for weeks, perhaps with intermissions, advancing to complete coma and death, which, however may be preceded by one or two epileptiform convulsions. Generally towards the end the other spmptoms of the "typhoid state," such as dry, brown, fissured tongue, and sordes on the lips and teeth, appear. Very often this greatly depressed condition of the nervous system is accompanied by an intense itching of the skin, so that the patient will constantly scratch himself though unconscious. There may also precede or accompany the mental disorder paroxysmal attacks of dyspnœa—so-called renal asthma, occurring generally at night, and perhaps due to arterial spasm,—as well as hiccough, vomiting and diarrhœa. The two latter symptoms would seem to be due to the irritation caused by the presence in the alimentary canal of ammonium carbonate derived from the decomposition of urea under the influence of alkalies (8).

PATHOGENESIS.

Some of the foregoing symptoms, or various combinations of them, generally arise when the normal function of the kidneys is seriously interfered with from any cause. The kidney is the main organ for getting rid of the nitrogenous waste materials of the body; therefore there is a strong presumption that at bottom uræmia depends on the non-excretion, or accumulation in the blood and tissues, beyond the normal amount, of these nitrogenous waste products, and perhaps derivatives of them, which are not formed in the normal state, but which may be developed in the abnormal condition in which the organism is placed. How does the non-excretion of these substances produce a deleterious effect? On what organs or tissues are their toxic influences exerted? What structural changes, if any, are produced which might account for the altered functions of the various organs? Can uræmic symptoms arise without organic disease of the kidneys? These are some of the questions which we must try to answer; and it seems to me that the best method to pursue in this inquiry is to begin with known and easily ascertainable facts, and from these advance as carefully as we can to the more difficult and intricate parts of the problem. The means to be employed are two—observation and experiment; observation and comparison of clinical facts when the abnormal condition recognized as uræmia is naturally presented to us, and experimental attempts to produce an analogous condition artificially. Both of these methods have been employed by numerous investigators, especially within the last few years; and I shall endeavor to collect the most reliable results and place them before you in the order indicated above.

It is an undisputed fact that suppression or diminution of urine, or the elimination of urine of more or less altered chemical constitution, due to certain organic diseases of the kidneys, is attended by symptoms described as uræmic.

Now let us first inquire what is the composition of normal urine, what is the origin of its various constituents, and what is the effect of their non-excretion. The following table (after Parkes) gives the amounts of the several urinary constituents passed in twenty-four hours by an average man of sixty-six kilogrammes (145 lbs.)

	GRAMMES:
Water	1500.000
Total solids	72.000
Urea	33.180
Uric acid	.555
Hippuric acid	.400
Kreatinin	.910
Pigment, and other substances	10.000
Sulphuric acid	2.012
Phosphoric acid	3.164
Chlorine	7.000(8.21)
Ammonia	.770
Potassium	2.500
Sodium	11.090
Calcium	.260
Magnesium	.207

The *water* of course comes directly from the blood, being derived from the ingesta, and its chief purpose is to act as a solvent for the other excrementitious matters, though a certain amount must be got rid of constantly to preserve the normal fluidity of the blood. The amount of water excreted as urine depends primarily upon the blood-pressure in the area of the renal artery, and follows therefore the laws of filtration; or,

(8). COHNHEIM. Vorlesungen über Allgemeine Pathologie.