tachycardia, that is correct. The pulse rate I see from the chart varies. It has been as high as 108. It is now, under rest and medication, below 95; varying from 85 to 92. When the patient remains quiet he is not conscious of palpation, but under excitement or exertion he feels a thumping in the chest with a sense of smothering. Percussion and auscultation show no heart lesion. The first sound is somewhat lacking in muscular tone. The pulse is full, equable, of low tension; systolic pressure is 100; diastolic pressure 80.

What else should we look for? An enlarged thyroid gland. How shall we look for an enlarged thyroid gland? "By inspection." Looking at the neck in front and from the sides we fail to observe any abnormal fulness. Sometimes fulness which is not manifest in one position becomes evident in another. We allow the patient to sit erect; to lie down with the head unsupported by pillowing; and we prop the head and neck at various angles. Still there is nothing to be seen indicating enlargement of the thyroid gland. There is no evident goitre. What next? "Palpation." Upon ordinary palpation we do not find any enlargement of the thyroid gland. I will now straddle the trachea with two fingers and tell the patient to swallow. As he swallows I feel the isthmus of the thyroid gland move up and down between my fingers and I should say that it is very slightly, if at all, enlarged. I have frequently found that amount of enlargement without any symptoms of thyroid intoxication. There is little, if any, goitre and only slight and occasional acceleration of the heart, but there is slight exophthalmos and with it those other phenomena to which I have called attention.

Now let us look at his hands once more. What do you observe? They are congested, cyanotic. We notice around the borders of the nails (Plate I, *A*, see frontispiece) that the skin is of a brick-red color; the nails are purplish or blue at the base; then in the middle we notice a pinkish-white area, and towards the end of the nail a rather sharp and narrow curved line, convex toward the tip, of somewhat brighter red. So we have red, white, and blue—tricolored nails. This also is a sign to which I called attention many years ago. I think you can see it from the benches as the man passes around the ring. The narrow bright red line near the tip of the nail, then a broad pinkish—by contrast almost whitish—area, and then the deep purple (or blue, as it sometimes is) at the very root of the nail. These colors differ somewhat in tint or extent in different patients (Plate II), in the same patient at different times, sometimes in different nails on the same hand. The distal line may be somewhat broader and deeper in tint than this, but it is always red—it is a loop, of course, of distended vessels in the nailbed, and becomes evident where the pressure of the nail is removed. The middle area may be yellowish, pinkish, or whitish; the proximal area deep red, purple of various shades, blue, or, as in one case I shall show you, almost black. Sometimes the whitish area is wanting and the colors are blue and red; sometimes the blue is wanting. Sometimes the nail is very flat and of deep or light leaden color. Like dermography, the tricolored nail, in some of its minor degrees—or more frequently a light pink nail with the distal bright red line—is not so uncommon as I at first thought. But in its full and sharp development it indicates vasomotor ataxia. As I hold up one hand and arm of this patient, you see that the color slowly runs out, leaving what we usually term a white—that is, a normally colored—hand (Plate I, *B*). I will make slight compression upon the vessels of the wrist with a bandage, and then put this hand down beside the other. You notice the great contrast in color. Now as I loosen the bandage and allow the blood to return to the hand, it first becomes pink, then mottled, now purple, and finally it will become as cyanotic as the other. These illustrations (Plates I and II) show a change similar to those in the hand of a patient whom I will show you later, the one with "black" nails. What does that indicate as regards the blood-vessels? The

blood, when allowed to return, comes first to the arteries and capillaries and gives the pink color because the terminal capillaries are dilated; then the mottling and the purple follow, as the blood runs into the dilated terminal veins; and finally the deep blue, as the venous congestion increases and masks the capillary congestion. So we notice that we have dilatation of both systems of peripheral vessels. Observe that when I stroke the hand the discoloration disappears; when I cease stroking the colors return in the same order as before. Notice also that if I press with my thumb on the back of his hand the whitish impression persists for quite a while. That is one way to make out slight degrees of passive congestion. You see that if I press upon his face the finger marks remain. When I press my hand upon his chest it is as if white paint were upon my fingers and the impression persists for many seconds. And so I might go on in many ways to emphasize the peripheral dilatation, but I wish to call your attention to certain other phenomena for which other patients must be exhibited. Although this man has no goitre, and although exophthalmos is slight and tachycardia is not prominent, the case is unquestionably one of Graves's disease, and I have shown you the prominence of tremor and of vascular paresis in its symptomatology. In connection with this tremor, the theory of parathyroid deficiency as a causal factor is quite attractive; and in one of my patients treatment with parathyroid substance did cause the tremor to subside. So also treatment with calcium salts is sometimes useful, symptomatically; but as yet we do not know enough to draw any definite conclusion from such facts.

