mortality rate as 12.3 per cent., but, as the result was not mentioned in 4 cases, there were really 16 deaths in 126 cases = 12.6 per cent.; adding my 9 hitherto unpublished cases and the patient of 92½ mentioned above, gives 136 cases with 17 deaths, or 12.5 per cent.—that is, 1 patient in 8 died from the operation.

If all the cases operated on had been published it is possible that the mortality would be higher; for if we take Kelly and Sherwood's table¹⁷ of those ovariectomists who have published at least 5 cases and add my cases we get the results shown in the following table:

Operation.	Cases.	Deaths.	Remarks.
Halliday Croom ...	6	2	One had cancer of uterus; the other was a parovarian cyst.
I. Homans ...	12	3	One was a sarcoma, the other benign.
A. Martin ...	5	1	Embolism.
Werth ...	5	0	
H. R. Spencer ...	10	0	
Together ...	38	6	A mortality rate of 15.7 per cent.

The mortality is shown in Wiel's table¹⁸ to be very high in malignant cases (which are fortunately rare), 4 out of 5 cases having succumbed; and in parovarian cysts, 2 out of 4 having died. One of the 8 cases of fibroma died (12.5 per cent.). The low mortality of the 17 recorded cases over 80 years of age (5.8 per cent.) has been already mentioned.

Remarks on Ovariectomy in Old Women.

These patients having outlived the allotted span of life show in their own persons a constitution of more than usual strength and in their family histories a tendency to longevity. If their organs are sound and the patients are not too fat they are good subjects for operation, especially if they are of a cheerful temperament.

The special points to be borne in mind in operating are their waning strength, their tendency to mental disturbance, and their liability to bronchitis and pneumonia. With regard to the anaesthetic, I think infiltration and spinal anaesthesia are generally unsuitable, as liable to upset the patient's mental equilibrium, though Igel,¹⁹ Wechsberg,²⁰ and Pfannenstiel²¹ have published very successful cases operated on under local anaesthesia, which offers many advantages for a simple ovariectomy in a courageous patient. I think ether is usually preferable to chloroform unless bronchitis be present. I should prefer to postpone operation if the weather were severe. The operation should be performed as rapidly as possible, with due regard to careful suturing. In case of urgency the abdominal wall may be sewn up with through-and-through stitches of silkworm gut by what I call the "reversed-B" suture, the loop of the B apposing the cut edges of the sheath of the rectus. This shortens the operation by several minutes, ensures good apposition of the fascia, and leaves no buried stitch. The head of the patient's bed should be screened from draughts, and the bed should be warmed. Old patients bear cold badly. When King David was old and stricken in years, though they covered him with clothes, yet he got no heat.²² The patient should be propped up in bed to prevent hypostatic pneumonia, and sedatives (not morphine) should be given, preferably by the rectum, if sleeplessness occurs.

It is fortunate that malignant tumours are rare in these patients, and a consideration of the results of ovariectomy for benign tumours in women over 70 years of age shows that the operation may be undertaken without selection of cases with every prospect of success, and the patients may survive beyond the fourscore years of the psalmist, and yet their days may not be "but labour and sorrow."

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Hunterian Lectures

ON

MAN'S POSTURE: ITS EVOLUTION AND DISORDERS.

GIVEN AT THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

BY

PROFESSOR SIR ARTHUR KEITH, F.R.C.S., F.R.S.,
CONSERVATOR OF THE MUSEUM.

[Abstracts.]

LECTURE IV.—THE ADAPTATIONS OF THE ABDOMEN AND OF ITS VISCERA TO THE ORTHOGRADE POSTURE.

VERY early in my inquiries I became impressed by the fact that in the anthropoid or orthograde apes the viscera of the abdomen were very human in shape and arrangement, and that they were fixed to the walls of the cavity in almost the same manner as they are in the abdomen of man. On the other hand, a distinctly different pattern prevailed in the bellies of pronograde monkeys, even in the higher kinds, which are most akin to the gibbons in point of structure. It became apparent, then, as we have seen to be the case with the spine and with the thorax, that the chief of these features in the human abdomen which we recognize as postural adaptations came into existence at that remote period when the gibbon type of anthropoid was evolved; these postural adaptations became further perfected with the appearance of the great anthropoid type, and reached their culmination in the human body with the evolution of the plantigrade mode of progression.

