symptom of uræmic poisoning being present. Christison[a] dwells forcibly on the fact that he had repeatedly had occasion to remark the absence of any affection of the head, notwithstanding that the blood was, so to speak, poisoned with urea, in the advanced stage of granular disorganization of the kidney.

Frerichs proposed an explanation of these facts which was ingenious, and which he claimed to have demonstrated by clinical observations as well as by physiological experiments. The phenomena of uræmic poisoning are not, according to Frerichs, caused either by urea itself or by any other constituent of the urine, but occur when the urea which is accumulated in the blood is changed within the vessels by means of a peculiar ferment, into carbonate of ammonia—a transformation which readily occurs, as is known, outside of the body. It is this carbonate of ammonia which causes the morbid phenomena; and it is possible, according to Frerichs, to produce the symptoms of uræmia by the injection of carbonate of ammonia into the veins. So that for the production of uræmia two things are necessary—firstly, an accumulation of urea in the blood; and, secondly, the presence of a ferment capable of decomposing it. If no ferment is present a large quantity of urea may exist in the blood without any morbid symptom being produced.

This explanation found many supporters after its first publication, but is now pretty generally discredited. Clinical observation has not confirmed the statement of Frerichs regarding the invariable existence of a notable amount of carbonate of ammonia in the expired air in fatal cases of uræmia, and experiments on the effects of the artificial introduction of urea have also gone to contradict this theory. A modification of Frerich's theory, proposed by Treitz, to the effect that the supposed decomposition of urea into carbonate of ammonia takes place, not in the blood but in the intestinal tract, and that carbonate of ammonia is thence absorbed into the blood, met with some acceptance especially as it fell in with a highly important discovery published by Bernard and Barreswil,[b] in 1847, regarding a mode in which urea is occasionally excreted. On the basis of numerous and highly interesting experiments these observers stated that after nephrotomy has been practised on an animal, urea does not immediately undergo an increase in the blood, owing to the fact that the stomach and the small intestine take on a vicarious action and secrete urea. Once, however, excreted into the cavity of the primæ viæ, urea becomes rapidly changed into carbonate of ammonia, so that no urea can be found after the death of the animal. The objections, however, to the theory of Frerichs are equally valid as against that of Treitz.

A different explanation of the formation of urea was offered by Oppler and by Zalesky, each of whom conducted an independent set of experiments in the laboratory of Hoppe-Seyler, and also by Perls;[a] all of these observers agreed that urea is not increased in the blood after the extirpation of the kidneys, but that it is greatly increased after ligature of the ureters, the increase being greatest in from 24 to 28 hours after the operation, and that the extractives and creatine are also much increased after ligature of the ureters.[c]

It has been objected to the value of this method of experimenting that ligature of the ureters does not give rise to true uræmia, but by causing the urine to be retained in the body, promotes its decomposition and reabsorption into the system.[d] This distinction has led Vogel[e] to suggest that a distinct name should be given to cases of this kind, and he has proposed ammoniaemia to designate these, while uræmia would be reserved for those cases in which the secretion of urine is diminished or suppressed.

These experiments and observations seemed to have settled the question, and the opinion accordingly was adopted that the kidneys really formed the urea which appears in their secretion, an explanation which is, it will be seen, directly opposed to that of Prevost and Dumas. Unfortunately, however, we are again met by a number of contradictory results. Meissner found that there was a notable increase of urea after extirpation of the kidneys, and he accounts for the contradictory results obtained by Zalesky by regarding them as exceptional and caused by the vicarious action of the mucous membrane of the stomach and small intestines, separating the urea, which is no longer excreted by the usual channels.

A good deal of interest was excited by the statements originally made by Heinsius and Stockvis, and confirmed by Meissner, that the liver in mammalia contains urea. Heinsius stated that in a liver removed from the body and kept at a temperature of 40° for 20 hours, urea was found in greater quantity than in the liver immediately after its removal.

On the other hand Gscheidlen[a] made a number of comparative experiments from which he came to a conclusion opposed to that of the observers we have named. He found urea in the liver, but not in greater amount, relatively, than in the blood. He found it not only in the liver but in the spleen, kidneys, lungs, brain, and in the lens and the aqueous and vitreous humour of the eye. On the other

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[a] On Granular Degeneration of the Kidneys. Edin, 1839, p. 230.

[b] Archives Gènèrales de Médicine.

[a] Qua via insufficientia renum symptomata uraemica efficiat, quoted by Falek, Virchow's Archiv., Bd. 53, S. 335.

[c] The conclusions of Perls are as follows:—

"Qui numeri haec docent:

"(1) In bestiis, quarum renes erant excisi, ureae accumulationem non observavi; in iis, quarum ureteres subligati erant, ureae copia aucta erat maximaque inter 24—28 horas post operationem factam videbatur esse.

"(2) Copia extracti aquosi post operationem crescit.

"(3) Copia Kreatinini et omnino et praesertim cum extracto aquoso, in quo salia diversa insunt, comparata magnopere crescit."

[d] Rommelaere, de la Pathogenie des symptomes uremiques. Bruxelles, 1867, p. 4.

Handbuch der Pathologie und Therapie. Erlangen, 1856-65, S. 428.

[a] (Leipzic Engelmann, 1871. Prager Viertelgahrschrift.