The next case is one who was in my service at Jefferson Hospital, and whom I exhibited to the class last year.

Case II.—Graves's Disease: *Persistent Headache the Chief Symptom.*—Mrs. W., aged about 45 years, was referred from the ophthalmic clinic of my friend and colleague Prof. Howard F. Hansell. She has suffered much of many oculists chiefly in the way of prisms and muscle-operations. For "as long as she can remember," she has had recurrent headaches; not strictly migrainous in type, as there is no nausea or vomiting; nor have the attacks shown any distinct relation to the menstrual period. The pain may be unilateral or bilateral, frontal or occipital, but is always accompanied by sharp stabbing pain referred to the eyeball. Dr.

Hansell found only dilatation of the vessels, and a refractive error, which he has corrected; and he did not believe the pain to be of ocular origin. We found the heart to be irregular, at times tumultuous, in its action. The systolic pulse tension was low, 100 to 110 millimetres of mercury; the diastolic pressure about 80 millimetres. The sphygmographic tracing was very irregular, showing a lack of sustained pressure either in the heart or vessels. The first sound lacked muscular tone, the second sound was weak and irregular, the pulmonic sound being sharper than the aortic; but we could detect no murmur. Precordial dulness was increased to the right. The apex beat was not visible and scarcely palpable. The patient has a slight enlargement of the thyroid gland, and exhibits dermographism and tricolored nails. The eyes, on fixation and elevation of the eyebrows, show a distinct rim of sclera above the cornea. The patient was put at rest and cactus administered in increasing doses, in the form of a solid extract termed by the manufacturer "cactin." The tracings which I exhibit show a gradual betterment of the heart's action, slight under rest, marked under drug influence, and now maintained for a month under activity. The pressure is now 125 systolic, 90 diastolic. The patient tells us that her pain has disappeared, and the date of her improvement coincides with the date of the marked change in the sphygmogram.

Now here is a case in which antipyrine, phenacetin, etc., which the patient has received from time to time for years, gave only temporary relief, and at last failed utterly. Indeed I am of the opinion that they made her worse. Treatment directed to the improvement of vasomotor tone—for that is the effect of cactus—has been of distinct benefit. Ergot or barium chloride might have been equally useful. I did not use digitalis or strophanthus, which would also have been useful, lest the result I hoped to reach might be attributed to the relief of congestion dependent upon cardiac dilatation. I do not find that cactus alone is an efficient remedy for the cardiac arrhythmia dependent upon muscular asthenia or dilatation from any other cause.

I have already said that I am unable to accept the view that hyperthyroidism is the fundamental difficulty in Graves's syndrome. Hyperthyroidism is a complication which in some cases ensues after the thyroid has become affected and hyperactive as the result of the original disorder or toxæmia, whatever that may be. You

have just seen a case in which there is but slight tachycardia and inconsiderable thyroid enlargement, yet the exophthalmos is there, the tremor is there, and the general relaxation of vessels is present. What seems to be the fundamental condition? Evidently the vasomotor failure. As to causation of this I am not now putting forth any theory. To the condition I have given the name of vasomotor ataxia, and it manifests itself in various ways. It appears sometimes in a syndrome the very opposite of that which we have just had before us in different degrees. In those cases abnormal relaxation was evident. Its opposite is contraction. We see this highly marked in a fully developed case of Raynaud's disease, in which there occur, usually on the hands, sometimes on the feet, often in the nose or ears, occasionally over the whole body, paroxysmal blanchings or discolorations. As a rule, but not invariably, this "local syncope" or "local asphyxia" is symmetrical. In severe instances gangrene follows, hence the name "symmetrical gangrene," sometimes applied. The fingers may first tingle, then become numb and white, and the name "dead finger" has thus been given to one of the numerous manifestations of Raynaud's syndrome. "Paroxysmal hæmoglobinuria" is another of its names, from the appearance in certain cases of large quantities of hæmoglobin with few or shadowy blood-cells in the urine. Now I am not systematizing or exhausting the symptomatology of this vasomotor spasm—merely illustrating its protean character. Exposure to cold is not infrequently the immediate determining cause of a paroxysm. It is not the cold, but the susceptibility to such extreme reaction from moderate chilling, that interests us. The phenomena of Graves's disease resemble in a measure the normal reactions to excessive heat; Raynaud's phenomena resemble the normal reactions to excessive cold; and both Graves's disease and Raynaud's disease exhibit some of the phenomena of severe fright. But the question is, why do some individuals show these symptoms under inadequate provocation? I have seen many cases, and published a few, in which symptoms of Raynaud's disease and of Graves's disease coexisted. In this connection the patient I now show is extremely instructive.