HOW ARE VISCERA SUPPORTED?

At the time I was making these inquiries my conception of the mechanism which supported and kept the abdominal viscera in place was crude and mechanical. I supposed that when we stood up the organs within the abdomen were suspended by their mesenteries much as our coats hang from pegs within a wardrobe. I accepted a belief, then widely current, that in the erect posture a negative pressure or suction arose under the diaphragm and that thus the pressure of the atmosphere assisted in visceral support. Soon after I went to teach anatomy at the London Hospital in 1895 a series of events happened which showed that the mechanism involved in supporting the abdominal viscera was infinitely more complex than had been generally supposed. My attention had been attracted by certain dissecting-room subjects in which the abdominal organs were placed at an abnormally low level, as if their supports had given way. Of 71 subjects I found 10 in which the diaphragm and the organs within its domes were 2 inches or more below what was the usual level; in 15 other subjects there was a partial dropping of the viscera. My friend Dr. Christopher Addison, who had not then taken on the cares of statesmanship, had published very exact observations on the position of the abdominal viscera of 40 subjects; in 2 of them the upper abdominal viscera had dropped downwards to a marked extent, in 10 there was present a condition of partial prolapse affecting one or more organs. Then, when I was regarding this matter as one of merely anatomical interest, there appeared, in 1899, Dr. Franz Glénard's great volume entitled *Les Ploies Viscérales*; he had become interested in the sagging of the abdominal viscera from a clinical point of view as early as 1885; in the patients who crowded to Vichy for the cure of dyspepsia and neurasthenia he found the condition of enteroptosis to be very common. In seeking for an explanation of how the dropping of viscera came about I turned to the out-patient department of the London Hospital, where an x-ray apparatus had been installed at an early date. It was possible then for all of us to examine the position of viscera in the thorax and abdomen of the living—particularly the organs which occupy the domes of the diaphragm. It became clear to everyone then that the viscera in the upper segment of the abdomen formed part of a respiratory piston. The upper end of the piston is covered by the diaphragm. When that muscle contracts during inspiration the upper end of the piston moves in a downward and forward direction; the piston is returned by a contraction of the muscles of the belly wall; the visceral piston is not only supported by muscles, it is delicately poised, in all phases of respiration, between the opposing

muscular groups. In those in whom the abdominal type of respiration is well developed the respiratory piston has a stroke of 3 inches, or even more when a deep breath is taken. Such observations compelled one to reconsider the mechanism of visceral support.

INTRA-ABDOMINAL PRESSURES.

It was an easy matter to show that subdiaphragmatic suction had nothing to do with keeping the viscera up. When the interior of the cardiac end of the stomach—which lies within the left dome of the diaphragm—was connected with a manometer the intragastric pressure was found, when the subject of the experiment was standing or sitting, to vary between +3 and +5 mm. of mercury. It was only when extreme inspiratory efforts were made to raise and expand the chest that a slight negative pressure appeared. When the subject lay on his back the intragastric pressure rose to 16 mm. Hg. On consulting literature concerning this subject I found my observations were not new; they had been made several times before.¹ Pressures taken within the rectum when the living subject was standing in an easy posture throws further light on the mechanism of visceral support. The intrarectal pressure in these circumstances varied between 15 to 20 mm. Hg. Now if the whole weight of the semi-fluid column of abdominal viscera—360 mm. in height, and with a specific gravity of 1.50—rested on the floor of the pelvis, the intrarectal pressure ought to have been twice the amount observed; there must be, therefore, a suprapelvic mechanism which partially sustains the weight of the visceral column. This clearly cannot be the system of mesenteries and ligaments which pass from the viscera to the walls of the abdomen, for when the abdominal walls are measured from a dead subject, and the trunk is placed in the upright position, the contents of the abdomen, liver, stomach, spleen, and great and small intestine slip downwards until they hang from their mesenteries and ligaments. The descent of the upper organs amounts to about 3 inches, the lower viscera to about 5 inches.

