

results suggest that the "S" organisms produce a soluble specific substance which may be analogous to the soluble specific substance produced by Pneumococcus.

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**Filterability and Mechanisms of Excretion of Certain Dyes by
the Frog's Kidney.**

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This report concerns a correlation of the filterability of certain dyes with the manner of their excretion by the kidney as tested by the method of perfusion. The details of the technique of this method may be found in previous publications¹ and the results of our present experiments briefly summarized as follows:

Filtration of a series of dyes through collodion membranes gave the following average values of filterability. Phenol red, 100%; indigo carmine, 90%; toluidin blue, 60%; and neutral red, 35%. Trypan blue was unfilterable as such, but the pink component of the dye passed through the filter in small amounts, and brilliant red was entirely unfilterable.

By perfusion of either the glomerular or the tubular circulation of frogs with these dyes, it was found that phenol red and indigo carmine were eliminated chiefly through the glomeruli. Toluidin blue and neutral red on the other hand were excreted principally by the tubules. Trypan blue was excreted in the relatively short period that our experiments continued only in traces, and these traces passed through the glomeruli most readily and showed the same separation of the components of the dye as was observed in the filtration process, for the urine was pink in color. Brilliant red did not pass through either tubules or glomeruli.

Anesthesia of the tubules and repression of their function during the course of dye excretion increased the rate of elimination of phenol red and indigo carmine, but decreased the rate of excretion of toluidin blue and neutral red. When the glomeruli were damaged in such a way as to increase their permeability, both components of trypan blue escaped into the urine, which assumed the bluish color

¹ *J. Exp. Med.*, 1929, 1, 15.

of the original dye solution. Damage to the glomeruli also allowed the passage of brilliant red through the glomeruli.

These findings are summarized and correlated in Table I.

TABLE I.

Filterability	Dye	Glomerular excretion	Tubular excretion
Easily filterable	Phenol red	Marked	Slight
	Indigo carmine	Marked	Slight
Moderately filterable	Toluidin blue	Moderate	Moderate*
	Neutral red	Slight	Marked
Slightly filterable	Trypan blue	Pink element—trace	Slight
Unfilterable	Brilliant red	None	None

* Some tubular damage from dye.

We interpret these results as indicating that dyes of small particle size pass readily through the glomerular filter whereas those of less filterability require the activity of the tubular epithelium for their elimination. The similar separation of trypan blue into its components by the intact glomerular membrane is further evidence that the processes of glomerular excretion and filtration are analogous.

It was later noted that neutral red in the acid form was excreted at a much greater rate than the alkaline form. Further analysis showed that this increase was due to an increased passage of this dye through the glomerulus, a process which as we have just noted is relatively slight under physiological conditions of acidity.

A new examination of the filterability of neutral red, comparing the alkaline and acid forms showed that the latter was from 3 to 4 times as filterable as the alkaline form. Direct observation of the two forms by ultramicroscopy proved that this increase in filterability was due to a decrease in the size of the dye particles.

It would seem, therefore, that one very important factor in the determination of the mechanism of the elimination of a dye, whether glomerular or tubular, is the size of the particles into which the substance is dispersed.