Case III.—*Pseudo Angina; Paroxysmal Tachycardia; (Larval) Graves's Phenomena; Acro-asphyxia; Acroparæsthesia.*—Mr. L. A., aged 26 years, a travelling salesman, is a private patient

and has been under my observation since he was five years of age. Of the diseases of childhood he has had measles, whooping-cough, and mumps. His father died of pulmonary tuberculosis after an illness lasting fifteen years, to which attention was first directed by pulmonary hemorrhage, and from which I believe recovery would have taken place had the patient been able to carry out more fully the advice given him concerning open-air work and a general hygienic life. His mother, who is living and well, is one of a highly neurotic family. He has one sister, who is healthy but who had, as a child, a rather marked case of chorea. Among his collateral relatives there have been many cases of hysteria and of chorea, and at least two of prolonged diabetes mellitus. At the age of fourteen this patient showed signs of tuberculous infiltration at the left apex. He was sent to the Adirondacks, where he remained for two years, returning home apparently perfectly well, and since then has given no sign of active pulmonary tuberculosis. He is six feet high and weighs 160 pounds. He has an expansion of four inches. At the age of eighteen he contracted specific urethritis from which he apparently recovered completely. After this he was well until about two years ago, when he began to have occasional "faint spells," which appear from the description to have been transient attacks of subjective vertigo. He was at that time living in a distant city and I cannot speak from personal observation. The present series of attacks began about six months ago.

He tells us that he has "a pain in the heart," at times very severe, which comes on suddenly and passes away quickly. When I ask him to indicate the locality he places his hand in the third interspace to the left of the sternum, at about the parasternal line. There is no tenderness upon pressure at this point. The attacks of precordial pain, we find upon further questioning, may occur several times in a day, or may occur only once or twice in a month. There is no regularity. They are much more apt to come on after excitement of any kind, pleasurable or the opposite; fright especially is likely to cause them. They are sometimes followed by a sense of faintness, but never by actual syncope; there may be dizziness, though this is not common. There is no radiation of pain, no sense of constriction in the throat or elsewhere, no dyspnœa. The pain is sharp, stabbing, and not accompanied by a sen-

sation of crushing. Sometimes the attack is followed immediately, or after an interval varying from a few minutes to half an hour, by violent palpitation of the heart, which may be so great that the patient has to stop, if he is walking, and sit down somewhere until the paroxysm subsides. At other times there may be a paroxysm of cardiac palpitation without the precordial pain. We cannot get any clear account of circumstances precipitating the attacks either of pain or of palpitation, beyond their coincidence with emotional excitement, as already stated. They may occur in the absence of such emotion; they occur when hurrying and when resting; after a meal and when the stomach is empty; and apparently independently of the occasional attacks of indigestion of which he complains. He cannot give us any idea of the duration of the attack of palpitation, or, as I shall now call it—for such it evidently is—the attack of paroxysmal tachycardia. As to the rapidity of the pulse-rate, its volume, and its pressure during the attacks, I have no information, as I have never been fortunate enough to see him in one. The pulse characteristics may be very different at different interviews. My notes show nothing of this variability in his previous history.

