

we have a reflection of the recent tendency to regard the symptoms as being due to perversion of the secretion of the gland, the changes in which therefore come to have a primary significance. It is plain that the symptoms are also explicable as being athyroidal, and I venture to suggest that where there is extensive perversion of secretion, that so in proportion there must be a certain degree of athyroidism. Take a single symptom such as the characteristic dyspnoea; that again is exactly the most prominent symptom of the acute athyroidal cachexia in all kinds of animals. Coupled with the dyspnoea is not infrequently a rise in temperature, and in cases where death has rapidly supervened after removal of one portion of an exophthalmic goitre, the temperature may rise to 105° or higher, and the patient die with marked dyspnoea, although of course there is no mechanical interference with the air passages.

I have quite recently had the misfortune, at University College Hospital, of seeing the same condition occur in a patient who was the subject of a very large parenchymatous goitre affecting the whole gland. The dyspnoea was considered to be due to the flattening of the trachea from the pressure of so large a tumour, and though the flattening was found at the operation, I regret to say it did not occur to me that the severity of the dyspnoea might have been in part due to the patient having been in a certain stage of athyroidal cachexia which had been brought about by the involvement of the whole organ in the disease change. Removal of the tumour, although in this case particularly easily accomplished, did not terminate the dyspnoea to which the patient succumbed. At the necropsy the two-thirds of the left lateral lobe left behind for carrying on the function of the gland were found to be extensively goitrous. In future I shall treat such patients with thyroid prior to undertaking the operation.

We may now return to the secretory epithelium, and the colloidal and other products of its secretory activity. Very interesting and valuable observations on this point have been made by Anderson and others who, following on the line initiated by von Wyss, have administered pilocarpin with the effect of obtaining heightened secretory activity on the part of the epithelium.

As regards the changes in the epithelium a great deal has been said by many observers as to the vacuolation of the epithelium and the appearances of vacuolation in the colloidal substance. In the most recent work on this subject—that by Anderson—these vacuoles containing secretion are supposed by him to move out from the epithelial cells and to migrate into the centre of the acinus. It seems unnecessary to do more than remark on this point that the secretion is supposed by many to collect as watery droplets, which naturally appear as vacuoles in the substance of the gland, and of course such secretion is simply extruded from the secreting cell, therefore the view of Anderson is so far coincident with prevailing views. In speaking of the question of the vacuolation of cells, especially in relation to the thyroid gland, I wish to draw attention to the vacuolation, not of the mere protoplasm of the fat cells in myxœdema (Microphotograph 11), which is in itself a common—in fact regular—state of things, but to the vacuolation of the nuclei of the fat cells, and which I believed to be a fairly constant phenomenon in myxœdema. I first observed it in 1885, but could not find any reference in the literature of that time to the matter, and subsequently Professor Boyce and Mr. Beadles independently observed the fact in a case of myxœdema published by them in 1894. Such vacuolation is well shown in these photographs of myxœdematous subcutaneous fat. Since then the question of the vacuolation of the nuclei of fat cells in general has been very thoroughly investigated by Sack, who goes much further and finds that vacuolation of the nuclei of fat cells occurs not only in diseased tissues, namely, lipomata, but also in normal developing fat and in fat undergoing senile degeneration. It is obvious, therefore, that vacuolation of the nuclei of the fat cells, although a very interesting biological condition, is not peculiar to myxœdema, and consequently cannot be regarded as pathognomonic of that disease change.

This photograph from Sack's monograph shows vacuolation of the nuclei not only of the subcutaneous fat in man, but also of the fat cells in marrow, and finally also in large nuclei of the salamander. The so-called vacuoles in the colloid sub-

stance I have referred to, and must now illustrate more fully, are of far less biological interest and significance. As these photographs show, they can be observed in all possible conditions of the epithelium, provided that the latter is capable of forming a colloidal secretion at all. Starting with a pilocarpin result by Anderson, we see actually in vacuolated spaces in the deeply stained colloid material shed epithelial cells containing droplets and granules of colloidal secretion. In this section of an adenoma removed by opening a large vacuole, the secretion contains numerous droplets of a different chemical constitution.

In another you see solid and granular secretion in neighbouring acini, and in another in even the same acinus. In another adenoma with flattened epithelium the colloid is little different as regards degree of vacuolation from this photograph by Hurthle, where the epithelium is heaped up (microphotograph, Fig. 12).

