

not arise very often, they do occur frequently enough and are important enough to demand increasing attention. In considering these difficulties we must keep in mind the following possibilities:

1. Cases of acute anterior poliomyelitis with no noticeable sensory symptoms. These are rare, at least in adults and in children old enough to express themselves.

2. Cases of acute anterior poliomyelitis with severe pain and hyperesthesia in the paralytic members in the onset and lasting for a variable time. These cases are also rare.

3. Cases of acute anterior poliomyelitis in which the sensory disturbances fall between the extremes of numbers 1 and 2. These are the usual cases.

4. Cases of multiple neuritis with unusual sensory symptoms and distribution.

5. Cases of so-called "multiple neuritis of the motor type," with little or no sensory symptoms.

6. Cases in which multiple neuritis and poliomyelitis are associated. Such cases have been pathologically demonstrated. They are difficult to diagnosticate; and certainly are not frequent. They are caused by some widespread and intense toxic process, producing grave general symptoms.

7. Miscellaneous conditions, as acute ascending paralysis, "family periodic paralysis," myesthesia, hysteria, etc., which, in the differentiation under consideration, will hardly create confusion when carefully studied.

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## SOME CLINICAL ASPECTS OF CHEMISTRY.

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Even the most superficial observer of the expansion of the medicine of to-day might accept without much question the claim of chemistry to be the first of the pure sciences which form the foundation of medicine, for the potent influence of its leaven may be perceived throughout the whole medical mass. Clinical laboratories are growing in favor and influence; publishers have produced a superabundance of text-books which purport to "make clinical chemistry easy"; medical journals accept at sight articles on almost any chemical subject, some of scientific value, some of practical value, some of no value.

At a recent large medical congress so much time was spent on the chemical side of internal medicine that one not interested in that subject must have had to exert unusual efforts to look interested and knowing. What did he care what the intermediate products of sugar metabolism are, or whether the body can recognize the difference between a "right-handed" and a

"left-handed" pentose with the same empiric formula? Of what "practical value" is it to discover an extra ferment in the stomach? Does the "practical man" care to know how a hen synthesizes uric acid?

Neurologists now examine urine with greater interest and demand that we find there the cause of a neuritis. Oculists and dermatologists awake to the fact that the whole body is one and that the chemistry of this whole may throw light on the organ in which they are interested. Students are required to take chemical courses before beginning to study medicine and it is a professor of anatomy who suggests the addition of another year of pure chemistry to the already long list of requirements of one school.

But chemical education does not emanate alone from medical schools, medical journals and medical congresses; every practitioner gets a free course through the mails. He is bombarded with pamphlets giving a detailed account of some recent "Arbeit" in chemistry, and advertising a new food or new preparation of some well-known substance, or some brand-new drug which is the tangible and expensive embodiment of the above-mentioned "Arbeit." The whole practical medical world, in fact, is studying chemistry.

But it is not alone medical men who are turning chemists for the pathologists are also studying chemistry—their hemolysins, bacteriohemagglutinins, anti-hemagglutinins, toxophores, heptophores, complementophilic groups and intermediary bodies are now or soon will be playthings of "pathologic chemists."

The physiologic laboratories have also felt the leaven. The kymograph is run down, the plethysmograph leaks, the nonpolarizable electrodes almost spark, burettes, test tubes and beakers cover the tables, for the physiologists are, many of them, studying chemistry. Here the recently-called professor of physiology is a pure chemist; there almost the whole physiologic staff is working on chemical problems. The journals which publish the mechanical side are termed by a pure physiologist "uninteresting," journals of physiologic chemistry grow in number and circulation and the physiologic chemical laboratories are admitted by eminent clinical men to be the centers from which the medicine of to-day is progressing.

The growth of the physiologic chemical laboratory is of the utmost importance to clinical medicine, for now the clinical laboratory will be provided with methods which are of practical use to the clinical man, and with men well enough trained to use them. Clinical chemistry is no new subject. Urinary examination has long been recognized as of the greatest importance, but the work has not been done by men especially fitted and the methods in use were many of them poor. Nevertheless, and in fact because of this, there has grown a very extensive literature of clinical chemistry and to increase this has been one of the earmarks of a "very scientific practitioner." The advent of physiologic chemistry, the occupation of the field by thoroughly-trained men, has sifted and weeded this literature to a surprising degree. Instead of a long list of diseases in which the xanthin bodies are increased or diminished we now read that the method used was so inaccurate that "our knowledge of the relations of xanthins to pathologic processes is as defective as it was years ago"; the alkalinity of the blood is not arraigned as often as a few years ago, although we still suspect it is an offender, but can not prove it; phosphaturia is now a name only. Compare a text-book of clinical chemistry of this year with one

\* Read before the Clinical Section of the Medical and Chirurgical Faculty of the State of Maryland.

of a few years ago and see how much less we know now than then.

