THE RELATION OF GLYCOGEN TO WATER STORAGE IN
THE LIVER

A REPLY TO THE COMMUNICATIONS OF PUCKETT AND WILEY AND OF
MACKAY AND BERGMAN

BY EDWARD M. BRIDGE AND E. M. BRIDGES

(From the Department of Pediatrics, the Johns Hopkins University, and the
Harriet Lane Home of the Johns Hopkins Hospital, Baltimore)

(Received for publication, February 11, 1932)

In a recent article in this Journal (1) we reached the conclusion
that it was not permissible to express the amount of water stored
with glycogen by an exact mathematical ratio. Puckett and Wiley
(2) and MacKay and Bergman (3) are now presenting data some-
what similar to our own, from which they conclude that each gm.
of stored glycogen is accompanied by an amount of water which
is essentially the same as that proposed by Zuntz et al. in 1906
(4). This discrepancy of views deserves clarification.

As Puckett and Wiley point out, one could not expect the ratio
of glycogen to total liver water to be arithmetically constant, for
a glycogen-free liver would then be water-free also, an obvious
absurdity. However, because present methods do not permit a
direct study of the water bound with glycogen, one is forced to
utilize either percentage of water, or total liver water in formulat-
ing any deductions. Both criteria were considered in our previous
report, emphasis being placed on the latter because of its employ-
ment by Zuntz and his associates in the original work on the
subject.

Puckett and Wiley present experimental data on a series of
eleven rats in which they found the percentage of liver water to
exhibit a high degree of constancy, while the glycogen varied from 0
to 7.62 per cent. They argue that since the sum of all liver solids
holds 2.4 gm. of water per gm. of solids \( \frac{70.3 \text{ (per cent H}_2\text{O)}}{29.7 \text{ (per cent solids)}} = 2.4 \)
therefore, glycogen, being one of them, must hold this same pro-
portion of water. Such an argument would be valid only (1) if protein, fat, salts, and in fact each one of the other liver solids caused exactly this proportion of water to be stored, or (2) if, in case the other liver solids bind varying amounts of water, the sum of their hydration properties alters with each change in the concentration of glycogen so as to maintain exactly the ratio of 2.4 gm. of water for each gm. of non-glycogen solids. The first of these possibilities has never been established; moreover, it has been repeatedly shown that, whereas the storage of protein and of minerals is accompanied by a large amount of water, the retention of fat binds little more water than could be accounted for by the supporting connective tissue. The second possibility is an obvious absurdity. It is, thus, apparent that the argument used by Puckett and Wiley is not justified under the condition of their experiment.

Based on the results of a series of measurements on rat livers, Puckett and Wiley postulate a constant percentage of liver water irrespective of wide variations in glycogen. In five of their eleven rats it will be noted that the liver glycogen content was below 0.4 per cent. If the contention of these authors were true and each gm. of glycogen held 2.4 gm. of water, such minute variations in glycogen would, at the most, have produced a change in water content of less than 1 per cent, which is well within the experimental error. For practical purposes, therefore, the glycogen of these livers must be considered constant. The thesis, thus, rests upon the remaining six experiments, one of which, with a liver water content of 63.9 per cent, they have arbitrarily excluded from the series. One may well raise the question as to how constant the percentage of liver water would have been had the authors studied a larger series of animals. The answer to this question is to be found in the data of our experiments, of those of MacKay and Bergman (3), of Lowrey (5), of Profitlich (6), and of others who have analyzed the water content of animal livers. All of these workers have found considerable variation in individual animals. This fact is illustrated graphically in Chart 1 where we have plotted our own data on rats and rabbits, the figures of Puckett and Wiley on rats, and the results of MacKay and Bergman with rabbits. While in the majority of animals the water content is not far from 70 per cent, variations are met with between
62 and 75 per cent. Unless such variations from the average are completely ignored, values could be calculated, even if the method of estimation of Puckett and Wiley were permissible, varying 30 per cent in both directions. It is, therefore, apparent that neither the premise nor the argument of these authors rests upon a firm foundation.