THE REFLEX POSTURAL MECHANISM OF THE BELLY WALL.

Now, as is well known, when a living subject raises his body to the sitting or standing posture the upper viscera do not drop more than a half or three-quarters of an inch; the ligaments and mesenteries can therefore take no part in sustaining the viscera. The supporting structures are the muscles of the belly wall; particularly is the transversalis muscle important in this respect; it is a living belt which girds the loins. The moment we assume a sitting or standing posture there is set going a reflex mechanism which throws the muscles of the belly wall into a state of postural tone. François Franck noted that when a dog was chloroformed in the upright position tone departed from the muscles of the belly wall and the viscera sagged. When the posterior roots of the abdominal spinal nerves are cut, or, as Sherrington has demonstrated, when the afferent nerves from the viscera are severed, the abdominal musculature loses its postural tone. Surgeons are well aware that dragging on a mesentery or visceral ligament in an imperfectly anaesthetized patient gives rise to a dragging pain and to nausea²; the parietal peritoneum has a rich supply of sensory nerves. At the roots of mesenteries and within them are numerous Pacinian-like corpuscles. Very probably the afferent stimuli which set the reflex postural mechanism into operation arise from some or all of these sensory terminals. Possibly, too, the mechanism may require the accessory action of one or more hormone substances. It is sufficient for our present purpose to realize that the assumption of the orthograde posture demanded an elaboration of the mechanism of visceral support. Under modern conditions of life, this postural mechanism of man's body is particularly liable to break down. The cause of this breakdown we do not know, but all available evidence points to its being connected with errors in feeding and living rather than with any imperfection in Nature's evolutionary workmanship.

THE FUNCTION OF MESENTERIES AND OF VISCERAL LIGAMENTS.

If, as I have stated, mesenteries and visceral ligaments do not suspend the abdominal organs, then what are they for? If they do not serve the purpose of support, why is it that as we pass from the higher pronograde apes to the lower orthograde apes the areas of visceral fixation become much more extensive and closer? Then, again, as we pass from the gibbon to the large anthropoid apes we note that the

process of adhesion has extended, and reaches its farthest point in the human body. There cannot be a shadow of doubt that the degree of peritoneal fixation keeps step with the degree of adaptation of the body to the erect posture. The explanation lies in a proper understanding of the law of ligaments. In the maintenance of posture Nature never uses ligaments; it is always muscle, striped or unstriped, she employs for this purpose. I know of only one exception, and that is where yellow elastic tissue is employed between the laminae of vertebrae and in the subcutaneous tissue in the ventral wall of pronograde animals. Ligaments only come into action when the muscular supports or guards have been overcome or have broken down; ligaments are a second line of defence—the first line is always held by muscles. Hence it is that if the postural tone of the abdominal musculature is damaged then the mesenteries and visceral ligaments come into action; the dropped organs become supported or suspended by their attachments. Very probably Mr. H. Tyrrell Gray is right in ascribing certain symptoms and disorders of intestinal function to tension on the nerves lying within the mesenteries. The increased areas of visceral fixation to be seen in the bodies of orthograde primates, particularly in the human body, are not for the suspension of organs, but to limit their movements and prevent entanglements. For example, it is not uncommon to find in the human body that the mesentery of the "ileo-caecal loop" has not become adherent to the posterior wall of the abdomen, but has remained free as in pronograde apes. In such cases neither the caecum nor ileum falls below its usual level; what does often happen is that the unfixed condition of the ileo-caecal tract permits a freedom of movement which may end in the loop becoming twisted and the bowel acutely obstructed.

INTRA-ABDOMINAL STRESSES.