The advances already made by study of the chemical side of internal medicine are great. Metabolism experiments in various diseases have thrown considerable light on the nature of these conditions and in the sphere of dietetics aided the practitioner to no small degree. They were clinical chemists who showed the importance of the test meal, the meaning of the hyperacidity and anacidity, of free and bound hydrochloric acid, the significance of lactic acid and lastly the importance of the increased bound chlorids in the early diagnosis of cancer of the stomach (Reissner). It was a clinical chemist who showed that in the pneumonic lung the exudate was digested as if it were a piece of meat in the intestine, and that from examination of the urine the amount of lung resolved could be each day weighed. The practical results from this may be considerable. They were clinical chemists who taught the profession so much about diabetes mellitus; a short review of this subject will be a good illustration of the contributions of clinical chemistry. The presence of sugar in the diabetic's urine had been long known and its amount followed by clinical chemists, but does this explain diabetic coma, the dyspneic coma of Kussmaul? Petters ascribed this to acetone, Gerhardt to a body later found to be diacetic acid, but neither of these is the poison, yet the qualitative tests of these are of great value and can be easily and repeatedly made by every practitioner in every case of diabetes. Following a suggestion from a pharmacologic laboratory Hallervorden demonstrated the increase of ammonia in the urine of diabetics—and in each severe case this quantitative determination should be made at stated intervals—this increased ammonia proved that in the urine was an increase of acid. Stadelmann proved this acid to be organic, showed the relation between its increase and coma, pointed out the similarity between diabetic coma and that of rabbits with acid intoxication (Walters), and deserves the greatest credit for introducing the alkali treatment of diabetes. It remained for clinical chemists, Minkowski and Külz, to isolate this acid, which they found to be oxybutyric acid, from the decomposition of which acetone and diacetic acid arise. The discovery of this body must have surprised chemists. They had interested themselves in many bodies present to about one-half a gram or less, and overlooked this often present to the amount of 20-30 gms. and in coma even one-quarter of a pound a day!

Before the alkali treatment, when rigid diet of diabetics was enforced, the practitioners noticed that many patients promptly went into coma and died—why? Again clinical chemists answer. That acetone and diacetic acid are present in a normal fasting person, or a patient with almost any disease causing severe malnutrition, clinical chemists had noticed. Gerhardt and Schlesinger then showed that a normal person who eats the diabetic's rigid diet will, on about the seventh day, show even nine grams of oxybutyric acid in his urine. Since this acid is then a product of metabolism of any person when the diet is too poor in carbohydrates, what wonder then that the diabetic, already on sugar-rich diet half poisoned by it, should, when sugar is withheld, at once succumb to the increase of this acid? How necessary it is that the practitioner should know whether or not his patient is already in a condition of partial acid intoxication, by the simple tests for acetone and diacetic acid, and, if this is the case, should give an abundance of sodium-bicarbonate, not "fifteen grains

with each meal," but even that number of grams and govern the size of the dose by the amount of the ammonia, for it is the absence of alkali which forces the body to increase the ammonia in the urine, and the accurate amount of this any practicing physician can determine, if he will. But physiologic chemistry (Hofmeister) has called the attention of clinical chemists to the importance of determining the assimilation limit of the patient and the diagnosis of diabetes mellitus is now made when the urine is sugar-free. Lastly, glycuronic acid is now well proven a first product of sugar metabolism and to find this increased, even though sugar be not present, may soon be ground for rejection by insurance companies as diabetic.

The above are a few of the contributions of chemistry, but it has only begun its serious work and promises much greater results.

