feeding. We feel that this is not the explanation of our negative results. In some of our pancreatectomized dogs the urine output was not more than in normal dogs of similar weight. Further, the polyuria observed after thyroid feeding is much greater than that in any of the diabetic dogs in the above series.

In some of the pancreatectomized animals the B.M.R. and heart rate were observed during thyroid administration or anterior pituitary injections. In each case a typical rise occurred, which suggests that the diuresis is not the result of accelerated metabolism. Further work will be necessary to explain the polyuria of hyperthyroidism and its absence in pancreatectomized animals.

Summary. The diuresis produced in normal animals by thyroid administration fails to occur in pancreatectomized dogs although the metabolic rate is increased.

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Van den Bergh Reaction of Bilirubin in Xanthochromic Cerebrospinal Fluid.

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It is well recognized that in blood serum normal bilirubin within certain limits of concentration gives a delayed reaction in the Van den Bergh test (diazo reaction). This type of reaction differs from the prompt reaction obtained with isolated bilirubin and that encountered in a variety of pathological states. In attempting to explain this difference numerous factors have been considered. The most thoroughly studied of these concern changes in chemical constitution of the bilirubin molecule, changes in adsorption of the bilirubin by blood colloids and bilirubin concentration. None of the explanations has been universally accepted.

An important reason for the lack of conclusive experiments which would solve this problem is that much of the work has been done on blood where it is practically impossible to control all of the factors properly. Not only are the colloids in relatively high concentration, but also the influence of the liver can not be excluded entirely even in dehepatized animals.

It would seem that much information could be gained from a study of the phenomena under less complicated conditions. Such conditions are found in the cerebrospinal fluid. Influence of the

liver can be excluded almost entirely and the colloids (proteins) are present normally in such low concentration as to be practically negligible. Even the concentration present under extreme pathological conditions is very low when compared with that normally present in the blood.

Soon after a small quantity of blood is introduced into the ventricles of the brain or into the subarachnoid space the cerebrospinal fluid becomes xanthochromic. Obviously the color is produced by a pigment derived from hemoglobin and is undoubtedly identical with bilirubin formed elsewhere in the body including that normally present in the blood serum.

The present paper deals with the type of Van den Bergh reaction obtained in 20 samples of xanthochromic cerebrospinal fluid taken from 15 patients. In the majority of the patients the cause of the xanthochromia was subarachnoid hemorrhage. In no case was the patient jaundiced. That no appreciable amount of bilirubin was introduced directly with the blood was determined in several of the cases where preliminary samples were taken soon after the hemorrhage and before xanthochromia developed.

The technique of the Van den Bergh was the same as that employed with blood serum except that a control tube of the test fluid diluted with distilled water was used as a blank to offer a contrast with the color reaction. This was necessary because the amount of pigment present was very small. The time of first appearance of pink color and that of its maximum development were noted. Quantitative determinations were made also whenever the degree of color was great enough to match with the standard. Protein content was measured roughly by the use of the Pandy and nitric acid ring tests.

In 13 of the 20 samples (65%), the color appeared promptly after the addition of the reagent. The full color developed in from 1 minute to 2 hours. These reactions corresponded with the "prompt direct", "prompt biphasic" and the "delayed biphasic" reactions of the literature but for the sake of simplicity they will be grouped together as "prompt" reactions in this discussion. The remaining 7 samples gave reactions that were delayed from 2 to 30 minutes. They attained their maximum colors within 2 hours.

By comparing the type of reaction with the concentration of pigment it was found that in every case where the concentration exceeded 0.3 mg. % a prompt reaction occurred. When the concentration was lower the types of reactions were equally divided between prompt and delayed.

In a similar manner the type of reaction was compared with the protein concentration. In all cases where the protein concentration was within normal limits the reaction was prompt. When the concentration was above the normal the type of reaction varied.

However, when the results were tabulated in such a way that there was a progressive increase in the pigment concentration with increasing protein concentrations for each pigment value the correlation was quite definite. Prompt reactions occurred in all cases where the protein concentration was normal and also where the pigment concentration was high regardless of the protein content. When the pigment level was relatively low and the protein content high the reactions were predominantly delayed.

From these results it can be concluded that the type of Van den Bergh reaction of the bilirubin in xanthochromic cerebrospinal fluid depends upon a reciprocal relationship between the pigment and protein concentrations. While it cannot be said definitely that the same relationship holds true in blood serum there are good reasons for believing that such may be the case. It seems significant that reactions quite similar to those described are found in the blood of many cases of anemia associated with over production or retention of bilirubin. It is quite possible that these reactions are comparable directly with those in this series where the pigment concentration was increased disproportionally over the protein concentration. This would lend support to the view set forth by Barron,[1] that the bilirubin of normal blood serum is prevented from reacting promptly by adsorption on colloids (proteins) and that its ability to react in this manner is restored when there is failure of complete adsorption. In the opinion of the authors this renders it unnecessary to introduce other factors such as the influence of liver cells to explain the prompt reactions in retention jaundice.

[1] Barron, E. S., *Medicine,* 1931, **10**, 77.