There is another line of evidence which helps us to understand why peritoneal fixation has assumed so extensive a development in the human body. We are apt to forget that the chief muscles of the belly wall, the two recti, the external obliques, and the internal obliques, are primarily muscles of the spine; they are the powerful postural antagonists of the component elements of the erector spinae muscles. The spinal muscles thus form a great cylinder, within which is packed the column of abdominal contents. Thus the abdominal contents are subject to the compressive action of the cylinder of postural muscle. During violent muscular effort the intra-abdominal pressure will mount up to 100 or 150 mm. Hg. In pronograde apes we cannot conceive that such high pressures can arise; the postural musculature of their trunks uses both fore and hind limbs as bases of action. With the evolution and maintenance of the orthograde posture, the shortening of the loins and extension of the thighs, the abdominal contents became subjected to greater degrees of compression and displacement, but even in the great anthropoids the maintenance of posture does not fall entirely on the musculature of the abdominal walls; weight in the upright position is partially borne by their upper extremities. It was with the evolution of the plantigrade posture of the human body that the postural compression of the abdominal viscera reached its highest point. The arms no longer assisted in supporting the body; the reverse became the case—the erect trunk had to afford a firm basis of action for the arms. For this purpose the postural complex of muscles which surround and enclose the abdominal cavity is called continuously into action. They tend to compress and displace the contents of the abdomen, and hence the human posture demands the most extensive system of visceral attachment.

It has also to be remembered that the upper viscera of the abdomen move with the respiratory tide. They must be fixed and shaped so that they may respond to all movements of the diaphragm and changes in shape of the thorax.³ The respiratory factor has to be kept in mind when we seek to explain the altered fixation of the abdominal viscera which occurred with the evolution of the orthograde posture.

TRANSFORMATION OF THE ABDOMINAL CAVITY.

Thus we see that the evolution of the orthograde posture was attended by a revolution in the attachment of the abdominal viscera and by an elaboration of the muscular mechanisms which keep the trunk erect and support the contents of the abdomen. Then, too, came a transfiguration in the shape of the abdominal cavity and a remodelling of such solid viscera as the liver and spleen. Everyone is familiar with the long loins of the commoner monkeys and the keel-like form given to the hinder part of their bodies. In

their usual pronograde or "four-footed" mode of progression the chest is more ventral in position than the flanks; hence the abdominal viscera tend to sag against the diaphragm. The iliac part of their pelvis is long, narrow, and situated dorsally, thus permitting the ventral musculature to exert an unfettered control over the contents in the hinder part of the abdomen. That part of their abdominal cavity which lies within the wings of the thorax is deep from back to front, but relatively narrow from side to side. We have seen that with the evolution of the orthograde posture the loins became shortened by the addition first of one lumbar vertebra to the sacrum, then of another. The dorsal wall of the abdomen was thus curtailed; so too were the abdominal aorta and the dorsal attachment of the mesentery. Attention has already been drawn to the widening of the orthograde trunk and to the flattening of its dorsal and ventral surfaces; the abdominal cavity necessarily underwent a corresponding change in shape: the domes of the diaphragm became wider and more capacious. A feature which is particularly worthy of note was the increased protrusion of the bodies of the vertebrae within the cavities of the thorax and abdomen. This vertebral protrusion led to a deepening of the hypochondriac recess which lies on each side of the vertebral column. In man, particularly after the lumbar curvature is fully developed, these recesses become deep and capacious. With the deepening of the recesses the viscera which lie within them, especially the kidneys, become withdrawn from direct muscular support, and hence are particularly liable to displacement. These changes in the shape of the abdominal cavity, which became more marked with each succeeding phase in the evolution of the orthograde posture, necessarily affected the form of the contained viscera and their mode of fixation.

THE EVOLUTIONARY RÔLE OF PERITONEAL ADHESIONS.

Having thus sketched in outline the chief changes which overtook the abdominal wall during the evolution of the upright body I now turn to note the postural adaptations to be recognized in the contained viscera. It is impossible in the course of a single lecture to deal with the matter fully; I shall restrict myself to one or two of the more significant changes, particularly those which have been brought about by a more extensive peritoneal adhesion of the viscera.

