Influence of *dl*-Methionine and Other Substances on the Nephrotoxic Action of *dl*-Serine

dl-SERINE introduced either by stomach tube or by intraperitoneal injection causes severe kidney damage in young rats^{1,2}. In view of the probable interaction of serine and methionine in the rat^{3,4}, the influence of methionine on the serine effect was studied. Male rats weighing approximately 100 gm. were given 100 mgm. *dl*-serine by stomach tube and killed 24 hours later. Litter mates received the same amount of serine, and in addition *dl*-methionine in amounts varying from 100 to 600 mgm. subcutaneously in several injections preceding and following the administration of serine. 24 rats given serine alone showed extensive renal necrosis localized in the region of the cortico-medullary junction (see Fig. 1). Of 39 animals given methionine in addition, 30 showed no lesions or only minute lesions (see Fig. 2). Only in two rats was no protective effect seen.

Fig. 1

Fig. 2

Fig. 1. NECROSIS IN THE KIDNEY OF A RAT ON A PROTEIN-DEFICIENT DIET FREE FROM VITAMIN B COMPLEX SACRIFICED 24 HOURS AFTER THE ADMINISTRATION OF 100 MG. *dl*-SERINE BY STOMACH TUBE. ($\times$ c. 50)

Fig. 2. COMPLETE PROTECTION AGAINST THE NEPHROTOXIC ACTION OF SERINE BY TWO INJECTIONS OF 100 MG. *dl*-METHIONINE IS SEEN IN THE KIDNEY OF A LITTER-MATE FURNISHING FIG. 1. ($\times$ c. 50)

Of other sulphhydryl compounds tested, *l*(+) cysteine hydrochloride was considerably less effective, while glutathione (glutamylcysteinylglycine) regularly afforded complete protection. *l*(+) Glutamic acid had a slight influence, but glycine exerted considerable protection. Similarly *dl*-alanin, glycolic acid (hydroxyacetic acid) and *dl*-threonine prevented the nephrotoxic action of *dl*-serine. *l*(+)Histidine monohydrochloride, *l*(+) arginine monohydrochloride, lactic acid, pyruvic acid and butyric acid afforded some protection, while sodium chloride and sodium acetate were without any influence.

These experiments are being extended and will be published in detail.

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Circulation in the Frog

MOST text-books of elementary zoology contain an account of the circulation of the frog. These accounts, which are based largely on the views of Brücke¹ and Sabatier², differ in minor details, but agree that the frog's heart, though possessing only a single ventricle, functions, nevertheless, so that the so-called arterial blood, returning by the pulmonary veins, is mixed only slightly with the venous blood. The mixed blood is sent through the systemic arches to the hinder part of the body. Meanwhile the head region is supplied through the carotid vessels with pure arterial blood, while the greater part of the venous blood is sent through the pulmo-cutaneous vessels to the lungs and skin.

This hypothesis, based on somewhat slender experimental evidence, proved very satisfactory, no doubt, to the nineteenth-century comparative anatomists. Then it seemed natural to seriate the incomplete double circulation of the frog, as an example of the Amphibia, between the single circulation of the fish on one hand and the double circulations of certain reptiles, birds and mammals on the other. Since the time of Brücke, however, many facts have been discovered. For example, the incompletely divided heart of *Lepidosiren* has been described³; again, the results of palaeontological investigation have shown that, so far as their skeletal elements are concerned, the modern Amphibia have departed widely from the structure exhibited by the earliest members of that group⁴. In addition, there have been described^{5,6} certain abnormal hearts of individual frogs in which the circulation could not possibly take place as the Brücke-Sabatier hypothesis requires; the fact that such frogs were apparently capable of leading a normal existence shows that the supposed selective distribution of the blood is, in fact, unnecessary.

In more recent years, Ozorio de Almeida⁷ and Noble⁸ claim to have demonstrated by experimental methods that in certain Amphibia in which the interauricular septum is complete and a spiral valve present in the conus, the arterial and venous bloods mix but little. However, Vandervael⁹, who was the first to place an illuminant under the heart and observe the passage through it of Indian ink particles by means of transmitted light, found that very considerable mixing does take place. This author also directed attention to certain physiological considerations, notably the extensive cutaneous respiration of the frog, and concluded that a mixing process is much more likely to be in keeping with the frog's mode of life; for when it is submerged the skin will be the only source of oxygen supply (apart from any stored in the lungs). He suggests that when lung breathing is used, it will supplement the oxygen content of the blood obtained from cutaneous and bucco-pharyngeal respiration, and that, by mixing, this increase will be distributed to all parts of the body.

Recently¹⁰, Vandervael's experiments have been repeated using methods which obviate both the possibility of the injection increasing the cardiac intake in such a way as to invalidate the results, and also that of affecting the heart by heat derived from the illuminant. The results obtained confirm Vandervael's observations. By the methods used it can clearly be seen that (a) the spiral valve of the conus does not direct the first blood to leave the ventricle into the pulmo-cutaneous vessels, as the old hypothesis requires; (b) that the blood commences to move and ceases movement in the carotid, systemic