sues the several compounds may be rated about as follows:

a. Acranil: liver > spleen > kidney > lung

b. Win 2390; liver > kidney > spleen > lung

c. Win 2389; spleen >liver > kidney > lung

d. Win 2333; liver > spleen > kidney > lung

It is of interest to compare the metabolism of these drugs with that of Atabrine, although the data available for comparison[9] were obtained with a higher dose than any used in this work: 675 mg/kg. None of these 4 drugs was absorbed as fast as Atabrine. Only at the lowest dose levels were as small (absolute) amounts found in the gastrointestinal tract as following Atabrine, and even less than 50 mg/kg of Win 2390 would have been required to produce an equivalent result. The reported tissue-distribution of Atabrine resembles that of Win 2389 in item[4] above. However, the latter compound was still only about half absorbed when the animals were killed. Win 2390 differed from Atabrine chiefly in giving higher liver concentrations. Even at the lowest dose level Acranil produced much higher liver concentrations than 675 mg/kg of Atabrine, and the other tissues contained amounts of the same order as following Atabrine.

It was noted that these compounds undergo some chemical alterations, probably in the liver, followed by excretion through the bile. This was shown by the fact that the ethylene dichloride extracts of both the intestinal (plus cecal) contents and of the feces contained an intensely yellow non-fluorescent substance which remained in the organic solvent, even when the latter was extracted with N HCl. This indicates that the basic side chain had been lost, leaving a neutral compound, possibly an acridone. A similar metabolic process has been observed by Hawking and Frazer in their studies of Miracil D.[15]

Summary. The absorption, excretion, and tissue-distribution of 4 compounds of the 9-aminoacridine series have been studied in rats at oral dose levels ranging from 50 to 500 mg/kg. At any dose level Acranil concentrates in the tissues to the greatest extent, while the other compounds follow in this order: Win 2390, 2389, 2333. For any single compound, the tissue concentrations ordinarily increase with the dose, the largest amount being found in the liver. In order of increasing rate of absorption the compounds are Win 2390, Win 2389, Acranil, Win 2333 but none of these is as completely absorbed within 24 hours as has previously been reported for Atabrine.

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Regeneration of the Neural Portion of the Retina from Pigment Cells in Adult Urodele Eyes.* (17439)

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In previous experiments on grafted adult salamander eyes, it has been shown by the author,[1-3] that degeneration of the neural elements of the retina is followed by regeneration. The retina can be regenerated with sub-

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[2] Stone, L. S., and Farthing, T. E., *J. Exp. Zool.*, 1942, **91**, 265.

[3] Stone, L. S., and Ellison, F. S., *J. E. Zool.*, 1945, **100**, 217.

sequent return of vision at least 4 times in the same eye repeatedly transplanted.[2] The functional patterns associated with each of the retinal quadrants are reestablished and the visuomotor responses of the host are determined by the orientation of the graft.[4-7]

Regeneration of the retina in amphibians especially in larval urodeles has been reported previously by other investigators. As to its source of origin iris tissue has been claimed by some authors.[8-10] Retinal tissue at the ciliary margin[8,11] and ganglion cells in the fully differentiated retina[12] have been proposed as the source. One of the above mentioned investigators[8] believed that the regenerating retina in larval urodeles could also be derived from the pigmented epithelial layer.

An extensive study has been made to settle the question of the source of origin of the regenerating neural portion of the retina in the eye of the adult urodele, *Triturus v. viridescens*. In various groups of experiments over 500 grafts of iris tissue have been placed in the aqueous and vitreous chambers of the eye. None of them has given rise to retinal tissue. A detailed study was made of the degeneration and regeneration of the retina in 200 grafted eyes preserved at close intervals for at least 3 months after operation. Degeneration spreads throughout the neural retina during the first 3 weeks. In some cases destruction proceeds at different rates in various parts of the same eye and when degeneration overlaps early stages of regeneration it is more difficult to obtain a clear picture of the origin of the new retina. However, when degeneration is simultaneous in all parts it is clearly demonstrated that the new neural portion of the retina derives its origin from the surviving retinal pigment cells. This fact was demonstrated also in a study of 100 eyes from which the entire neural retina was successfully removed intact through a dorsal slit along the corneo-scleral junction after it had been detached from the underlying retinal pigment layer by a gentle stream of Ringer's solution emerging from a micropipette. The excised retinae were preserved and later served as controls for the eyes with regenerating retinae.