MacKay and Bergman (3) have made a study of the question under discussion, proceeding in a manner entirely similar to our own. Their method of calculation, based on the increase of liver water over and above that contained in a glycogen-free liver, is theoretically, we believe, the only correct approach to the problem. Examination of the data presented by these authors will show that our findings in regard to the limits and variability of the concentration of liver water and glycogen are entirely confirmed. Only in the interpretation to be placed on the findings does the difference in opinion occur.
A cursory perusal of the results of MacKay and Bergman gives one the impression that a relationship between glycogen and water in the liver has been satisfactorily established. However, on more careful examination of the experimental results and discussion, the relationship seems less clearly defined. In the first place, if such a correlation exists, it should be demonstrable in their Table I (Columns 4 and 6) and Fig. 3 in which the experimental facts are featured exclusively, uncomplicated by the somewhat questionable method of calculation used in Figs. 1 and 2. Examination of Fig. 3 will show that in their low glycogen livers variations were present between 16.5 and 30.9 gm. of water per kilo of body weight (the latter figure has been omitted from Fig. 3). Of the higher glycogen livers only five points on Fig. 3 extend outside of this range. It should also be noted that these five points were obtained in animals subjected to distinctly abnormal procedures. The amount of water administered was comparable in quantity to that used by Rowntree (7) to produce a moderate degree of water intoxication in rabbits. When there is added to excessive water intake prolonged administration of large amounts of glucose, the results of the experiments become increasingly difficult to evaluate. Conceivably, the excess of water in these high glycogen livers might be an expression of water intoxication, and not necessarily an indication of the water-binding properties of glycogen. But regardless of this uncertainty, if the attempt is made to formulate a linear relationship between the points of Fig. 3, one is confronted with the dilemma of deciding on a point of origin, since the variations at the origin cover a large extent of the ordinate. The slope of the line, and hence the ratio in question, would depend wholly on the origin chosen.

MacKay and Bergman have used the average figure of 71.0 per cent water in their low glycogen livers as the basis for all their calculations and in the formulation of their conclusions. Upon the accuracy of this figure stands or falls the value of their entire argument. That the authors themselves feel uncertain about this basis is illustrated by their discussion. If their average figure of 71.0 per cent water (actually 71.7) as the correct composition of a glycogen-free liver is used, their calculations show the series of rabbit livers to average 2.96 gm. of water per gm. of glycogen. However, because of recognized errors they believe
2 gm. of water per gm. of glycogen to be more nearly correct. If they use the water content of two out of three of our low glycogen livers as a basis, they again obtain the figure 3 gm. for their more trustworthy experiments. Our own experimental data are brought into agreement with this finding by excepting two more of our animals. In reality the true average of our experiments was 5.63, with a range of 2.9 to 14.3 gm. Incidentally, it should be noted that their own animals varied from 0.0 to 9.0 gm. of water per gm. of glycogen, these limits occurring in rabbits having identical concentrations of liver glycogen. Obviously, in spite of the best possible approach to the problem, the conclusion depends on whether one uses as a basis for calculation the average results of all available experiments or a few carefully selected ones. While these authors conclude that their studies do not oppose the statement that every gm. of glycogen stores with it 3 gm. of water, we feel that their evidence supporting the statement is entirely meaningless when considered in the light of the selective methods used and the wide variations found.

Obviously, as MacKay and Bergman suggest, factors other than glycogen must be operating in regulating the water content of animal livers, for otherwise a low glycogen liver would contain a constant minimum of water. In all probability it is the presence of these other unknown factors which so shrouds the water-binding properties of glycogen alone. It seems only reasonable to suppose that the liver water is controlled by the same physicochemical mechanism which regulates the rest of the body water, probably with a glycogen factor in addition. Until factors other than glycogen are better understood and more completely controlled, we believe it to be premature to attempt an exact mathematical formulation of the relation of liver water to liver glycogen alone. Herein lies the essential difference between our own conclusion and that of the authors mentioned above.

It has not been our aim to deny entirely the claim of Zuntz et al., of Puckett and Wiley, and of MacKay and Bergman, that glycogen is a factor in holding water in the liver. It is quite inconceivable that glycogen could be stored in the body in a dry state. It is generally accepted that proteins and salts are held in certain definite concentrations in the body; and in all probability glycogen, fats, phospholipids, etc., are also fixed with water.
However, we should like to reaffirm our original contention: that, from the data available, it is unjustifiable to define an exact mathematical relationship between the storage of glycogen and water in the liver, and that the water bound to glycogen is not of sufficient magnitude to explain the tremendous shifts in body water that occur with changes in the proportions of fat and carbohydrate in the diet. To accept a mathematical expression as the explanation of the phenomenon, as has been done in the past, tends to close the door upon further investigation of the matter. If the recent discussion has succeeded simply in pointing out the fallacies and dangers of the present orthodox conception, and has indicated the way toward a more sound physiological approach, then it has achieved its primary purpose. What the exact mechanism of the phenomenon is, will only be clarified by careful investigations of the future.

**BIBLIOGRAPHY**

THE RELATION OF GLYCOGEN TO WATER STORAGE IN THE LIVER
Edward M. Bridge and E. M. Bridges


Access the most updated version of this article at [http://www.jbc.org/content/96/2/381.citation](http://www.jbc.org/content/96/2/381.citation)

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 0 references, 0 of which can be accessed free at [http://www.jbc.org/content/96/2/381.citation.full.html#ref-list-1](http://www.jbc.org/content/96/2/381.citation.full.html#ref-list-1)