IV. "The Physiology of Sugar in relation to the Blood.—No. 2." By F. W. Pavy, M.D., F.R.S. Received June 21, 1877.

In my communication read at the last Meeting of the Society I described a gravimetric process of analysis adapted for the quantitative determination of sugar in blood and such like organic products. This process, after a little practice, is easy of application, and with proper care in manipulation admits of great accuracy being attained. I purpose, in this communication, giving results obtained by its means, showing—

(1) The amount of sugar existing naturally in the blood;

(2) The comparative states of arterial and venous blood;

(3) The spontaneous change ensuing after the removal of blood from the system.

From the rapid and marked manner in which the amount of sugar in the blood becomes influenced by altered states of the system, it is necessary that certain precautions should be strictly observed in order to obtain a representation of the natural condition. From what I have said upon former occasions it will be evident that if the blood is collected for examination during life, the animal must be at the time in a perfectly natural or tranquil state, and, if after death, the opportunity must not be given for the *post mortem* change occurring in the liver to exert its influence upon the contents of the circulatory system.

Subjoined are given three series of results illustrative of the amount of sugar existing naturally in the blood of the dog, sheep, and bullock. In two of the series six and in the other seven observations are supplied, and it is hardly necessary to remark that they represent observations taken just as they happened to present themselves. In every observation two separate analyses of the sample of blood were made. The results obtained in each are stated, and the mean taken as representing the amount of sugar present.

The blood from the dog (in Observations 1 to 6) was obtained by pithing the animal and *instantly* inserting a scalpel into the chest and freely incising the heart and large vessels. The chest was then quickly opened and the blood dipped out and treated for analysis before coagulation had occurred. In Observation 7 the blood was obtained by division of the jugular vein instantaneously after the process of pithing. So quickly does sugar in quantity find its way from the liver into the blood after pithing has been performed, that it is necessary the steps of the operation of collection should be carried out with the utmost speed.

The blood from the sheep was obtained from animals slaughtered for consumption as food, the mode of killing being that commonly practised, viz. passing a knife through the neck and dividing the vessels. The results represent the condition of the first portion of the blood that

escaped, and the time elapsing between the collection and the commencement of the analysis did not exceed a quarter of an hour. As coagulation had taken place, the clot was snipped into fine pieces with a pair of scissors, and a fair sample of the whole thus taken.

In the case of the bullock the blood was obtained from the Jewish method of slaughtering, which consists of drawing a sharp knife across the neck and cutting through all the soft structure down to the vertebral column. It is arterial blood that is thus yielded. Owing to the distance of the slaughter-house from my laboratory one hour elapsed between the time of collection and the commencement of the analysis.

Blood from Dog.

		Sugar per 1000 parts.	
Observation 1.	*a.*	·743	·751 (mean).
	b.	·758	
" 2.	*a.*	·776	·786 "
	b.	·797	
" 3.	*a.*	·706	·700 "
	b.	·694	
" 4.	*a.*	·770	·766 "
	b.	·762	
" 5.	*a.*	·777	·786 "
	b.	·795	
" 6.	*a.*	·795	·803 "
	b.	·811	
" 7.	*a.*	·932	·921 "
	b.	·910	
Average		·787 per 1000.	

Blood from Sheep.

		Sugar per 1000 parts.	
Observation 8.	*a.*	·456	·470 (mean).
	b.	·484	
" 9.	*a.*	·538	·490 "
	b.	·447	
" 10.	*a.*	·509	·517 "
	b.	·526	
" 11.	*a.*	·577	·559 "
	b.	·542	
" 12.	*a.*	·590	·569 "
	b.	·548	
" 13.	*a.*	·527	·526 "
	b.	·525	
Average		·521 per 1000.	

Blood from Bullock.

			Sugar per 1000 parts.	
Observation 14.	a.	·698	·703 (mean).	
	b.	·709		
„ 15.	a.	·515	·525	„
	b.	·535		
„ 16.	a.	·500	·492	„
	b.	·484		
„ 17.	a.	·464	·456	„
	b.	·449		
„ 18.	a.	·510	·499	„
	b.	·489		
„ 19.	a.	·589	·588	„
	b.	·588		

Average .... ·543 per 1000.