In the lowest and oldest primates known, as in the more recent and more highly specialized, the alimentary tract, from oesophagus to anus, falls into four natural sections or loops. These are: (1) the gastric loop, (2) the duodenal, (3) the ileo-colic, (4) the recto-colic. In the lowest primates these four loops are attached to the median line of the dorsal wall of the abdominal cavity by a continuous peritoneal sheet—the common mesentery. Even in this earliest of stages the gastric loop is seen to have undergone a rotation and its mesentery has become ballooned out to form a great omental sac—an occurrence which shows us that mesenteries are more than mere ligaments and that peritoneum is much more than a passive lining for the abdominal cavity. Even among pronograde monkeys the mesentery of the duodenal loop and the omental sac show various degrees of adhesion to the posterior wall of the abdomen. In the pronograde monkeys of the old world adhesions have already become extensive. The duodenum and pancreas have become sealed to the posterior wall of the abdomen. The rotation of the ileo-colic loop is now so complete that the proximal part of the colon falls into the right lumbar region in front of the duodenum. In the duodenal or right lumbar area an interesting complex of peritoneal adhesions is formed; chiefly out of the right extremity of the omental sac, which is attached to the pyloric end of the stomach and commencement of the duodenum. The fringes of the right end of the omentum have become plastic and adhesive in nature; they help to bind the colon to the right lumbar region and represent the initial stage in the evolution of the so-called Jacksonian membrane. In the old-world monkeys, too, is to be seen the first stage in the adhesion of the mesentery of the small bowel and transverse mesocolon—which collectively represent the common mesentery of the ileo-colon. The area of adhesion is restricted to the neighbourhood of the "root" of the mesentery. The mesentery of the distal part of the colon retains its primitive median attachment.

Then, when we pass from the highest of the pronograde apes to the lowest orthograde form represented by the gibbon, we find the process of peritoneal adhesion has proceeded apace. The omental sac has not only become adherent to the posterior abdominal wall but has become fused with the mesentery of the transverse segment of the

colon. Its right or hepatic extremity forms adhesive colic bonds in the loin, while its left or splenic extremity does the same in the left hypochondrium. The spleen has become adherent over the left kidney. The posterior aspects of both oesophageal and pyloric ends of the stomach have become more adherent. The fixation of the mesentery of the ileo-colon, which has reached only an initial stage in old-world monkeys, has become more extensive in the gibbon, but the extremity of the loop, including the terminal part of the small intestine and the beginning of the large intestine, is still free. It is in the gibbon we see the first stage in the process of sealing down the mesentery of the distal segment of the colon. The mesentery attached to the splenic flexure becomes fixed to the posterior wall of the abdomen, while the mesentery of the descending and sigmoid colons remains almost as free as in pronograde apes. In the great anthropoid apes we see a stage of adhesion which takes us almost to the extent seen in the human body. The colic adhesions developed out of the omental extremities at the hepatic and splenic flexures have become particularly abundant. The posterior aspect of ileo-colic mesentery has become adherent almost to the termination of the ileum. The mesentery of the descending colon has become sealed down to the left lumbar region, and the root of the meso-sigmoid shows signs of wider attachment. The human is but a slight exaggeration of the anthropoid stage.

Thus in the degrees to which the viscera are bound to the abdominal wall by a process of adhesion we have a complete series of evolutionary stages leading from the lowest stage seen in pronograde monkey to the stage seen in the highest orthograde primate—man. Nature has used the process of peritoneal adhesion as part of her evolutionary machinery. That she has done so is made manifest by the recapitulation of the evolutionary series in the developing abdominal system of the human foetus. It is but seldom that the developmental processes of the human body recapitulate evolutionary history with any degree of clearness; but in the development of the mesenteric adhesions I think there can be no doubt evolutionary history is repeated.

HOW DO POSTURAL ADAPTATIONS OF THE PERITONEUM ARISE?

Long ago Sir William Arbuthnot Lane recognized that there was a connexion between posture and the formation of peritoneal adhesions. He spoke of such adhesions as being "crystallizations in the lines of force." This explanation may be true, but it does not help us to understand how adhesions occur in the foetus. A more profitable approach to the problem is the recognition that all the cells which line the peritoneum have in them, as an inherent quality, the power to form adhesions; that power becomes manifest whenever an irritant or toxic substance is applied to them. We must suppose, then, that this quality which is inherent in living peritoneal cells can be evoked somehow during embryonic and foetal life. The stimulus, whatever its nature may be, acts in a controlled manner on a sequence of definite areas, and produces a series of adaptational adhesions which serve to meet a need of the body.

