Brodie suggests that teleologically these metabolic transformations are unnecessary as the gills act as a dialyzing membrane allowing foreign compounds to diffuse from plasma to an almost infinite seawater environment. We investigated plasma half times of various agents and studied oxidative and reductive drug metabolic pathways in vitro. The following points summarize our findings:

1. Plasma half-times of very lipid soluble and readily diffusible substances did not suggest a rapid diffusion of these substances from dogfish (Squalus acanthias) plasma to seawater. The plasma half-time of 4-aminoantipyrine and sulfanilamide after intraarterial injection was approximately 4 and 6 hours.

2. Dogfish liver homogenate fortified with a proven TPNH ($NADPH_2$) generating system was unable to oxidize hexobarbital or chlorpromazine and was also unable to convert aminopyrine to 4-aminoantipyrine.

3. Reductive metabolic pathways were investigated using either tissue homogenate of 9000 x g supernatant fortified with a TPNH generating system and incubated under nitrogen for one hour at 37°C. There was no difference in results obtained with homogenate when compared to 9000 x g supernatant. Homogenates of dogfish liver, spleen and testes were able to reduce the azo linkage of neoprontosil yielding the metabolite sulfanilamide. None of these tissues were able to reduce the aromatic nitro group of p-nitrobenzoic acid to produce p-aminobenzoic acid. Homogenates of livers from embryonic, male (adult), and adult female dogfish showed no difference in their capacity to reduce neoprontosil. Skate, lungfish (Lepidosiren), and hagfish (Myxine glutinosa) liver homogenates were also able to reduce neoprontosil. However, only skate liver homogenate was able to reduce the aromatic nitro group of p-nitrobenzoic acid.

Azo-reductase activity of dogfish liver homogenate was shown: a) to be TPNH dependent; b) to increase with increasing temperature from 5 to 37°C; c) to increase with increasing levels of TPN; d) to be stimulated fivefold by flavin-adenine dinucleotide (FAD) 10^{-3}M; e) to be inhibited only 50% by an atmosphere of oxygen; f) to be relatively unaffected by SKF-525a, a drug metabolizing enzyme inhibitor, whether added directly to the incubate; preincubated; or injected into the animal 30 min prior to sacrifice; g) to increase with increasing pH to an optimum at 7.4 - 8.0; h) to increase with increasing levels of substrate as high as 10^{-2}M; and i) to indicate a very low affinity of the enzyme for the substrate.

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ULTRA STRUCTURE OF 1) FISH KIDNEYS, 2) THE URINARY BLADDER OF THE FROG

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During the summer of 1964, two projects were carried out, one dealing with the fixation of fish kidneys, the second with the study of the microcirculation in the frog's urinary bladder. Primarily, the kidneys of the goosefish, Lophius piscatorius, were fixed with a variety of fixatives, since earlier studies of this kidney had demonstrated a poor preservation of some cell types. The fish were obtained by deep sea dragging, and upon capture the kidneys were removed imme-

diately. In one type of experiment, a large part of the kidney was immersed in the fixative; in a second type, small pieces of the kidney were cut out and subsequently immersed. Glutaraldehyde and osmium tetroxide were used separately or combined as fixatives. The best results were obtained with a combination of the two fixatives, although it did not represent the very best preservation. An analysis of these specimens is under way.

As a second project, the microcirculation was studied in order to establish the fine structural details of the arterial and the venous capillaries. It was found initially, that the urinary bladder of the frog represented an ideal situation where the microcirculation could be studied advantageously in vivo, since the bladder wall contains a monolayer of small blood vessels. However, it was subsequently discovered that the fixatives applied directly at the surface of the bladder would cause the smooth muscle components of the wall to contract, and thus distort the microcirculatory pattern observed.

1965 #35

ULTRA STRUCTURE OF 1) THE ABDOMINAL SKIN OF THE FROG, AND 2) FISH CHROMATOPHORES

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During the summer of 1965, two projects were carried out, one dealing with the microcirculation of the abdominal skin of the frog, the second with fish chromatophores.

During the winter of 1964, the study of the microcirculation continued on rabbits in order to improve the preparation technique by using a double technique: examination and filming of the living material, and then fixation of the material and restudy of the same site, first with phase contrast microscopy, and then with low and high magnification electron microscopy. This technique was used in studying the circulation of the abdominal skin of the frog, where the capillary network is embedded in the dermal connective tissue, and thus does not move upon application of the fixative. During the first several weeks, the microcirculation was also studied in the wings of bats. However, it turned out that the circulation could not be stopped momentarily by the local application of several kinds of fixatives, and as a consequence, study of this animal had to be abandoned.

Various types of chromatophores were studied in the marine teleost Fundulus heteroclitus. Light and dark adapted fish were used, and the dorsal scales of males were removed from the living fish and immersed in glutaraldehyde or osmium tetroxide. Initially, the epidermal melanophores were studied during pigment dispersion and concentration. Subsequently, xanthophores and iridoleucophores were fixed for detailed studies. A peculiar, flat chromatophore was discovered in the dermal connective tissue which did not respond readily to a light or a dark background. This type of chromatophore had central enclosures of probably crystalline nature, since they were colorless when observed with direct light, but gave a blue reflexion when observed with incident light.