In the above experiments the blood was collected in such a manner as to give a reliable representation of the state existing during life; and it is necessary to bestow attention upon this point, for unless the proper precautions from a physiological point of view are observed, we may be led as much into error as by the faulty method of analysis. This is strikingly exemplified by the following analyses of the blood of bullocks obtained by the ordinary process of slaughtering; that is, by the animal being felled with a pole-axe, a cane being then passed down the spinal canal to destroy the medulla oblongata and spinal marrow, and blood being afterwards allowed to escape by an incision from the neck into the superior vena cava, or possibly the right auricle of the heart. I gave instructions to my assistant to get the incision made as soon as possible after the animal was felled. The first day the samples of blood of two bullocks (Observations Nos. 20 and 21) were procured for analysis, the same time elapsing between the period of collection and the commencement of the analysis as in the instances belonging to the other method of slaughtering. On the following day samples from two more bullocks (Observations Nos. 22 and 23) were procured in a similar way. The results derived from the blood obtained the first day do not differ to a material extent (strictly speaking, the sugar is a little higher) from those displayed above. The blood obtained on the second day, however, showed a notably larger impregnation with sugar; and this difference, I have reason to believe, arose from a longer time having been allowed to elapse between felling the animal and making the incision for the blood to escape.

Blood obtained from the Bullock slaughtered by the pole-axe.

		Sugar per 1000 parts.	
Observation 20.	....	a. ·595 b. ·597	·596 (mean).
„ 21.	....	a. ·655 b. ·662	·668 „
„ 22.	....	a. 1·037 b. 1·070	1·053 „
„ 23.	....	a. 1·091 b. 1·097	1·094 „

From the above results the conclusion may be drawn that the amount of sugar naturally existing in the blood of the sheep and bullock is, speaking roundly, half per 1000, or 1 part in 2000, and in the dog $\frac{3}{4}$ per 1000, or $1\frac{1}{2}$ part in 2000. There is a remarkable uniformity, looking at the results as a whole, in the constitution of the different samples. In Bernard's observations there is a striking want of uniformity, and he places his lowest limit at 1 per 1000, and says that in the normal state the amount of sugar varies from 1 to 3 per 1000 ('Comptes Rendus,' 1876, p. 1409).

In my observations upon the dog I have purposely varied the time of collecting the blood in relation to the period of taking food, but have not found that any difference is noticeable whether the collection is made a few hours after food or after an interval of 24 hours. In all the cases the animals have been kept, whilst under my notice, upon a purely animal diet.

The comparative state of arterial and venous blood possesses a bearing of the deepest physiological importance, and Bernard has given results derived from the application of his process which tend to show that an extensive disappearance of sugar takes place whilst the blood is passing from the arterial to the venous system. In the 'Comptes Rendus' (t. lxxxiii. no. 6, p. 373) five observations are given referring to the blood of the crural artery and vein, and three to the carotid and jugular. There is great discordancy in the results of the different observations. In one instance, where the least difference is noticeable, the figures stand 1·100 part per 1000 for the arterial blood and 1·080 for the venous. In the instance of greatest difference the figures are 1·510 per 1000 for the arterial and ·950 for the venous, and this relates to the carotid artery and the jugular vein. The mean difference between arterial and venous blood, drawn from all the observations, is ·300 part per 1000; and if this represented the truth it would undoubtedly imply, as is urged by Bernard, that a sufficient destruction of sugar occurs to harmonize with his glycogenic theory.

My own observations, however, supply strikingly antagonistic evidence; and, looking at Bernard's results, I am forced to the conclusion that

they show a want of proper precaution in collecting the blood, as well as the effect of a fallacious method of analysis. It is necessary that both the physiology and chemistry belonging to the course of procedure should be free from sources of error; and if the blood be collected directly after the vessel has been cut down upon, it may be expected, as a result of the effects of the operation upon the animal, to present a deviation from the natural state, and more so especially after the exposure of the carotid artery, on account of its deep situation and close contiguity to the pneumogastric nerve. As I have stated, it is between the blood of the carotid artery and jugular vein that the greatest disparity was noticed by Bernard, the difference in one case amounting to ·560 part per 1000, which is actually a larger proportion of sugar than what I have found exists naturally in the blood of the sheep and bullock.