THE DESCENT OF THE TESTES.

To understand the protean and plastic qualities of developing peritoneum one has only to recall Hunter's account of the nature of the process which brings about descent of the testicle. The gubernaculum testis may be described as a peritoneal growth plug; it is a cellular mass formed out of peritoneum and subperitoneal elements. The gubernaculum as it approaches the groin brings about a proliferation and an evagination of all the strata of the inguinal wall. The descent of the testicle, whatever the physiological reason for it may be, is not a more obscure or a more wonderful process than the formation of a peritoneal adhesion. Both are manifestations of developmental or growth qualities inherent in the lining membrane of the abdomen. Hunter has been criticized for using the phrase "stimulus of perfection" to designate the cause which set the machinery of descent in motion. If we translate Hunter's phrase "stimulus of perfection" to mean a hormone substance which is produced by a normal developing testis, we are only giving his language and his explanation a modern garb.

One other instance I may cite to illustrate the active qualities of developing peritoneum. In all forms of primates the ileo-colic loop of intestine undergoes a rotation during development, the rotation bringing the beginning of the colon into the right lumbar region. In the human embryo the

rotation of this loop takes place as it is withdrawn from the umbilical sac at the end of the second month of foetal life. My friend Professor J. E. S. Frazer has made a very thorough study of the mechanism¹ which brings about the turning over of the colic end of the loop. From his observations there can be no doubt, I think, that the retraction of the loop from the umbilicus and its rotation are produced by certain growth bands—or rather retraction bands—which develop along certain sectors of the mesentery of the loop. The rotation of the ileo-colic intestinal loop is a growth phenomenon not unlike in nature to that which we see manifested in the descent of the testicle.

It would take us too far afield in this lecture to discuss the modifications undergone by the liver and stomach with the evolution of the orthograde posture. I shall content myself, so far as the liver is concerned, by drawing attention to the fact that the change in posture was attended, as in the adjacent right lung, by the disappearance of the large caudate lobe. In the human liver a vestige of the caudate lobe is always present, showing that man has come of an ancestry which was pronograde in posture. As for the stomach, I shall merely mention that in the human child this organ is shaped as in anthropoid apes, and occupies the same high horizontal position. At what period of adolescence the infantile form is replaced by the elongated, vertically placed stomach of adult life has yet to be ascertained, but the change in shape must certainly be attributed to man's erect posture.

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A NOTE ON THE NATURE OF THE SUGAR IN BLOOD.

BY

J. A. HEWITT, PH.D., B.Sc.

(From the Department of Physiology, King's College, University of London.)

THE recent important advances made by Irvine and his co-workers as to the constitution of the carbohydrates lend themselves admirably to speculation regarding the possible function and significance of the now definitely established "γ" sugars in the metabolic processes of both plant and animal.

Direct evidence of the formation of these reactive isomerides in biological reactions was lacking until the present author and Pryde (Hewitt and Pryde, 1920) showed with some certainty that γ glucose and γ fructose are formed and can be detected when the stable α and β isomerides are in contact with living intact intestine. We contented ourselves with recording the experimental facts, and refrained from discussing any theoretical extension of the work, attractive and obvious as such discussion was, beyond saying, "The possibility thus suggests itself that in the rapid transformation of carbohydrate in living tissues γ sugars may play an important if not an essential part." Later Hewitt and de Souza (1921) remarked with similar reserve on this question, "It may be presumed on *a priori* grounds that a structural change of the nature referred to has some fundamental reason."

Since the communications mentioned above, three publications have appeared in which Hewitt and Pryde's results are quoted in some detail, and in each case are accepted, extended, and employed for the formulation of a theory as to the causation of diabetes mellitus.

Before discussing the evidence adduced in these researches, on which this theory is based, it is perhaps advisable to emphasize the extreme difficulty that exists in interpreting results in this field of work. Most, if not all, of the biochemical data are and must necessarily be indirect; considerable caution is required, therefore, both in devising experiments and in deducing conclusions therefrom if advance is to be made and erroneous conception avoided.

