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CAN AMMONIUM SALTS REPLACE PROTEIN AS A SOURCE OF NITROGEN FOR THE TISSUES?

It has long been a dictum of physiology that the nitrogenous needs of the body cannot be supplied by all types of compounds of nitrogen or even by a considerable variety of them. The organism, continually enveloped in an atmosphere rich in gaseous nitrogen, makes absolutely no use of it in its chemical life. The experience and scientific observations of many decades have narrowed the sources of physiologically available nitrogen to the proteins or to their immediate cleavage products, the amino-acids. These are the indispensable nitrogenous foods which the body is evidently unable, for the most part, to construct anew. For some of the amino-acids, no adequate substitute in protein construction in the organism has yet been discovered.

Several years ago, Grafe[1] and his co-workers at Heidelberg ventured the belief that protein might be synthesized in a more simple manner. They maintained animals on diets rich in carbohydrate and fat supplemented with ammonium salts. A notable retention of nitrogen occurred, and this fact was corroborated by Abderhalden. The results have been subjected to severe criticism, notably by Underhill and Goldschmidt[2] at Yale, who pointed out that in any consideration of the influence of ammonium salts on intermediary metabolism, a distinction must be recognized between ammonium salts of organic acids and those of inorganic nature. The ability of the organism to dispose of these two types of salts is radically different. Ammonium chlorid, for example, may become "a distinct detriment to nutritional rhythm, whereas there may be some storage of nitrogen when organic salts like ammonium acetate or citrate are fed as indicated."

It is conceivable, of course, that ammonium salts might in some way protect body protein from disintegration. In other words, if when they are fed along with carbohydrate they do not lead to a direct production of amino-acid complexes, the ammonium salts perhaps "spare" or prevent the usual extent of tissue breakdown in some way. There is a method by which this can be ascertained. True protein contains sulphur as well as nitrogen. The sulphur is none the less important because we usually happen to place the greater emphasis on the nitrogenous component. Organic sulphur is qualitatively as indispensable as is organic nitrogen to the organism. When protein disintegrates, catabolites containing both nitrogen and sulphur appear in the excreta. Hence physiologists are wont to speak of the parallelism of the two elements in metabolism. If ammonium salts lead to protein sparing, the loss of sulphur from the organism should be correspondingly decreased. According to recent investigations of Gessler[3] at Heidelberg, this is not the case. The hypothesis of the advantageous rôle of ammonium compounds in nutrition must be definitively abandoned. It would simplify the solution of many problems of far-reaching importance if we could dispense with the expensive proteins built up for us so laboriously by animals and plants and replace them by a product—ammonia—which the ingenuity of man can derive from the omnipresent air. The answer is: "Not yet!"

1. Grafe, E., and Schläpfer, V.: Ueber Stickstoffretentionen und Stickstoffgleichgewicht bei Fütterung von Ammoniaksalzen, Ztschr. f. physiol. Chem. **77**: 1, 1912.
2. Underhill, F. P., and Goldschmidt, S.: Studies on the Metabolism of Ammonium Salts, III, The Utilization of Ammonium Salts with a Non-Nitrogenous Diet, J. Biol. Chem. **15**: 341, 1913.

FORMIC ACID IN THE BODY

One of the scientific consequences of the menaces to human health which have arisen from the alarmingly frequent cases of consumption of methyl alcohol, or wood spirits, has been the more careful study of the behavior of this toxic substance in the organism. Methyl alcohol, CH_3OH, is not completely burned up to simple end-products in the organism; one of the products of its metabolism is formic acid, HCOOH, as Pohl[4] demonstrated many years ago. The excretion of formic acid thus becomes an indicator of the fact that methyl alcohol has been taken into the body.[5]

It would be a comparatively simple plan to examine the urine for the presence of formic acid whenever information is sought as to possible instances of poisoning with wood alcohol. It happens, however, that formic acid has been known for many years to occur in the urine of persons living under supposedly normal conditions. Autenrieth[6] found that the daily output may approximate 0.25 gm. so that, without a quantitative measurement of the formic acid in the urine, definite conclusions as to its source and origin could not be drawn. The mere test for the presence of formic acid will not suffice to point to methyl alcohol as its predecessor.

3. Gessler, H.: Zur Frage des Wesens der Stickstoffretention bei Fütterung mit Ammoniaksalzen, Ztschr. f. physiol. Chem. **109**: 280 (April 15) 1920.
4. Pohl, J.: Arch. f. Exper. Path. u. Pharmakol. **31**: 286, 1895.
5. Methyl—Wood—Alcohol and Its End-Products in the Body, editorial, J. A. M. A. **74**: 33 (Jan. 3) 1920.
6. Autenrieth, W.: Ueber den Ameisensäuregehalt des Harns, normalerweise und nach Eingabe verschiedener Substanzen, München. med. Wchnschr., Aug. 1, 1919, p. 862.