In conclusion, I wish for the opportunity of saying a further word on the retrogression of thyroïdal epithelium. In myxœdema, as is now well known, the thyroid gland atrophies, and there is found a round-celled infiltration of the remnants of the lobes and acini. A photograph taken from a patient who died from myxœdema nine years ago, and a photograph of Mr. Lapidge's drawing of another section from the same specimen, show that in retrogression the cells resemble more particularly the parenchyma cells of Baber; that they are polyangular, and that they occupy the lumen of the shrunken acinus, in which there is consequently no secretion; but it is to be observed that this confirms the importance of the morphological change in the epithelial cell. By way of contrast compare the myxœdematous retrograde cell with that of the compensating active transplanted thyroid in one of v. Eiselberg's striking experiments. In this last there is no colloid, and the secretion must have been a watery one, yet adequate. Estimation of the athyroidal condition, therefore, is rather to be looked for as yet in the changes in the epithelium itself than in the products of its secretory activity.

To summarise our present position and knowledge of the whole question, it is, I think, now generally agreed (and the more so since the recent extensive researches of Mr. Edmunds) that whereas myxœdema and cretinism result from simple loss of the function of the thyroid gland, exophthalmic goitre in its various degrees results from a perversion of that function.

## REMARKS

ON

### THE EFFECTS OF ANHELONIUM LEWINII (THE MESCAL BUTTON).<sup>1</sup>

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THE history of the use of mescal by the Indians of New Mexico is very well known in the United States, and especially through the valuable papers of Dr. Prentiss, of Washington, D.C.<sup>2</sup>

These so interested me that I asked him to favour me with some of the extract. Profiting by his kindness, I made a trial of the drug on May 24th, 1896, by taking it as I shall now relate.

At 12 noon of a busy morning I took fully 1½ drachm of an extract of which each drachm represented one mescal button. I had in a half-hour a sense of great gastric discomfort, and later of distension. At 1 P.M. I took a little over a drachm. Between 2 and 3 P.M. I noted my face as flushed; the pupils were dilated midway, the pulse 80 and strong. I had a slight sense of exhilaration, a tendency to talk, and now and then I misplaced a word. The knee jerk and station were normal. Between 2 and 4 o'clock I had outside of my house two consultations, and saw several patients. I observed that with a pleasing sense of languor there was an unusual

<sup>1</sup> Read before the American Neurological Society.

<sup>2</sup> *Therapeutic Gazette*, September, 1895.

amount of physical endurance. I went rather quietly, taking two stairs at a time and without pause, to the fourth storey of an hotel, and did not feel oppressed or short of breath. This is akin to the experience, as I learn, of the mescal-eating Indians, and to that of many white men.

Meanwhile my stomach was more uncomfortable, and I saw the first evidence of any change in my colour records. On closing my eyes (while in my carriage), I held longer than usual any bright object just seen. As to this, however, I am not as sure as I am concerning the later phenomena. About 4.10 P.M. I drove home, and after taking half an ounce of extract in three doses I lay on a lounge and read, becoming steadily more conscious, at first of a left frontal pain (not severe) and soon after of a dull occipital ache felt on both sides and at or about the occipital bosses. Yawning at times, sleepy, deliciously at languid ease, I was clearly in "the land where it is always afternoon." At 4.30 P.M., rising to make notes, I became aware that a transparent, violet haze was about my pen point, a tint so delicate as at times to seem doubtfully existent.

At this stage of the mescal intoxication I had a certain sense of the things about me as having a more positive existence than usual. It is not easy to define what I mean, and at the time I searched my vocabulary for phrase or word which should fitly state my feeling. It was vain.

At this time, also, I had a decisive impression that I was more competent in mind than in my every-day moods. I seemed to be sure of victoriously dealing with problems. This state of mind may be easily matched in the condition of some men when pretty far gone in alcohol intoxication. My own mood was gently flattering—a mere consciousness of power, with meanwhile absolute control of every faculty. I wrote a long letter of advice dealing with a rather doubtful diagnosis, and on reading it over was able to see that it was neither better nor worse than my average letter. Yet the sense of increased ability was so notable that, liking to test it, and with common-sense disbelief in its flattery, I took up a certain paper on psychology, which a week before I had laid down in despair. I grieve to say that it was less to be comprehended than ever. My ignorance would have remained bliss had I not made the experiment. I next tried to do a complicated sum, but soon discovered that my ordinary inefficiency as to figures was not really increased.

