5. The similarity of this drug in its action upon the circulation, the central nervous system, as an emetic, and in toxicity to emetine, has influenced me to recommend to Professor Lloyd that the name of this substance be changed from Kryptonine to Emetoidine, to which Professor Lloyd has agreed.

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THE OCCURRENCE AND SIGNIFICANCE OF CREATININE IN URINE.*

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Much interest has been shown of late by physiological chemists, physiologists, and others in this body, creatinine, which is excreted with normal urine of the average adult male to the extent of about 14 Gm. per day; that is, about 0.08 percent in normal urine.

This interest is no doubt due in part to the discovery of fairly accurate methods for its isolation and determination. Its isolation in pure crystalline form has been followed by the determination of its molecular and constitutional formulae and by its synthesis, so that to-day we can call it the anhydride of creatine, which, in turn, depending upon how one looks upon it, is the ureide of sarcosine or methyl-glycocoll; or, methyl-guanidine-acetic acid.

By the direct union of methyl-glycocoll and cyanamide creatine is easily synthesized:

$$CH_3.NH.CH_2.COOH + NH_2CN \longrightarrow NH_2.C(NH).N(CH_3).CH_2.COOH.$$

The last product, creatine, is a colorless, crystalline substance which readily passes over to its anhydride creatinine. Aqueous solutions of creatine are neutral, but of creatinine are distinctly alkaline. Such alkaline solutions are unstable but the solution becomes stable upon acidifying.

Creatinine will reduce Fehling's solution, and will also reduce picric acid to picramic acid in alkaline solution. The picramic acid solution is distinctly reddish and upon this property of creatinine is based Folin's colorimetric method for its determination.

The process by which creatinine may be obtained in pure form is given in Hawk's "Physiological Chemistry," last edition.

It is probable that the creatinine of the urine is derived from the creatine of

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the tissues of the body. Creatine, as is known, occurs widely spread throughout the body (about 120 Gm. to the average adult) in the blood, brain, thyroid body, but particularly in the muscles. Where the change from creatine to creatinine occurs is not definitely known, but the liver tissue and muscle tissue are, among several others, capable of producing it; may be an enzymatic action. The source of creatine is even more problematical. Urea may be concerned in its synthesis; recall its chemical relation to that body. By some it is thought to be produced by metabolism notable within muscle tissue; that is, not represented in the products resulting from catabolism, but in the "filings" and "scraps" unused or brushed aside in repair work.

Several interesting facts are cited to show that "creatine and creatinine are products of endogenous metabolism in the body." That the amount of creatinine excreted varies directly as the weight of the body is significant. Again its excretion does not depend in amount on the quantity of protein in the food. During starvation its excretion (or creatine + creatinine?) is remarkably constant. How different is this excreted nitrogenous body in this respect from urea. The two have been compared repeatedly by Folin, who suggests that the excretion of creatinine is "an index of the real catabolism of the vital machinery of the body proper, in distinction from that catabolism which increases the free energy;" that is, it indicates the upkeep necessary, not the "gasoline" consumption. Hence the study of its determinations should be a basis for diagnosis as to general cell vitality.

Sufficient clinical data of its occurrence and amount in pathological urines are as yet not at hand. Shaffer found a low creatinine content in a large number of pathological urines representing a variety of conditions which forced him to conclude that an "abnormally small amount of this substance is by no means peculiar to any one disease." But against this is the fact that creatine and creatinine both appear in the urine at times and cannot with certainty as yet be distinguished between quantitatively. Shaffer's urines might have greatly varying amounts of creatine in them.

Upon the accurate separation and determination of these two, creatine and creatinine, many perplexing and interesting problems can be solved, such as the possible part played by creatine in muscular contraction, or whether the quantity of creatine in urine is an index to the rejuvenescence of cell protoplasm. Possibly it is creatine and not creatinine that may have the greater significance in urine. The whole problem is interesting and its solution may be of much value.

The writer does not claim to have presented any new lights bearing upon this subject, but rather to have presented a combination of certain of the discoveries and opinions of others.

If he has aroused renewed interest in this hackneyed subject of urine analysis the purpose of the paper has been fulfilled.

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