Sometimes I find the pressure elevated perhaps to 145 or 150 millimetres of mercury systolic pressure, with 100 or 120 millimetres of mercury diastolic pressure; at other times the systolic pressure is as low as 110 and the diastolic pressure perhaps 70 or 80. Usually the volume of the pulse is full and the artery is easily compressible, yet there is a suspicious hardness of the vessel at times, even at periods of low pressure. As a rule the pulse is regular, but the rate may be, on different occasions, anywhere from 60 to 90 beats to the minute. The area of precordial dulness is not usually enlarged; but may perhaps be a trifle greater to the right—I speak with caution—sometimes, during a period of low pressure and rapid rate. The apex beat is normally situated and at present is somewhat increased in force, while there is a faint, soft, blowing systolic murmur just above the apex, not transmitted. This is not constant. To-day, the first sound is lacking in muscular tone; the pulmonic second sound is about normal in character; the aortic second sound is heightened. These findings correspond with a pulse-rate of 72 and a systolic blood-pressure of 140, the artery being full and somewhat hard.

In December of last year (1908) the patient noticed for the first time that when he became cold his nails turned blue. I have a memorandum that at that time he stated that otherwise his hands would sweat; that the nails, when I saw them, were pinkish with a red line at the tip; and that the half moon was clearly to be seen, though a little dusky. The eyes showed a rim of sclera above the cornea on voluntary wide opening when the balls were fixed by looking at a stationary object. There was no lagging of the lids and no tremor; no tremor of the hands was seen, no lesion of the heart detected. While the blueness of the nails occurred upon exposure to cold, the patient stated that he felt "generally bad" in a hot or close room. A month later, January 4, 1909, he reported that the hands became cold and the nails black for ten or fifteen minutes every morning as soon as he got out of doors or upon washing in cold water. He was therefore using hot water for his ablutions. The discoloration passed away gradually. He had noticed it to be greatest upon the left side and most marked in the little finger and second finger upon both sides. Occasional tingling and numbness was felt in both hands, chiefly in the ulnar distribution. The paræsthesia was independent of the local asphyxia, of temperature, or of emotion, and could not be attributed to pressure at the "crazy bone," although usually most marked in the morning and relieved by motion and friction. The color phenomena had disappeared when I saw him, and he was requested to come in sometime when they should be present, which he accordingly did on January 25, 1909. The illustrations show the condition of the nails at that time. The hands were mottled, the color slowly running out upon elevation; the nails were dark, with three distinct areas of different color—dusky blue, almost slate-color at the root, deep red just below the tip, and in the middle dusky pink. Immersion in cold water intensified the lividity, while immersion in hot water caused the hands and nails to become bright pink, which color could be temporarily stroked out or pressed out, and slowly disappeared as the heat passed away. Under treatment this condition has slightly improved, but the patient tells me to-day (April 13), that yesterday, being disturbed by bad news—the sudden death of a business associate—he had a chill and the nails became intensely black for a few minutes. This has passed away, although we can now note three areas, deep red at the tip,

purple at the base, with a lighter area between; but by no means so marked as in the illustration. The hands are warm and of normal color, but upon asking him to open the eyes widely we note a considerable margin of sclera both above and below the cornea; in other words, we have the picture of an apparent exophthalmos; apparent only, however, because with the cessation of the voluntary effort of opening, the eyes resume a normal appearance in this respect. We note, however, that the pupils are much and equally dilated. There is prompt response to light but with quick exhaustion; a similar promptness and quick exhaustion marks the response to accommodation. After wide opening, if we make the Von Graefe test we find that the upper lids do not lag as the eyeballs descend; but there is a sign to which I have frequently called attention, a sticking, hitching, or interrupted descent of the lids. When lightly closed, the lids show a fine tremor. There is a fine tremor of the hands upon extension. The thyroid gland is not enlarged, though it is easily palpable. Dermographism in this patient exhibits a peculiar modification. Thus a probe drawn across the cheek leaves behind it a deep crimson streak. This fades away and is followed by a wider white streak. In other words pressure has caused dilatation, followed by quick contraction of the vessels. I may add that examination of the eye-ground by Dr. Hansell shows distinct dilatation and engorgement of both veins and arteries.