A mood is like a climate and cannot be reasoned with. I continued to have for some two hours this elated sense of superiority. I was for this while in that condition in which some people permanently abide.

The further test of writing a few lines of verse was tried. I found there was much effort needed. I lay down again about 5.20, observing that the outer space field seemed to be smoky. Just at this time, my eyes being closed, I began to see tiny points of light, like stars or fire flies, which came and went in a moment. My palms were now tingling, my face a little flushed. About 5.40 the star points became many, and then I began to observe something like fragments of stained glass windows. The glass was not very brilliant, but the setting, which was irregular in form, seemed to be made of incessantly flowing sparkles of pale silver, now going here, now there, to and fro, like, as I thought, the inexplicable rush and stay and reflux of the circulation seen through a lens. These window patterns were like fragments coming into view and fading.

Hoping for still better things in the way of colour, I went upstairs, lay down in a darkened room and waited. In a few minutes the silver stars were seen again, and later I found that these always preceded any other more remarkable visions.

The display which for an enchanted two hours followed was such as I find it hopeless to describe in language which shall convey to others the beauty and splendour of what I saw. I shall limit myself to a statement of a certain number of the more definite visions thus projected on the screen of consciousness.

During these two hours I was generally wide awake. I was comfortable, save as to certain gastric conditions, which were not so severe as to distract attention. Time passed with little sense for me of its passage. I was critically attentive, watchful, interested, and curious, making all the time mental notes for future use.

Especially at the close of my experience I must, I think, have been for a while in the peculiar interval between the waking state and that of sleep—the "prædormitum"—the time when we are apt to dream half-controlled stories; but as to this I am not very sure. As a rule, I was on guard with every power of observation and reflection in full activity.

My first vivid show of mescal colour effects came quickly. I saw the stars, and then, of a sudden, here and there delicate floating films of colour—usually delightful neutral purples and pinks. These came and went—now here, now there. Then an abrupt rush of countless points of white light swept across the field of view, as if the unseen millions of the Milky Way were to flow a sparkling river before the eye. In a minute this was over and the field was dark. Then I began to see zigzag lines of very bright colours, like those seen in some megrims. I tried to fix the place and relation of these tints, but the changes were such as to baffle me. One was an arch of angled lines of red and green, but of what else I could not determine. It was in rapid, what I may call minute, motion.

The tints of intense green and red shifted and altered, and soon were seen no more. Here, again, was the wonderful loveliness of swelling clouds of more vivid colours gone before I could name them, and, sometimes rising from the lower field, and very swiftly altering in colour tones from pale purples and rose to greys, with now and then a bar of level green or orange intense as lightning and as momentary.

When I opened my eyes all was gone at once. Closing them I began after a long interval to see for the first time definite objects associated with colours. The stars sparkled and passed away. A white spear of grey stone grew up to huge height, and became a tall, richly finished Gothic tower of very elaborate and definite design, with many rather worn statues standing in the doorways or on stone brackets. As I gazed every projecting angle, cornice, and even the face of the stones at their joinings were by degrees covered or hung with clusters of what seemed to be huge precious stones, but uncut, some being more like masses of transparent fruit. These were green, purple, red, and orange; never clear yellow and never blue. All seemed to possess an interior light, and to give the faintest idea of the perfectly satisfying intensity and purity of these gorgeous colour-fruits is quite beyond my power. All the colours I have ever beheld are dull as compared to these.

As I looked, and it lasted long, the tower became of a fine mouse hue, and everywhere the vast pendant masses of emerald green, ruby reds, and orange began to drip a slow rain of colours. All this while nothing was at rest a moment. The balls of colour moved tremulously. The tints became dull, and then, at once, past belief vivid; the architectural lines were all active with shifting tints. The figures moving shook the long hanging lines of living light, and then, in an instant, all was dark.

After an endless display of less beautiful marvels I saw that which deeply impressed me. An edge of a huge cliff seem to project over a gulf of unseen depth. My viewless enchanter set on the brink a huge bird claw of stone. Above, from the stem or leg, hung a fragment of some stuff. This began to unroll and float out to a distance which seemed to me to represent Time as well as immensity of Space. Here were miles of rippled purples, half transparent, and of ineffable beauty. Now and then soft golden clouds floated from these folds, or a great shimmer went over the whole of the rolling purples, and things, like green birds, fell from it, fluttering down into the gulf below. Next, I saw clusters of stones hanging in masses from the claw toes, as it seemed to me miles of them, down far below into the underworld of the black gulf.