I will mention the course of procedure I have myself adopted to obtain a true representation of arterial and venous blood in a natural state, and give the results of the analysis of the samples. Experience has shown that the effect of anæsthetics is to occasion a preternatural amount of sugar in the blood. To strictly attain, therefore, the object in view it is necessary that the collection of blood should not be made whilst the animal is under their influence.

In my first experiment I was under the necessity, on account of the restrictions of the Vivisection Act, of collecting the blood instantly after the destruction of life. Pithing was performed, and instantaneously afterwards an incision was made across the jugular vein on the one hand and the crural artery on the other. These vessels were selected from their convenient situation for the expeditious performance of the operation in a manner to admit of the respective kinds of blood being obtained in a pure or unmixed state. The following are the results of the analysis of the counterpart samples of each. It will be seen that the amount of sugar in the blood corresponds with what I have before represented as naturally present, thus showing that no time was given between the period of pithing and collection for the influence of *post mortem* change in the liver to be exerted.

Sugar per 1000 parts.

Crural artery.			Jugular vein.		
a.	·799	·795 (mean).	*a.*	·793	·792 (mean).
b.	·791		*b.*	·791	

Four days ago the legal restriction I was before labouring under was removed, and time has just been allowed previous to the termination of the present session of the Royal Society for the performance of two experiments, in which the blood was collected under natural conditions during life. In these two experiments ether was administered to remove sensibility during the exposure of the carotid artery and jugular vein. The animals were then allowed to remain for an hour and a half to recover

from the unnatural state induced by the anæsthetic. Without occasioning any disturbance of tranquillity the two vessels were now drawn forward by means of loose threads which had been placed around them, and openings made to allow of the escape of blood. The respective specimens of blood were thus collected at the same moment; and, before coagulation had time to occur, the process of analysis was commenced. The following were the results obtained :—

Sugar per 1000 parts.

Carotid artery.			Jugular vein.		
a.	·806	·811 (mean).	*a.*	·808	·798 (mean).
b.	·817		*b.*	·788	
a.	·854	·863 ,,	*a.*	·863	·879 ,,
b.	·873		*b.*	·896	

I must allow these results to speak for themselves. The circumstances I have alluded to have prevented my obtaining a larger number for this communication. Taking the evidence as it stands, it is not clearly apparent that any decided difference exists in the amount of sugar contained respectively in arterial and venous blood. More observations, however, shall be made, and the results communicated at a later period. Meanwhile, it may be confidently looked upon as settled that Bernard's representation is shown to be erroneous.

I have now to refer to the spontaneous change ensuing in the blood after removal from the system. Bernard, in his recent writings (Comptes Rendus, 19 Juin, 1876, p. 1406) has drawn attention to this subject, and represents the rate of disappearance of sugar to be such as to give weight to his results regarding the extent of destruction alleged to occur in the systemic capillaries during life, contending, as he does, that the *post mortem* phenomena observed, both as regards sugar-formation and sugar-destruction, stand as representations of the natural actions of life. The following is the record he has given of the results derived from an analysis of a sample of blood at different periods on a warm summer's day :—

	Sugar per 1000.
Analyzed immediately	1·070
,, after 10 minutes...............	1·010
,, after 30 minutes	·880
,, after 5 hours	·440
,, after 24 hours..................	·000

The results derived from the observations conducted in my laboratory with the gravimetric process of analysis furnish evidence of a very different nature. Subjoined are the particulars relating to five observations made during the present year at the dates mentioned.