As soon as the pigment epithelial cells lose contact with neural retinal tissue they can be followed step by step as they change their structure and function. At first they become flattened oval densely pigmented bodies. Soon they increase in size and undergo mitosis. One daughter cell migrates inward, loses its pigment and gives rise to a chain of cells which later form the new neural retina. The other takes on the characteristics of a retinal pigment cell. Its pigment granules regain their ability to migrate in the presence of light only when the rod and cone cells of the new retina above them differentiate. It was also noticed in these experiments that the lost vitreous body was eventually replaced.

In another group of 63 eyes various injuries were made by inserting a micropipette through a wound in the cornea and removing by suction limited areas of the neural portion of the retina. In the larger wound areas the denuded pigment cells responded in the same manner as in those eyes from which all of the neural retina was eliminated. On the other hand if the wound area was small a rapid proliferation and migration of the heavily pigmented cells partially filled the space before depigmentation spread among them. As in other wound areas repair was carried to completion to replace the lost retinal tissue. There was always a sharp demarkation between the surrounding intact neural retina and the regenerating one. No evidence was found to support the idea that surviving cells of the neural portion of the retina bordering the wound ever contributed to the formation of the new retina.

To bring forth a response from the retinal

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pigment cells it is not essential to destroy or completely remove the neural portion of the retina. If a segment of the fully differentiated or regenerating neural retina becomes detached as an elevated fold it may survive. In the arch beneath it the retinal pigment cells immediately give rise to a secondary neural retina.

In 59 experiments segments of the eye wall containing the retinal pigment layer were implanted in the vitreous chamber of recipient eyes from which the lens had been removed. They also showed the development of neural retina from the pigment layer. It is therefore concluded that the regenerating neural portion of the retina in the adult urodele eye has its only source of origin from the cells of the retinal pigment layer.

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Enhancement of Hemolytic Activity of Complement by Polyethylene Glycols.* (17440)

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In the course of an investigation designed to test the ability of various substances to prevent the deterioration of complement, it was found that certain of the polyethylene glycols greatly enhance the hemolytic activity of complement. The polyethylene glycols, a series of polymers with the general formula $HOCH_2(CH_2OCH_2)_xCH_2OH$, are soluble in water and in many of the aromatic hydrocarbons. The compounds with average molecular weight up to 700 are liquids; those with average molecular weight above 1000 are wax-like solids, sold under the trade name "Carbowax".† This paper constitutes a preliminary report on the effect of the polyethylene glycol carbowax-4000 on the hemolytic activity of complement, as determined by complement titrations in the presence and absence of this compound.

Procedure. Complement titrations were carried out according to the 50% hemolysis end-point method developed by Mayer *et al.*,[1] and Kent *et al.*[2] The reaction mixtures, 20 ml in volume, had the following composition: 1) 1 part complement, the dilution so adjusted as to yield final dilution values ranging from 1:3300 to 1:950; 2) 1 part standardized suspension of sensitized erythrocytes; 3) either 2 parts of buffered saline,[3] or 2 parts of an 8% solution of carbowax-4000 in buffered saline. The sensitized erythrocytes were well mixed with either buffered saline or carbowax-4000 solution, and then the complement added dropwise with constant agitation. All components were kept in ice-water until time of incubation. The reaction mixtures thus prepared were incubated at 37°C for 60 minutes, with frequent agitation. After centrifugation of the mixtures, readings of per cent hemolysis in the supernates were made at 5500 Å in a Coleman spectrophotometer, an optical density of .500 representing complete hemolysis. Titrations were carried out in duplicate. Controls were set up of 1) sensitized erythrocytes and carbowax-4000, 2) unsensitized erythrocytes and carbowax-4000, and 3) complement, unsensitized erythrocytes and carbowax-4000.

Results and discussion. None of the control tests showed any hemolysis. The results of the titrations are shown in Fig. 1, in which

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† Carbon and Carbide Chemicals Corporation, New York.

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2 Kent, J. F., Bukantz, S. C., and Rein, C. R., *J. Immunol.*, 1946, **53**, 37.

3 Mayer, M. M., Osler, A. G., Bier, O. G., and Heidelberger, M., *J. Exp. Med.*, 1946, **84**, 535.