This was the most distinct of my visions. Incautiously I opened my eyes, and it was gone. A little later I saw interlaced and numberless hoops in the air all spinning swiftly and all loaded with threaded jewels or with masses of colour in long ropes of clustered balls. I began to wonder why I saw no opals, and some minutes after each of these circles, which looked like a boy's hoop, became huge opals; if I should say fluid opals it would best describe what was however like nothing earthly.

I set myself later to seeing if I could conjure figures, for so far I had seen nothing human in form, nor any which seemed

alive. I had no luck at this, but a long while after I saw what seemed a shop with apothecaries' bottles, but of such splendour green, red, purple, as are not outside of the pharmacies of fairy land.

On the left wall was pinned by the tail a brown worm of perhaps a hundred feet long. It was slowly rotating, like a catherine wheel, nor did it seem loathly. As it turned, long green and red tentacles fell this way and that. On a bench near by two little dwarfs, made, it seemed, of leather, were blowing through long glass pipes of green tint, which seemed to me to be alive, so intensely, vitally green were they. But it were vain to find in words what will describe these colours. Either they seemed strangely solid, or to possess vitality. They still linger visibly in my memory, and left the feeling that I had seen among them colours unknown to my experience.

Their variety and strange juxtapositions were indeed fascinating for one to whom colour is more than it is to most men; nor is it possible to describe the hundredth of what I saw. I was at last conscious of the fact that at moments I was almost asleep, and then wide awake. In one of these magic moments I saw my last vision and the strangest. I heard what appeared to be approaching rhythmical sounds, and then saw a beach, which I knew to be that of Newport. On this, with a great noise, which lasted but a moment, rolled in out of darkness wave on wave. These as they came were liquid splendours huge and threatening, of wonderfully pure green, or red or deep purple, once only deep orange, and with no trace of foam. These water hills of colour broke on the beach with myriads of lights of the same tint as the wave. This lasted some time, and while it did so I got back to more distinct consciousness, and wished the beautiful terror of these huge mounds of colour would continue.

A knock at my door caused me to open my eyes, and I lost whatever of wonder might have come after.

After dinner I ceased to be able to see any further display of interest. Now and then a purple or pink fragment appeared, but that was all. For a day after I noted the fact that my visions could be easily recalled by a memorial effort, but with less and less sharpness.

These shows are expensive. For two days I had headache, and for one day a smart attack of gastric distress. This came after the first dose, and was most uncomfortable. The experience, however, was worth one such headache and indigestion, but was not worth a second.

Dr. Prentiss and others describe mescal as causing insomnia. My first experience with the tincture was made early in the morning. I became deeply flushed by noon, but had no visions. I felt drowsy and slept very well the following night. The extract used, as stated, did make me sleepless up to 4 A.M., but neither restless nor uneasy.

Some interesting reflections are suggested by my experience with this vision-breeding drug, mescal. The effect on me was more or less like what is experienced in some ophthalmic megrims, and even my most brilliant visions can be matched by those I reported in 1887, and by some to be found in Dr. de Schweinitz's more recent paper.

The following extract from my own paper will sufficiently illustrate what I desire to point out. It concerns one of the several cases of megrim with visions which I reported:

"The symptoms of onset are these: frontal and occipital sense of tension lessening towards night, good sleep follows; next day he awakes with some pain between the eyes and slight photophobia. The second night, or the morning after it, he is aware of being flushed, but has no cerebral throbbing. In a few moments the lids feel as if pulled towards the inner canthus, and fortification zigzags appear, with next partial blurring of vision, which seems in twenty minutes to efface the lines and include more or less of the field. The lines seem to be projected one inch from the eye, and flash, and come and go with shimmering prismatic colours. The dimming of vision lasts some twenty minutes, and leaves him with slight vertigo and a feeling of fullness of the head, but pain always begins over the eye which has distinct vision, and of this he is sure. It increases as the eyesight clears, and is about one inch above the eye. Exertion, stooping, anxiety increase it. The pain lasts from one to three hours, and ceases without nausea. When it occurs over the left eye he has sometimes slight aphasia for five minutes, and in youth this was more severe and more lasting.