Here, then, we have a patient who exhibits, in larval form, unmistakable phenomena of Graves's disease; who has definite acro-asphyxia, acroparæsthesia; with attacks of pseudo-angina and of paroxysmal tachycardia. Is it the more scientific to make four separate diagnoses in his case—each merely a syndrome name—or to include all the phenomena under one comprehensive term, suggestive at least of a definite pathologic physiology, vasomotor ataxia? And observe, also, that in this patient we have the signs of Graves's disease without the goitre and without evident or persistent hyperthyroidism. That in future we may have goitre and hyperthyroidism or persistent tachycardia is possible, though of course we shall do our best to prevent the full development of the syndrome. On the other hand it is possible that the Raynaud syndrome may become more pronounced; and, should this be the case, it is quite possible that

arteriosclerosis and even evidences of neuritis, especially in the ulnar nerve, might be discovered years hence, at autopsy. But none of these developments of either extreme, Graves's or Raynaud's, would alter the fact that in the beginning the disorder depended upon a congenital instability of the vasomotor system, and that the particular phenomena developed are to be attributed to accidents of environment or of toxæmia.

You have heard that this man's father had pulmonary tuberculosis and that he himself has recovered from the same affection.

Dilatation of the pupils and low pulse-tension are not uncommon in tuberculosis. I believe them to be important signs of the "susceptibility" to this form of infection. Others may regard them as evidences of existing infection and toxæmia. This opens for discussion a wide field which we have not time to enter now; but whenever you observe these signs make a careful study for possible tuberculosis.

Other disorders frequently associated with signs of imperfect vascular co-ordination are the metabolic perversions, especially gout and diabetes; not rarely arthritism—rheumatism or arthritis deformans. Additional manifestations of vasomotor ataxia are migraine, urticaria, asthma, and hay fever. Hemorrhages are not rare; epistaxis, hæmoptysis, hæmatemesis, melæna, purpura, hæmaturia. Often the blood is occult. Some patients show a curious "marbling" or mottling of the skin in general, though rarely of the face. It may be permanent, or developed on exposure to air, sometimes only appearing in cold weather. In one of my cases the appearance was of red, white, and blue geometrical designs, almost like a "tattooed" man. In most instances some permanent vascular abnormities of the skin can be detected on careful search, frequently on very casual observation. These may occupy the face, the trunk, or the extremities. They vary from minute red or blue spots, scarcely more than petechiæ, to large or small angiomata or telangiectases. Their occurrence indicates the constitutional vascular peculiarity upon which the very various symptomatology of this interesting group of disorders is builded.

I have by no means exhausted the subject, merely introduced it. I should like to talk to you of treatment, but our hour is up and I can only be brief and general. You have gathered at least that I do not favor surgery in exophthalmic goitre except as

a last resort. In the various conditions of vasomotor disorder, the internal secretions as represented by thyroid, parathyroid, thymus, adrenal, and ovarian preparations—aided by some such drugs as the calcium salts, the barium salts, picrotoxin, ergot, digitalis, strophanthus, cactus, aconite, veratrum, the nitrites, hyoscine, atropine, asafœtida, musk, sumbul, valerian, camphor, and strontium bromide—are to be used, choice being made among these various agents according to the particular group of symptoms that is to be dealt with. Sodium sulphocyanide is sometimes useful—a suggestion I owe to Paulli's studies of ionic pharmacology; and I have lately used with apparent good result in cases marked by a tendency to hypertension, a preparation modeled upon thiosinamin, but with the addition of bismuth to render it more acceptable to the stomach, which Dr. Frederic S. Mason, who has prepared it for me, characterizes as allyl-sulph-carbamide-bismuth-diiodide. Diet is to be carefully regulated; and, as it is quite possible that absorption of toxins from the intestine may precipitate the crises or maintain the established disorder, digestive ferments, lavage, purgatives, intestinal antiseptics, find place. In some cases rest, in others regulated exercise, is indicated. Perhaps the most important of all measures in mild and early cases is the education of the vascular responses by mild thermic stimulation—some appropriate form of "water-treatment"—as the alternating hot and cold douche, or simple sponging with hot water followed by a brisk rub with cold water. The details must be carefully prescribed and modified according to the conditions and the result in the individual case. But I cannot elaborate further. I have chiefly wished to impress upon you the importance of systematic interrogation of the vasomotor system as well as of the other organs and systems before formulating a diagnosis in any case.

The examination of the chest or the eyes or the urine does not imply that the individual patient has thoracic, ophthalmic, or renal abnormity; yet such examinations are always necessary, if only for exclusion. So with the vasomotor system, now neglected unless it obtrudes itself. Its disorders, when systematically sought for, will prove to be more common than is supposed, and their development into distressing and often fatal disorders will be prevented by timely discovery and appropriate treatment.