THE RENAL THRESHOLD FOR BILIRUBIN

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There appears to be scanty evidence as to the exact renal threshold for bilirubin. Van den Bergh (1928) states that it is 1/50,000 (2 mg./100 ml.) with remarkably few exceptions, but does not say how exact this estimate is, apparently basing his statement on numerous disconnected observations. This figure appears to be quoted by others.

Weiss (1935) observes: “It is stated that bile does not appear in the urine until four units (i.e., 2 mg./100 ml.) are present in the blood. In haemolytic jaundice this relation does not hold, since it is quite possible to have between five and 18 units present in the blood with no bile in the urine.” Whithy and Britton (1946) quote the same figures, and Harrison (1947) quotes Weiss directly, but suggests that the use of sensitive urine tests would modify his claims for the threshold value, and that this can be 0.5–1.0 mg./100 ml. With (1943), on the other hand, states that the threshold value lies between 2 and 6 mg./100 ml., with considerable variation.

An opportunity to investigate the question occurred during an epidemic of infective hepatitis among Service patients in a military hospital. As soon as a clinical diagnosis was made twice-weekly estimations of plasma bilirubin content were made by the van den Bergh method and the Lovibond comparator (to the nearest 0.2 mg./100 ml.) on 53 patients, together with simultaneous urine tests by Fouchet’s method for bile. Although this is not quite the most sensitive method, it is not considered that its use has led to any material error in the final conclusions.

Method

The plasma bilirubin level at the time when bile was last found in the urine during recovery from the condition was noted, and for convenience was called the “above threshold” value. Similarly the plasma bilirubin level when bilirubin first ceased to be found in the urine during recovery was noted and called the “below threshold” level. It was argued that the true renal threshold must lie between these two levels. The number of occasions on which the various values for these two levels were found have been plotted as superimposed frequency diagrams in Fig. 1.

Discussion

The figure shows two significant features: (1) the definite modal values, and (2) the pronounced scatter of values.

Modal Values.— There are definite modal values of 1.0 and 0.8 mg./100 ml. for the “above” (13 cases) and “below” (18 cases) threshold levels respectively.
Fig. 1.—Superimposed frequency diagrams of 53 observations of bilirubin levels. "Below threshold" values show a standard deviation of 0.11, a mean of 0.71, and a variance of 15%. "Above threshold" values show a standard deviation of 0.93, a mean of 1.32, and a variance of 70%.

which strongly suggest that the renal threshold itself has a modal value between those levels. Both levels were recorded in the same patient on six occasions. That this did not happen more often is probably due to the fact that the rate of fall of plasma bilirubin was often too fast for the exact recording of the two levels in the same patient by the method adopted.

Scatter of Values.—This is marked and could have been due to the following factors.

True Variation in the Renal Threshold.—This possibility was suggested by the observation that, in certain cases, urinary excretion of bilirubin apparently ceased while the plasma bilirubin level remained constant or even rose slightly. A very similar phenomenon was noted by With (1943). This mechanism could account for the scatter immediately around the modes.

Variation in the Chemical Nature of Bilirubin.—It is of interest that Vaughan and Haslewood (1938), when attempting to estimate normal bilirubin levels, found a coefficient of variation of 45.93%, which is of the same order as those found in the present investigation (70 and 15%). It is not certain whether this was entirely due to variations between the persons investigated or partially to unrecognized difficulties in estimating bilirubin. That there may be unrecognized difficulties in estimating bilirubin was shown by Weiss (1935) when he drew attention to the inconstant relationship between serum bilirubin and the icterus index. The effect of any such factors on the present investigation need not be elaborated.

A well-recognized difference exists between the nature of "direct" and "indirect" bilirubin, and each is known to have its own renal threshold, which in the latter case is very variable. This has been mentioned indirectly in Weiss's statement which I have quoted. In fact, as With (1943) points out, it may be misleading to think of bilirubin as a true threshold substance at all. Both forms of bilirubin occur in the
plasma of infective hepatitis and it is considered that this is the main cause of the present findings. Those cases with a predominantly "direct" bilirubinaemia showed the modal threshold and neighbouring levels, whereas those cases with an "indirect" bilirubinaemia showed the variety of much higher threshold levels.

**Summary**

There is no one renal threshold level for bilirubin. There is a modal level, seen in a minority of cases, which lies between plasma bilirubin levels of 0.8 and 1.0 mg./100 ml. This and similar low levels occur in "direct" bilirubinaemia. A variety of much higher levels may occur in "indirect" bilirubinaemia. True variations in the threshold may occur in the same person independently of the type of bilirubin excreted.

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**References**


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