"As the zigzags fade he has exalted sense of hearing; loud voices hurt him for a half hour, and this is the period of vertigo. At one time he had at this period of the attack tingling in the fingers of the side opposite to that of the pain. After a number of these headaches he is subject to the curious and exceptional illusions which have caused me to report his case. At times these replace the zigzag lines, but later in a series of headaches they come on independent of the hemicrania, and occur at night, while awake or in full daylight.

"1. A common delusion with him is to see about twenty feet distant a trellis of silver covered with vines and flowers of brilliant tints. This is seen best when the eyes are open, and comes and goes.

"2. He sees a series of complex geometrical figures at the centre of the field. These are brilliant pink or red.

"3. Quite commonly he sees multiple red circles intertwined and in rapid rotation, and once a red eye which seemed to approach him from a distance. Sometimes there is a milky cascade before both eyes.

"4. He saw once a crescent of silver on the wall, and suspended from it numerous heads in profile. Some were strange to him, and some were vivid revivals of faces which he had long forgotten.

"5. Six years ago he saw, during an attack, a huge red spider, which melted into a series of red rectangles revolving in swift motion.

"6. He has several times, and first on awakening, seen the door opened and a procession of white-robed veiled figures enter. They did not fade until he arose and lit the gas. These were seen with his eyes open or shut, and he could not double them by causing himself to squint by pressure on one eye."

It will have been seen that mescal supplied me with one-sided (left) frontal headache—later with occipital pain on both sides, with coloured zigzags or fortification lines—the rain of silver and disorder of the stomach. I ask myself now if the megrims with visions are apt to be found in association with occipital pain in the region of the convolutions, which we believe store up our ocularly acquired memories. It is worth an inquiry.

The mode of action of mescal is somewhat curious, and may vary with the dose and the man. At first, even at the height of drug action, the visions require one to wait with closed eyes for a minute or more. To open the eyes is to dismiss the vision, no matter how dark be the room. Suggestion availed me but little, and no act of will was competent to hold my dream unaltered.

I found in these seeming laws some resemblance to those which—in my case, at least—appear to govern a quite ordinary and normal phenomenon. From childhood I, like some others, can at night, before sleep arrives, summon visions. These are not always just what I desire. Once present I cannot alter them; they shift, change, and disappear under influences not within my capacity to control or to analyse. To open my eyes, even in the most intense darkness, dismisses these visions. Is it true of opium visions? The same law certainly applies to some hysterical phantasms; but the explanation does not as yet seem attainable. My normal power to summon visions was entirely lost under mescal action. I tried to see faces, gardens, etc., but none came at command so long as I was under the influence of the drug.

For the psychologist this agent should have value. To be able with a whole mind to experiment mentally upon such phenomena as I have described is an unusual privilege. Here is unlocked a storehouse of glorified memorial treasures of one kind. There may be a drug which shall so release a mob of verbal memories, or of musical records, or, in fact, of tastes and odours. I naturally speak of things seen under mescal influence as glorified memories—certainly nothing seen in these visions was altogether outside of my known experiences—but everything was excessive—forms were gigantic—colours marvellously intermingled. In fact, nothing was simply the vision of a thing remembered and recognised except the familiar Newport Beach.

I see no obvious therapeutic uses for mescal in massive doses. It is yet to be tested by continuous employment in moderate amounts, and may be of value.

I sought so to limit the influence of mescal as to remain in full

possession of all my faculties. The larger doses secure, as Dr. Prentiss has shown, more remarkable results, but may lessen the power to observe and to comment. I should dread a little lest excessive amounts might leave too permanent effects. In fact, I constantly carried for days a quite vivid image of one of these jewel clusters, seeing it mentally whenever my mind was turned upon the subject of my visions.

I could match this also by a painful experience of some years ago, but I have said enough to show the great interest of this drug for physicians and psychologists. I predict a perilous reign of the mesal habit when this agent becomes attainable. The temptation to call again the enchanting magic of my experience will, I am sure, be too much for some men to resist after they have once set foot in this land of fairy colours, where there seems to be so much to charm and so little to excite horror or disgust.