Substantiation of this general conclusion has now been afforded by Stepp[7] at the Medical Clinic in Giessen. He has detected formic acid as a frequently recurring if not ever-present constituent of human blood. Fifty years ago the Berlin physiologic chemist Salkowski[8] reported the presence, in this fluid, of a substance that was identical in behavior with formic acid, but the observation received little if any further experimental consideration. Among the persons whose blood was examined by Stepp were several diabetics. These afforded the surprise of yielding negative results. Little if any formic acid could be detected in their blood which gave evidence of pronounced hyperglycemia. As the destruction of sugar is profoundly disturbed in such cases, Stepp has offered the tentative suggestion that formic acid may be a stage in the usual metabolism of carbohydrates—a stage that might not be represented when the normal transformations of the latter are interfered with. Thus, the problem of the physiologic significance of the traces of formic acid commonly present in both blood and urine of man has become a by-product, so to speak, of the investigation of the toxicity of methyl alcohol.

THE RIGHT TO STRIKE

The employees of a small railway that furnishes the sole access to a town at the head of a valley go on a strike and demand an absolute acceptance of their terms. As this shuts off all supplies from the local hospital, its directors institute a motor truck service to meet the needs of the institution. On the first day of this arrangement, a car is overturned by a steel wire stretched across the road, and the newly wedded doctor, son of the local practitioner, is killed on the spot. Under the leadership of the chief surgeon of the hospital, an agreement is made by which all medical service is withheld from the strikers and their families. The wife of the leader of the railway strike has an obstructed labor which the physician in attendance (who has declined to side with his professional colleagues) is unable to handle. The surgeon, who is a close friend of the young physician who is killed, declines to aid in caring for the woman who is in labor until he is appealed to by the widow of his dead friend, when he accedes to her importunities and goes to the assistance of the wife of the leader of the railway strike.

This is the plot of a play, by Mr. Ernest Hutchinson, which has been appearing at the Garrick Theater, London. It has created general public interest probably more because it portrays an interesting sociological possibility than for its exceptional histrionic merit. The *Lancet* concludes a not very flattering criticism of the play as a dramatic effort with the statement that it "may be helpful to those members of the body politic, whether medical or no, who cannot otherwise picture the results of withholding their professional services." In a later issue, the *Lancet* publishes letters from Dr. Arthur Cox, medical secretary of the British Medical Association, and from Dr. Alfred Welply, general secretary of the Medico-Political Union, commenting on the subject of the plot of the play.

Dr. Cox says:

> I have always held that in this country a *real* strike by doctors is almost unthinkable. The idea of witholding service from one's own patients—people you may possibly have known since birth—revolts every professional instinct. . . . But I do not say that a refusal to serve would in *any* circumstances be wrong. If I were practicing in a country cursed with a set of bloodthirsty scoundrels who had temporarily got the upper hand and who declared their intention of wiping out the "bourgeois" class to which I belong, I should think it quite right to decline to give my services to anybody expressing that intention. In the words of Clough, "Thou shalt not kill, but needst not strive officiously to keep alive." . . . No medical man who remained amongst his own people could, I think, persist in refusing his services if faced by a real emergency such as occurred in the play. It would be illogical to give then, for "what is sauce for the goose is sauce for the gander"; but, after all, logic has very little to do with most of our actions.

And this from Dr. Welply's letter:

> I think that the title is appropriate on the ground that the right to strike applies equally to all sections of the community; but it is difficult, in my opinion, to apply the word "strike" to a withholding of services for no other reason than a reprisal. . . . Whatever may be said of their action in combating the strikers, it comes as some surprise to learn that the dependents—many of whom might already be suffering through the stoppage of work—are to be vicariously punished. Such an attitude of mind is not generally associated with the medical profession, and I feel that it does not reflect our outlook on men and things. . . . In the fact that the striker endeavors to reach his purpose by imposing suffering or loss upon others is to be discovered the disfavor in which he is so generally held:
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> 1. He threatens his employer with financial ruin by rendering idle his capital, plant or machinery, and by undermining the stability of his market.
> 2. He threatens the public by depriving it of a necessary commodity or of an indispensable service.
> 3. He may use the language of intimidation toward imported labor if he does not give employment to illegal violence.

If we are in accord with the three foregoing definitive paragraphs, it would seem clear that the action taken by the physicians in the play was not a strike but a measure of reprisal. According to Dr. Welply's definition, there is nowhere record of a strike by the medical profession. Under the ethics of our profession, it is doubtful whether there ever will be. Physicians recognize the right to refuse or terminate attendance on a patient under certain circumstances. In the Principles of Medical Ethics of the American Medical Association is a definite statement regarding this subject: A physician is free to choose whom he will serve. He should, however, always respond to any request for his assistance in an emergency or whenever temperate public opinion expects the service. Once having undertaken a case, a physician should not abandon or neglect the patient because the disease is deemed incurable; nor should he withdraw from the

7. Stepp, W.: Ueber den Befund von Ameisensäure im menschlichen Blute, Ztschr. f. physiol. Chem. **109**: 99 (March 1) 1920.
8. Salkowski: Virchows Arch. f. path. Anat. **50**: 174, 1870.