We hope that one of these will be to convince the medical world that eggs and milk are not only a good, but the best diet for a patient. At present the tendency is to prescribe predigested proteids, various peptone preparations and many other specially prepared foods, so that in a long fever the bill for these may well appall the wage-earner of the family. Nevertheless, it is questionable whether there is any good evidence in favor of such foods, which justifies such expense. Certain it is that their superiority over simple eggs and milk has scarcely any, if any, physiologic basis. It is not proven that albumoses have even the same nutritional value as the native albumins of milk and eggs, or that these latter if properly given are at all hard to digest. As for "peptone" each new work seems determined to destroy our faith in it as an important product of digestion (Zuntz and especially Cohnheim). Meat extracts may have a stimulating effect and do, hence the certain benefit which the patient derives; but as for their nutritional value, one may as well feed a fire from the ash heap. On the whole, we can assert that the weight of physiologic evidence is against artificial foods, including in that list all predigested foods. Predigested they may be for a test tube but not necessarily for a patient—the normal body and more so the diseased, demand albumins. These it digests to suit itself, breaks them down to amidoacids and then synthesizes these to the proper albumin and at the present state of our knowledge it is much better to furnish even the diseased body with the raw material than to try to aid it by furnishing products of artificial digestion which, so far as we know, it can not use. Clinical evidence that such foods are unnecessary may be obtained from Dr. Osler's wards where they are never given. Seldom it is that a patient can not digest properly diluted milk, still less seldom that he can not well-prepared egg albumin or beef juice. Of course, the tendency now, when few medicines are prescribed, is to prescribe foods, but the practitioner may well bear in mind that their nutritional advantage is questionable, the chief person to benefit being the manufacturing chemist, and that eggs and milk, if properly prepared, may be even superior and do not cost one dollar a bottle.

One of the most promising fields for clinical chemistry is anemia and it is of interest that hematologists are turning from the morphologic to the chemical side. We read less now of blood counts in pernicious anemia, more about specific gravity, potassium and sodium percentages of the plasma, fat determinations, etc. This is only natural as the plasma is by far the most important part of the blood; red corpuscles, and leucocytes also per-

haps, have a very limited function compared with that of the plasma. When in a case of anemia we count the reds, determine hemoglobin and estimate the percentage of eosinophiles and lymphocytes and polymorphonuclear neutrophiles we gain excellent clinical information, but so far as approaching the question of the anemia we have only begun—the cause of such changes as we find lies farther back in the plasma or blood-forming organs, and in the latter case the plasma may still be to blame. Ask a student what the hemopoietic organs are and he will doubtless answer, bone marrow, lymph glands and spleen, thus omitting three just as important, I think more so, intestinal wall, liver and kidneys, for these determine the composition of the plasma. No, chronic anemia is not oxygen starvation. Clinically, we must depend almost entirely on a study of the morphologic elements, but the laboratory worker must and is already going much further and over two-thirds of the recent communications on blood have dealt with its chemical side.

We read much and hear more lately of the practical value of blood examination. Some would give it first importance evidently as much as the physical examination of the patients; some, because they can not rely on it alone, deny it any importance, while others insist it is of value when well done and rationally interpreted. It is certain that blood examination to many means merely leucocyte counting. Our experience may be briefly stated: In practical internal medicine, leucocyte counting is invaluable. In surgery it is very important, usually throwing some light on the case; sometimes it alone determines the course of action, on other cases its evidence is disregarded. In all cases it must be interpreted by one who understands that leucocytosis is a biologic chemical reaction, hence must not be asked to conform to mathematical standards as a purely chemical reaction might be. He also should be one who has made just a few leucocyte counts himself and knows whether or not a slightly higher count means a rise of leucocytes. Counting red corpuscles is in internal medicine very valuable. Hemoglobin determination is for both physician and surgeon indispensable. Differential leucocyte counting is for the physician always of interest, often of considerable value, but will never have the importance claimed for it until the chemist has shown us the "why" of our staining reactions, and the physiologist the origin of the cells. Further blood examination, alkalescence, the composition of the plasma may in the future be a matter of routine, but at present they belong to the clinical chemist.