Were I to take mesal again I should dictate to a stenographer all that I saw and in due order. No one can hope to remember for later record so wild a sequence of colour and of forms. But since to talk does not disturb these visions, a perfect account might easily be given. No one has told us what visions come to the Red man. I should like to know if those of the navy would be like those of the artist, and above all, what those born blind could relate; and, too, such as are born colour blind. In fact, a valuable range of experiment is here to be laid open.

I append to my own statement that of Dr. Eshner, one of the clinical staff of the Infirmary for Nervous Disease. It will be seen that, although the symptoms were not unlike my own, there were some interesting differences. There was nausea, whereas I had none; there was no distinct headache, whilst mine was notable. In general the experience was in Dr. Eshner's case more unpleasant than in mine or in those Dr. Prentiss has reported, neither were the visions so remarkable nor the colours as vivid as were those I saw. It is as well to add, as concerns my own statement, that when twice in my life, I have had to take hypodermic injections of morphine for several successive nights, the drug ceased to cause sleep after the third night. Later it gave rise to visions of very remarkable character, which I have elsewhere described. These were seen whether or not the eyes were closed, if only the room in which I lay was entirely dark.

Dr. Eshner writes me as follows: From doses varying from 10 to 50 drops I noticed no effect other, perhaps, than slightly diminished frequency of the pulse. Thus, an hour after taking 20 drops the pulse had fallen from 80 to 70. Fifteen minutes after a dose of 50 drops the pulse had fallen from 82 to 69, although in fifteen minutes more it was again 74. The same effect was noticed after larger doses.

On May 30th, at 3.50 P.M., with a pulse of 78, I took a fluid drachm. At 4.25 P.M. my pulse was 73, and I took another fluid drachm. At 4.45 my pulse was 65, and I took a third fluid drachm. At 5 P.M., with a pulse of 61, I took 40 minims, all of the preparation I had left. At 5.15 my pulse was 59; at 5.30, 64; and at 6.30, 65.

As the constitutional facts appeared, I found I could not keep at serious work; I felt some distraction, and lacked my usual mental concentration. I soon began to feel badly, lapsing into a condition of general *malaise*, with not a little prostration, and had to give up any attempt at work, however small. I found some comfort in lying down, and when my eyes closed I became conscious of a series of visual impressions, in most of which colour sensations were present. The pictures were characteristically kaleidoscopic, particularly as regards uniformity of arrangement. They changed frequently at times, like lantern pictures on a screen. The designs were various; some were Oriental, with stars and crescents, and points of light interspersed; others were mosaic in arrangement; some were screen-like; some fern-like; some showed chased figures. Neither the images nor the light were very vivid, although as a rule quite distinct. The intensity at times appeared related to the vigour with which the eyes were closed.

At about 6.30 P.M. I arose and attempted to eat a little, but failed. Nausea was quite pronounced, and there was total loss of appetite. At no time did vomiting occur.

I then lay down for half or three-quarters of an hour, and

the visions were repeated. I had intended going out in the evening, and, in the hope of gaining relief, I equipped myself for a bicycle ride, and started off, despite my languor and general depression. I made my way to the Park without the slightest difficulty, and at Girard Bridge met and spoke to an acquaintance, stopped under the bridge to view the Memorial Day illumination, and went on. I rode in all about eight miles, going down a fairly steep declivity with ease, and descending a longer and perhaps steeper declivity with almost equal ease. I perspired *en route*, not unduly, but perceptibly. I felt that my pupils must be dilated from the brilliancy of the light, with prismatic radiations and the large amount that entered my eyes. I think ocular accommodation may also have been affected, although the visual languor may have been only a part of the general languor. Vision seemed not alert. I was in a state of placid indifference, free from enthusiasm, free from aspiration, without spontaneity. I imagine there was a little dryness of the secretions of the mouth and throat, because my voice appeared a little deeper and fuller than usual. I was scarcely conscious of ordinary movement, and felt as though I could scarcely make any extraordinary movement, although I was conscious of the necessity of making the effort, and of the increased exertion necessary in mounting the hill of which I have spoken. In general, however, I seemed to go on by virtue of my own momentum. In a figurative way, I felt as if I were of the same density as the medium in which I floated, so that I would yield to slight external physical impulses. The feeling is one that I can best describe as muscular insensibility or motor anaesthesia. I was a little indifferent as to how I rode, yet not careless nor without a sense of responsibility, but I made little effort to avoid the rougher places, and appreciated very little jolting. I sustained my equilibrium perfectly, and was not compelled to dismount other than intentionally. I rode slowly down Broad Street by the side of a four-in-hand, and listened with enjoyment to the strains of the trumpeter. I met a little messenger boy on a bicycle who made a ludicrous impression on me, and whom at his request I helped to a match without dismounting.