			Sugar per 1000 parts.
January 29th.			
Taken immediately.........	a.	·797	·786 (mean).
	b.	·776	
After 1 hour			·739.
April 25th.			
Taken immediately.........	a.	·706	·700 ,,
	b.	·694	
After 1 hour	a.	·681	·670 ,,
	b.	·660	
May 18th.			
Taken immediately.........	a.	·770	·766 ,,
	b.	·762	
After 1 hour	a.	·765	·751 ,,
	b.	·738	
After 23 hours	a.	·280	·285 ,,
	b.	·291	
May 24th.			
Taken immediately.........	a.	·777	·786 ,,
	b.	·795	
After 1 hour	a.	·731	·728 ,,
	b.	·726	
After 24 hours	a.	·321	·302 ,,
	b.	·283	
May 26th.			
Taken immediately.........	a.	·932	·921 ,,
	b.	·910	
After $1\frac{3}{4}$ hours			·793.

The *gradual* destruction of sugar shown by the above observations to occur after the removal of blood from the system is nothing more than a confirmation of what has been known for many years to take place. A communication presented by me to the Royal Society in 1855, and published in abstract in vol. vii. of the 'Proceedings,' contains the following remarks :—" Under the changes of the decomposition of blood, normal animal glucose is very readily metamorphosed. The rapidity of the metamorphosis depends on the activity of the decomposition of the animal substances present, and when the destruction of the sugar is complete, the blood has assumed an acid reaction. This acid reaction of decomposing blood is only observable in that which was previously pretty largely impregnated with sugar. It appears to be owing to the formation of lactic acid. . . . . The disappearance of sugar is more rapid where the fibrin and corpuscles are present than when the serum is exposed alone; and in accordance with this the blood, in the one case, undergoes decomposition much sooner than in the other."

Thus as far back as 22 years ago I directed attention to the phenomenon here referred to. The phenomenon constitutes a change, the occurrence of which, from the known properties of sugar, might be looked for under the circumstances. Taken by itself it implies nothing physiologically, but simply stands in subordinate relation to the physiological position shown by other evidence to exist.

The conclusion to which the evidence contained in this communication leads is that if the gravimetric application of the copper test used in the accustomed manner is to be accepted as affording trustworthy information with reference to the quantitative determination of sugar, and I confidently submit that it is, the results which Bernard has obtained by the experimental *modus operandi* he has been recently employing are shown to be seriously fallacious. The results being fallacious, his inferences must be looked upon as correspondingly in error.

V. "Note on Dr. Burdon Sanderson's latest Views of Ferments and Germs." By J. Tyndall, D.C.L., LL.D., F.R.S. Received June 21, 1877.

While writing the paper which the Council of the Royal Society has recently done me the honour of accepting for the Philosophical Transactions, the abstract of a lecture delivered by Dr. Burdon Sanderson to the Association of Medical Officers of Health was placed in my hands. The esteem in which the author's name is justly held will certainly give weight and currency to the views enunciated in this lecture. Speaking of ferments Dr. Sanderson says :—" In defining the nature of ferment action we are in a dilemma, out of which there is no escape except by compromise. A ferment is not an organism, because it has no structure. It is not a chemical body, because when it acts upon other bodies it maintains its own molecular integrity. On the whole, it resembles an organism much more than it resembles a chemical body, for its characteristic behaviour is such as, if it had a structure, would prove it to be living. Ten years ago the opponents of spontaneous generation were called Panspermists, because it was supposed that in the so-called *generatio equivoca*, in every case in which *Bacteria* appeared to spring out of nothing, the result was referable to the influence of unseen but actually existing germs. The researches of the last few years have carried us beyond this stage....the outer line of defence, represented by the aphoristic expression *omne vivum ex ovo*, has been for some time abandoned. The ground which the orthodox biologist holds now, as against the heterodox, is not that every *Bacterium* must have been born of another *Bacterium*, but that every *Bacterium* must have been born of something which emanated from another *Bacterium*, that something not being assumed to be endowed with structure in the morphological or anatomical sense, but only in the molecular or chemical sense. It is admitted by all, even by Professor Tyndall, that, so far as structure is concerned, the germinal or life-producing matter out of which *Bacteria* originate exhibits no characters which can be appreciated by the microscope; and other researches have proved that the germinal matter is capable of resisting destructive influences, particularly those of high temperature, which are absolutely fatal to the *Bacteria*