But one point deserves further mention and that is the staining reactions of the blood cells. Following Ehrlich's work we have in the past few years learned another language, the nomenclature of blood staining. We are asked to recognize amblychromatic and trachychromatic nuclei, to distinguish carefully between eosinophilic and fuchsinophilic reds and not to mistake the latter for polychromatophilic degeneration. This little thread of chromatin is the trademark of bone-marrow-made cells; this cell is the daughter of that; these have no relation. With each new stain are the granulations multiplying rapidly and, worst of all, the technic is long and results uncertain. And what does it all amount to? With all these studies in stains do we know much more than a fresh specimen would teach us? With all these names which label cells with a source, do we know any more of the origin and relationship of leucocytes than Virchow knew fifty years ago? Very

little. I don't wonder Ehrlich changed the subject. Has since the work of Neumann and Bizzozero one well accepted fact been added to our knowledge of the origin or the structure of the red corpuscles or their relation to the leucocytes? No. Is it necessary for the busy practitioner to spend hours getting his stained specimens? A most emphatic, no. We have satisfactory methods which give beautiful specimens in three minutes, and he doesn't look at fresh specimens nearly long enough. A trained man can guess at a blood-count and hemoglobin percentage and often get it closer than a less experienced man can with counter and hemoglobino-meter.

And the uric acid diathesis. What shall we say of that? Can clinical chemistry deal it any harder blows than it has received? Yet many still would insist that uric acid is really important. Thirty-nine separate morbid conditions are already ascribed to it and the fortieth recently added by an oculist, astigmatism against the rule! Now we know something, not much, about uric acid. We know it is a product of metabolism of proteid. We know the body can also form it by the synthesis of simpler bodies. We know no small part of that which is excreted is from similar bodies in the food and, lastly, that the body can oxidize uric acid. Hence it can not be considered the criterion for the metabolism of any one proteid body. We deny any relationship well proven between an increase of uric acid and leucocytosis; we deny that an increase has been well proven in any disease except fever and leukemia. We do not doubt but that the clinical picture is well marked which bears the name uric acid diathesis, but we do ask does uric acid have any more to do with it than has science with "christian science"?

In conclusion I make a plea for the more general use of the clinical laboratory. The practitioner depends on the bacteriologic laboratory because he knows he can not do this work. Should he not depend almost as much on the clinical laboratory? There are no tests more frequently made by a practitioner than the albumin and sugar tests; can he do these in a doubtful case? He should the former, yet we are certain many a faint trace escapes notice, but the latter he can not in a doubtful case, do, and not now so well as he could a few years ago. An illustration may explain this. Not long ago a patient in a distant city brought us a bottle of urine with the question, "Is sugar present?" The urine reduced copper fairly well, Nylander's test was decidedly positive. Here the physician must have stopped, yet these two tests do not prove sugar. The urine was not dextro-rotatory, it would not ferment, an increase of glucosazon crystals could not be determined, and in a doubtful case all of these tests should be found positive before glycosuria is diagnosed. But what was present? The patient when questioned solved the difficulty. When told to send another specimen and to add camphor to keep it in good condition she replied, "But my doctor told me something much better than that, he told me to add formalin." Formalin is the aldehyd of formic acid, glucose the aldehyd of sorbite and they both reduce copper and bismuth well. I then read clinical chemistries on the subject. One, the most pretentious in this country, advises to add a few drops of formalin to the urine to preserve it. If this advice is followed and it certainly will be by many, what will save the practitioner from finding sugar in many urines? Of course, we know that the text-book says "two or three drops, not more," and a very few drops in a twenty-four-hour specimen will not

trouble the chemist very much, but the "two or three drops" in a four-ounce bottle of the patient who wishes to do the matter thoroughly will, and in this case did, give a splendid reduction test. Almost at the same time another specimen was sent. It reduced copper and bismuth well, but the practitioner was sure it was not glucose, it must be lactose since the patient was pregnant. If lactose, its presence was of no moment; if glucose, of the greatest moment. Hence we say the practitioner in a doubtful case often needs a clinical chemist to aid him, especially if he believes in Nylander's test and allows his patients asparagus. In this connection I would say that one of our students recently showed us that thymol, an excellent preservative for urine, can impart to it good Gmelin-bile-reaction-giving properties. If the practitioner has sent to him a highly-colored urine with a crystal of thymol in it let him beware of making the diagnosis of bile in the urine. The practitioner, on the other hand, does not do nearly enough of some chemistry. With a few test tubes, reagents and a burette, he can do a surprising amount if he will, but let him send doubtful cases to the expert—and cryoscopy to any one with more time than he.