I reached home about half-past nine, and called at the house of Dr. S. Weir Mitchell, and in his absence left a note for him. I was more fortunate in finding Dr. J. K. Mitchell at home, who noticed the deepening in my voice, dilatation of the pupils, some injection of the eyes, a little flushing of the face, increased knee-jerks and active muscle-jerks, a heart beat of 72, and, as he thought, some evident effort in speech. My own feeling was one of partial release of inhibition, of relaxation of restraint and of repression. The state was not a pleasurable, but rather a helpless one. I could write freely and with ease about what I had passed through and was passing through, and experienced a certain freedom and fluency of expression.

I sat up and read from about ten until half-past twelve, the visions returning whenever I closed my eyes. Now I was again able to see all sorts of new designs, fresco work, porcelain decorations, tapestry figures, intricate laces, parquetry, diagrams, various kinds of scroll work, etc. I endeavoured to picture an American flag, but only partially succeeded after I had retired, and then my flag was furled. I saw coats of arms and shields and the like. All colours were represented. I looked especially for blue, as Dr. Mitchell had told me that he had seen all colours but blue, and I was successful. At one time I saw various shadows of green, and at another especially purples, violets, lilacs, etc. In none of the images were people or animals or other objects than designs represented.

As I read I was easily pleased. At this time I experienced a sense of nausea, with a suggestion of burning and weight in the umbilical region; but this was gone by the following morning.

Before going to bed I partook of a sandwich and some milk. I found the sense of taste benumbed. I was not able to fall asleep for some time. My sense of hearing seemed to be more receptive, but less acute. The condition might be described as an impairment of the auditory accommodation comparable to the corresponding ocular state. My breathing failed specially to attract my attention, but seemed shallow. I was conscious of pain on being pinched.

The night was a restless one, with some snatches of sleep of varying length, but I arose with ease at the usual hour, feeling not much the worse for my late experiences, and not at all sleepy. There remained a sense of fulness in the head, but no other reminder. I partook of my usual breakfast with ordinary relish. The preparation had a disagreeable nauseous taste, with suggestion of pungency.

### OBSERVATIONS ON THE SERUM REACTION IN TYPHOID FEVER AND EXPERIMENTAL CHOLERA BY THE DRIED BLOOD METHOD.

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and the Montreal General Hospital.)

#### THE METHOD AND ITS APPLICATION.

WE wish to record the result of 290 blood examinations made by the method already described by one of us.<sup>1</sup> Instead of employing fluid blood serum as recommended by Widal, a large drop of blood is allowed to dry upon a folded piece of sterilised non-absorbent paper, and is examined by moistening with a drop of sterilised water, mixing the solutions with a drop of pure broth culture of the typhoid bacillus, and examining the mixture as a hanging drop preparation under a dry lens of medium power. Instead of using the hollow-ground glass slide one may employ the simple old method suggested to us by Dr. Adami, of cutting a hole out of the centre of a piece of thick blotting paper, laying this moistened on an ordinary slide, and inverting the cover glass.

This method gave good results for diagnostic purposes. The preliminary drying of the blood did not appear to interfere with the production of the reaction, and enabled the sample to be taken more easily, and transmitted more readily, especially when received from a distance. Several of our samples came by mail from points from 500 to 700 miles distant. There is always difficulty in sending fluids by mail. There is none in forwarding an ordinary envelope containing a slip of paper.

A gratuitous public service of serum diagnosis was introduced last September by the Board of Health in the Province of Quebec. Suitable outfits for taking samples, consisting of pieces of sterilised paper enclosed in envelopes with printed directions and blank spaces for information to be filled in, have been placed at those dépôts (chemists' shops) which already keep and supply outfits for diphtheria diagnosis. In case a negative result is obtained, and the suspicions of typhoid continue, a glass tube is furnished in which a duplicate sample of fresh blood is also required to be sent.

