

298, and 386 days. The livers of 3 of these animals showed a severe diffuse fibrosis and in all of them a severe fatty infiltration was observed. A typical protocol follows:

Dog F41 was placed on the high fat diet on November 29, 1938, and died December 20, 1939. Its weight at the start was 11.2 kg and at death 12.8 kg. It attained a maximum weight of 16.5 kg during the course of the experiment. The liver weighed 695 g. It was uniformly green in color, firm and rubbery in consistency. It cut with resistance and was lobulated on the surface.

Microscopically (Figs. 1 and 2) the liver showed marked fibrosis and a fatty infiltration. The liver cords were broken up into fragments and in no place had the original pattern of the liver been retained. Fragments of cells were found between proliferating strands of connective tissue that were growing in all directions but had no particular distribution with respect to portal areas or central veins. Blood sinuses were engorged and appeared like fibrous walled blood vessels rather than sinusoids. Some bile duct proliferation had taken place but their duct cells were difficult to recognize because they, too, were enmeshed in connective tissue. Many plugs of inspissated bile were present in large and small masses.

It is of interest to note that the diffuse character of the fibrosis reported here distinguishes this type of cirrhosis from that previously described for dogs receiving alcohol,<sup>3</sup> although the outstanding anatomical change preceding the fibrosis in both instances, as well as in the depancreatized dogs, was severe fatty infiltration of the liver.

## 11288 P

### Immediate Generalized Skin Reactions in Hypersensitive Guinea Pigs.\*

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Immediate generalized skin-reactions following contact with or ingestion of allergens have been observed in humans but not hitherto in animals, although Dienes and Simon<sup>1</sup> reported a generalized

<sup>3</sup> Connor, C. L., and Chaikoff, I. L., *PROC. SOC. EXP. BIOL AND MED.*, 1938, **39**, 356.

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<sup>1</sup> Dienes, L. and Simon, F. A., *J. Immunol.*, 1935, **28**, 321.

delayed reaction in guinea pigs treated with human serum. No observations of generalized skin-reactions in animals, due to simple chemical substances, have been noted in the literature. It seemed of interest, therefore, to report recent observations of such effects in a number of guinea pigs sensitized to citraconic anhydride, together with the sensitization of guinea pigs to new anhydrides having similar properties.

The animals were rendered hypersensitive to citraconic anhydride by a method previously described<sup>2</sup> and were tested by scratching the skin through a 25% dioxane solution of the same substance, usually at intervals of 2 weeks.

It was regularly observed that the more hypersensitive the guinea pig the quicker the onset of the reaction. Animals developing generalized reactions showed within a very few minutes a large local wheal and erythema surrounding the scratch, often several centimeters in diameter. At the same time in both contiguous and remote parts of the skin some pigs showed a diffuse pinkishness apparently accompanied by slight thickening, while others exhibited discrete, urticaria-like wheals with distinct elevation and pinkness. Often some of the old injection-sites on the back flared up at the same time, with marked wheal-formation. The erythema reached a maximum 20 to 30 minutes after the test, following which it gradually faded. Edema associated with reactivated sites and other lesions distant from the original scratch increased for about 2 hours and then also diminished. By the next day all such subsidiary reactions had completely disappeared. In striking, possibly significant contrast to this, the reaction in the vicinity of the scratch after receding to a minimal color and edema in 4 to 5 hours, gradually increased in pinkishness and induration to a second maximum reached about 24 hours after the test. This secondary or delayed reaction at the original site slowly disappeared in the course of several more days. At no time were there any definite symptoms of anaphylaxis although coughs and shivering were occasionally observed. The mechanism of these effects requires further study.

These phenomena invite comparison with the occasional severe generalized skin-reactions from drugs observed in humans. Practically all guinea pigs treated with citraconic anhydride become hypersensitive but in our experiments only 6 out of 61, about 10%, gave generalized reactions. Other pigs less strongly sensitized, however, produced similar but less intense reactions, the subsidiary

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<sup>2</sup> Jacobs, J. L., Golden, T. S. and Kelley, J. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **43**, 74.

lesions being fewer in number and not present on areas far from the scratch. Unsensitized control animals were quite negative.

In small-scale experiments with 2 new substances, maleic and acetic anhydrides, using the same technic as with citraconic anhydride,<sup>2</sup> extensive immediate wheal-and-erythema reactions were produced, with subsidiary reactions in some cases. With maleic anhydride such isolated reactions appeared many centimeters from the site of scratch. It would seem profitable to examine, on a larger scale, the capacity of these compounds to produce generalized reactions.

Excellent sensitization-effects have been produced by the same method with a third substance, propionic anhydride, using patch-tests with a 25% dioxane solution. Scratch-tests, however, did not yield definite wheal-and-erythema reactions, which is interesting in view of the close chemical relationship between this compound and acetic anhydride.

## 11289 P

### Solubility of Fluorosed Enamel and Dentine.

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The reduction of caries incidence in humans and rats ingesting fluorine may be the result of a decreased acid solubility due to the incorporation of fluorine in the dental tissues. Support for this belief is apparent in the finding of more fluorine in caries-resistant than carious enamel and dentine.<sup>1</sup> If this assumption is correct, we might expect the greatest reduction in acid solubility in the enamel and dentin from mottled teeth since it has been shown that these teeth contain the greatest amounts of fluorine.<sup>2</sup>

The acid solubility of normal and fluorosed rat teeth was studied. The upper incisor teeth were used in all cases. The fluorosed human teeth were obtained from areas where dental fluorosis is endemic and showed a mild degree of "mottling". The fluorosed rat incisors represented were of 2 grades, (1) *mild*, produced by a diet

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<sup>1</sup> Armstrong, W. D., and Brekhus, P. J., *J. Dent. Res.*, 1938, **17**, 339.

<sup>2</sup> Armstrong, W. D., and Brekhus, P. J., *J. Dent. Res.*, 1938, **17**, 27.