The occurrence of renal blood urea contents markedly higher at times than arterial urea contents appears to be proof of the occurrence of reabsorption of urea from the kidneys.

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Production of Anatomical Lesions in the Isolated Organ.

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Since the frog's kidney has proved such a suitable organ for the investigations of the physiologist it seems likely that an examination of its structure and activity under abnormal conditions might be of value. The present report concerns one aspect of such a study. We have previously described the lesions in the frog's kidney when renal toxic agents, including potassium bichromate, corrosive sublimate, uranium nitrate and snake venom, are injected into the living animal.[1] The next step has been the elaboration of a method to test their functional activity, and in this procedure it was found advisable to isolate the organ and perfuse it with a modified Locke's solution.[2] While it was functioning normally under these controlled conditions the same toxic agents were administered by way of the perfusion fluid and the resulting disturbance of functional activity noted. These will be described at another time.[3] The tissues were then fixed and examined histologically.

In this study our first procedure was to determine that normal perfusion of the organ produced no structural changes. It was found that after 6 hours of such treatment the most delicate cytological structures such as the brush border of the epithelial cells, the mitochondrial elements and the achromatic spindle of mitotic figures, which are occasionally found in the frog's kidney, were entirely normal in appearance.

In the tissues of the damaged kidneys all the pathological lesions that had developed in the kidneys of the living animal after poisoning with the same toxic agents were observed, except those which

[1] Oliver, J. and Smith, P., *J. Exp. Med.*, 1930, **52**, 181.

[2] Oliver, J. and Shevky, E., *J. Exp. Med.*, 1929, **50**, 15; *Am. J. Physiol.*, 1930, **93**, 363; MacKay, E., and Oliver, J., *J. Exp. Med.*, 1930, **51**, 161.

[3] *J. Exp. Med.*, in press.

require a longer time for their development than was available in the experiment or which depend on the presence of the circulating blood. The epithelial lesions were localized to that part of the tubule which was most susceptible in the living animal. They consisted of necrosis with the typical nuclear changes of pyknosis and karyolysis, desquamation and cast formation. The granular changes involving the mitochondrial apparatus, cloudy swelling, agglutination and clumping or solution of the granular structures were especially well reproduced. In the glomeruli, the lesions were modified from the appearance seen in the lesion in the living animal by the absence of blood in their capillaries, but the same deposits of fibrinoid material were present in Bowman's space, and similar areas of necrosis were evident in their tufts. In the interstitial tissues of the organ, areas of edema identical to those found in the kidneys of the poisoned animals were seen.

These findings can be summarized by the statement that an experimental nephritis was produced extra-vitally, if we may use such a term, with all the essential lesions that develop *in vivo*. The structural changes are obviously not the result of mechanical effects due to variations in such physical forces as the osmotic pressure of the artificial perfusion fluid, for these kidneys were functioning in an entirely normal manner before the lesion was produced, concentrating urea or dyes many times, retaining sugar or diluting salts, and as we shall show later, the disturbances of functional activity were similar to those which follow the action of the same toxic agents on the kidney of the living frog. The lesions can therefore only be explained as the result of pathological processes which were apparently similar to those which occur *in vivo*, since their structural and functional effects were similar.

The method of Ludwig may, therefore, also serve as a means of study of anatomical as well as functional processes. The value of a single approach towards these two aspects of vital activity is obvious. The possibility of control that the method makes possible is analogous to that obtained by tissue culture, but with it not only tissue reactions may be examined, but the reactions of an entire organ to controlled conditions may be followed both structurally and functionally.