The dried blood method was selected more on account of the great facility it afforded for the collection and transmission by post to the laboratory of samples in proper condition for examination, than in the expectation of any greater delicacy over the fresh serum method as used in ordinary hospital work. In fact, we had anticipated a somewhat less delicate reaction by the dried blood method. Widal<sup>2</sup> has recorded the results of five blood examinations in which, for comparison, typhoid blood and typhoid serum were dried for forty-eight hours on sponges, and examined at the end of that time. The typhoid serum gave the reaction typically when in a dilution of 1 to 10 with typhoid broth culture, while the dried blood also gave the reaction somewhat less promptly in dilution of 1 to 5. This shows under these conditions a lesser delicacy with dried blood than dried serum, but the fact remains that, according to Widal, a positive reaction was obtained by the dried blood in all 5 cases. Previous to learning of these experiments of Widal, we had used with success absorbent cotton-wool swabs used in our diphtheria outfits; but we discarded these, and adopted the collections of the blood on non-absorbent surfaces as being more efficient.

We have not yet fully decided as to the relative merits of the dry and moist methods of collection, which is a matter depending chiefly on the conditions under which the samples

have to be transmitted and collected. We anticipated that the dried blood would be less delicate than the fresh serum, and that though the positive results would be equally reliable in either case, the negative would have less weight. On the other hand, with the fluid method the after-growth of contaminating bacteria during transmission might obscure a positive reaction if these were motile forms. Fluid samples received by us in a state of decomposition were found difficult to examine, though in some cases the heating of the sample to 65° C. to destroy the bacteria previous to mixing with the typhoid culture, enabled the reaction to be obtained. Decomposition does not in itself destroy the specific substance which produces the reaction, nor does a heat of 65° C.

In view of the assumed superior delicacy of the fresh serum, we obtained whenever possible duplicate samples of fresh and dried blood for re-examination when the first result was negative. To our surprise, when a negative result was obtained by the dry method, the result by the fluid serum was also negative, and where we obtained a positive result on re-examination with the fluid serum without exception the duplicate sample of dried blood also gave a positive result.

We would explain this apparent deviation from what one would theoretically expect, by the fact that there seems to exist in typhoid serum an intensity of reaction beyond what is ordinarily necessary for the test, so that dilutions of 1 to 10, or even 1 to 100, may be practised in a case showing well-marked reaction, without interfering with the result. By our method we use a concentrated solution which may explain the fact that our results appear to be, so far, quite as good as those already recorded by the Widal method, although Widal and others record almost uniform success with the reaction in suitable cases.

Thoelen and Mills<sup>3</sup> report that by the Widal method the blood serum taken between the sixth and twenty-second days only gave the reaction six times out of twelve re-examinations, in cases which had been shown to be typhoid by the positive result of the test.

In addition to the samples obtained through the Board of Health we examined a number of hospital cases to see what percentage of positive results could be obtained under favourable conditions, and at a period of the disease when the reaction could be expected with certainty. This was the more necessary as a great many of the samples sent to the Board of Health were taken at periods prior to the fifth day, a date at which, according to the statements of the best authorities, the reaction would not yet be present.

In public health laboratory work in which samples are largely obtained from obscure and doubtful cases, the proportion of positive results is less than when samples are taken indiscriminately from ordinary cases of typhoid, which form the basis of hospital observations. The effect of this circumstance upon the statistics of diphtheria has been pointed out by Welch,<sup>4</sup> who says: "We attribute the special differences in the reported statistics of results of different investigators, mainly to the class of cases selected for investigation. If only typical and characteristic cases of diphtheria be selected, the proportion of cases in which the diphtheria bacilli are missed will certainly be small and may be nil. If, however, the less characteristic cases of diphtheria, concerning which in many cases no one can be sure without a bacteriological examination, whether these are genuine diphtheria or not be included, there may be a relatively large percentage of negative results." This applies equally to typhoid.

It seems self-evident that where samples have to be taken by persons without special training, the same degree of accuracy cannot be expected as where a persona's supervision can be exercised over all stages of the work by the bacteriologist himself. Thus in organising our public diagnosis, preliminary sterilisation of the skin previous to taking the sample had to be omitted, lest an accidental inclusion of some of the disinfectant might disturb the result.

As we found that about 90 per cent. of the cases could be diagnosed by means of the dry method at the first examination, we thought it better to leave the more refined and careful study of the negative result to be dealt with by re-examination, as this would only be necessary then in 10 per cent. of the cases.