## A PLEA FOR THE EARLY TREATMENT OF SQUINT.\*

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The majority of laymen and a great many of our professional brethren regard squint with a great deal of indifference. This arises largely from the prevalent idea that the child will outgrow it, is too young to be treated or, if treated, will have to always wear glasses. Yet when children grow up with this horrible deformity, they and their parents often seek for relief without success. What I wish to try to make clear is the fallacy of the above reasons, why the squinting eyes of children should be attended to as soon as the first appearance of even a tendency to squint is noticed.

1. In rare instances in some cases the squint disappears as the patient grows older, but nearly always with vision much impaired in the deviating eye and binocular vision very imperfectly developed.

2. The earlier one can get a case after he has commenced to squint, the better the prognosis as to the parallelism of the eyes, binocular vision and visual acuity of each individual eye, because the case is in the developmental stage.

3. In regard to wearing glasses, the contrary is true. If a case can be obtained for treatment soon enough after the squint is noticed, the glasses, in the majority of cases, can be laid away about or soon after puberty, being only needed for close application of the eyes, except, of course, in cases of high hyperopia, myopia or astigmatism.

These deductions are reached through the latest theory advanced by Mr. Claud Worth of London regarding the etiology of squint, i. e., that the potential factor in the cause of squint, of course taken together with the several other etiologic factors, as hyperopia, myopia, anisometropia, congenital amblyopia, fundus changes, changes in the refractive media, heredity, local changes in an ocular muscle, etc., is the defective or non-development of the fusion sense.

We all know that binocular vision is produced by similar portions of the retina being acted upon by rays of

light and these afferent sensations fused centrally. Now, if the condition of the eyes is such that through hyperopia, myopia, anisometropia, congenital amblyopia or any of the above enumerated etiologic causes, which produce central sensations of different intensity, the sensation carried to the brain by the poorer eye can not compete with the clear, distinct image of the better eye and is disregarded, as we disregard the image formed by its fellow when we use the microscope with both eyes open; the eye is thus without a point of fixation and turns in or out. This occurring at a time when the fusion sense is in the process of development and the eye receiving no help in the way of improving the retinal image so it can compete with the fixing eye, the fusion sense is defectively developed or lost, and the eye remaining in the mal position, the squint is established and the organ becomes more and more amblyopic from non-use. The eye usually turns in in hyperopia as the relation of convergence and accommodation converges the visual axis. Instead of both eyes appearing to converge equally, the better eye fixes and the poorer eye turns through the additional arc to allow of this fixation. This explains also the so-called alternating squint, when the patient fixes with one eye or the other, the one eye turns through an additional arc to allow its fellow to fix. In myopia the general tendency is for the eyes to diverge; this is explained on the ground that the myopic eye not having to accommodate there is no effort to converge, consequently the eye diverges.

Then come the class of cases where there are no refractive errors or any of the before-mentioned etiologic factors; yet the child squints. The history of these cases usually develops that the squint commenced after a fright or during an attack of whooping cough or followed some severe illness, and is explained by the fusion sense being in a rudimentary state of development; it is thus rudely interfered with, the fusion center greatly disturbed and binocular vision thus lost for a time and one eye or the other allowed to deviate from parallelism.

The fusion sense, Mr. Worth has determined, is fully developed by the sixth year; after that the question of establishing it is almost beyond hope.

The factors to be dealt with in a case of squint are: 1. The deformity. 2. The suppressed vision of the deviating eye. 3. The more or less amblyopic condition of the deviating eye in the majority of cases. 4. The refractive errors. 5. The fusion sense.

The suppressed vision of the deviating eye produces a loss of central fixation, that in turn causes a deterioration of the vision in the deviating eye, as the rays of light are focused on other portions of the retina than the visual center or fovea and the eye becomes amblyopic; so in our treatment the first step is, after measuring the angle of the squint, to prevent the loss of central fixation and so prevent deterioration of the deviating eye. This is accomplished by refracting the eyes, fully correcting the hyperopia, myopia and astigmatism and ordering glasses to be worn constantly. The determination of the visual acuity is first desired for refraction and this is accomplished in cases who are not old enough to know their letters by the aid of five ivory balls, from  $\frac{1}{2}$  to  $1\frac{1}{2}$  inches in diameter in the following manner: By covering the poorer eye of the patient and starting a game of marbles with him. The mystery is solved! If at 5 meters he can go directly for the smallest ball without hunting about for it, it is safe to say his vision for that eye is about normal, then trying the other eye in the same manner, its visual acuity is determined approximately.

\* Read before the Milwaukee Medical Society, April 22, 1902.