As the known reactions and properties of γ sugars must furnish the final grounds of appeal in discussing their formation or existence in metabolic processes, it might be well to summarize the relevant salient features of such sugars as deduced from the study of their methylated derivatives.

1. They contain an ethylene or propylene oxide ring in place of the butylene ring ascribed to and accepted for the crystalline α and β hexoses.

2. Two γ isomerides exist in the case of each hexose, analogous in their mutual relations to the α and β modifications. Possibly these γ isomers undergo mutarotation *inter se* as well as stereochemical change to the stable form; the last reaction is undoubtedly extremely rapid.

3. The chemical reactivity of γ sugars is very great, and condensation with alcohols to form glucosides takes place rapidly at room temperature. Fehling's solution is reduced in the cold, they unite readily with oxygen to form oxy-compounds, which in turn easily undergo disaccharide formation.

4. Unsubstituted γ sugars show marked instability to traces of acid or alkali.

Such properties manifestly render detection a matter of difficulty, which is further increased when it is remembered that one isomeride of γ glucose is strongly laevo-rotatory, while β glucose is only feebly dextro-rotatory. Apart from isolation of derivatives of these sugars, identification in biological reactions depends on polarimetric determination of optical behaviour and on the reduction of alkaline potassium permanganate.

Polarimetric evidence alone, therefore, must exclude rigorously the presence of β glucose in amount greater than that found normally in aqueous glucose solution in equilibrium. This is referred to in further detail below. The dangers attending the use of permanganate with biological material are obvious; the employment of this reagent requires careful control, and at best can be applied only with extreme caution to such complex solutions as blood or urine.

In my opinion the evidence on which Cooper and Walker (1922) and Winter and Smith (1922) base their theory is insufficient when the essential properties of γ sugars are considered. Cooper and Walker separated blood from a hexose solution (glucose or fructose) by a dialysing membrane and examined, with negative results, the sugar polarimetrically and with permanganate. Several objections can be raised to this technique:

(a) The blood was extravascular and, having undergone at least preliminary stages towards coagulation, was not normal. If it were citrated or oxalated (this is not stated) its condition is possibly still more abnormal.

(b) Owing to physical properties no enzyme could pass from the blood inside the dialyser to the sugar outside. Before any action could take place the hexose substrate would have to pass through the membrane. Unless preferential dialysis of one of the α or β isomerides had occurred no change in the specific rotation would be found, if the sugars were in equilibrium at the beginning of the experiment.*

(c) As the concentration of hexose outside the dialyser was greater than within, no transference of sugar from within outwards would be produced. The value, therefore, of examining the sugar outside does not seem apparent.

(d) Inherent dangers in the use of potassium permanganate exist; as, however, no reduction took place, the inference is perhaps not without reason that no dialysis of any component had occurred in either direction, for the various extractives of blood are far from inactive as regards this reagent, and owing to relative concentration would be removed from the blood inside to the solution which was tested.

Negative results obtained from experiments based on such technique do not warrant the superstructure of theory erected thereon. Hewitt and de Souza (*loc. cit.*) had previously clearly demonstrated what Cooper and Walker attempted.

Winter and Smith (1922), in a more elaborate study, reached the conclusion that the normal blood sugar is γ glucose, and that an enzyme exists (not in the blood) for effecting the transformation of the stable butylene oxide glucoses into γ glucose.

I agree that no such enzyme can be demonstrated in the blood (see Hewitt and de Souza, *loc. cit.*), but am of opinion that objections may be raised both to Winter and Smith's view of blood sugar and to the experimental evidence on which they found their theory.

Dealing with the technique employed by these authors it is to be observed that in the course of preparing their final filtrate for polarimetric examination the following manipulative operations, among others, were performed: (1) precipitation with tungstic acid; (2) heating to 40° C.; (3) addition of ethyl and propyl alcohol and contact with these alcohols for twenty minutes at moderate temperature; (4) concentration

* Possibility of preferential dialysis was apparently not considered. It may be stated, however, that alteration of optical values due to such cause cannot be detected. (Unpublished experiments.)