position of their bases according to the method developed by KIRBY[8,9].

In the Table, the results of chromatographic and oscillopolarographic analyses of the A content in RNA are given for the sake of comparison.

Zusammenfassung. Auf dem Prinzip der Komparationstitration wird eine schnelle oszillographische Methode für quantitative Adeninbestimmung in saurem Hydrolysat der RNS entwickelt.

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STUDIORUM PROGRESSUS

Local Metabolic Response to Physio-Pathological Demands: The Pentose Phosphate Pathway

In the effort to understand and combat disease, the study of the pathways and intermediate products of metabolism plays an ever-increasing role. It is obvious that any qualitative or quantitative changes occurring in the metabolic pattern will produce consequent functional alterations in the cells affected.

In vitro studies have shown that, under normal conditions, glucose breakdown takes place *via* both the Embden-Meyerhoff (glycolytic) and pentose phosphate (direct oxidative) pathways in the arterial wall, liver, kidney, pancreas, adrenals and the spleen; whereas, in the veins, cardiac and striated muscles, central nervous system and gastro-intestinal tract, glucose is metabolized *via* the glycolytic route only[1–7].

This diversity in the pattern of glucose metabolism in different tissues implies that their requirements and utilization of the various intermediate metabolites provided by these pathways vary according to their structure and function. Metabolic needs alter under different physiological and pathological conditions. It has been shown, for instance, that the pentose shunt is increased in the lactating mammary gland[8]; while the opposite is found to hold true in the erythrocytes taken from patients with thyrotoxicosis[9].

The present communication reports results concerning the metabolism of glucose *via* the pentose phosphate pathway during (1) digestion, and (2) inflammation and repair. These particular physio-pathological processes have been selected for study because they are representative of the basic continuous functional responses by living tissues to maintain the integrity of the milieu interieur.

Experimental. The method of BLOOM and STETTEN[10] was used to indicate the relative utilization of the glycolytic and direct oxidative routes in glucose metabolism. The radioactive material (glucose-1-^{14}C and glucose-6-^{14}C, obtained from the Radiochemical Centre, Amersham) was diluted with inert substrate to give a specific activity of about 1.5 μc/mg. The glucose concentration in the Warburg flasks was 0.1%. Details of tissue preparation, incubation conditions and CO_2 determinations have been described in an earlier communication[1].

(a) *Study of glucose metabolism during digestion.* Adult, male Wistar rats, weighing 200–250 g, were fasted for 12 h. They were then allowed to feed for 15 min on a mixture of condensed milk, sugar and assorted grain, as well as being given water to drink. 2 h later they were decapitated, and slivers of the stomach wall (weighing about 100 mg) were taken and transferred to Warburg flasks. Sections were taken from the upper and lower half of the lesser curvature of the stomach, the latter tissue in the rat comprises an infinitely larger proportion of smooth muscle fibers.

(b) *Study of glucose metabolism during inflammation and repair.* Under light intravenous sodiumpentathol anesthesia, the femoral artery or vein was exposed in adult male mongrel dogs weighing about 10 kg. The vessel was then traumatized, by being crushed with artery forceps; by intramural injection of an irritant (0.2–0.5 cm^3 1% phenol or 0.5 cm^3 of 50% ethyl alcohol); or by being cut across and anastomozed. The animals were sacrificed 48–96 h after the intervention, at which time the affected part of the vessel was carefully dissected out and transferred to Warburg flasks.

Results and Comments. The results in the Table indicate that under conditions of digestion and during inflammation and repair glucose metabolism *via* the pentose phosphate pathway was considerably increased, although the quantitative increase cannot be precisely established because of the limitations of the technique employed[11,12].

Chemical reactions in biological systems are responses to physiological exigencies. Glucose, the major basic nutriment of animal tissue, is metabolized *via* at least two pathways – the glycolytic and the pentose phosphate. The former is the major and, in some tissues, the only measurable route of glucose metabolism under normal physiological conditions. The intermediate metabolites formed are utilized for the synthesis of the necessary cell constituents and, together with the Krebs cycle, this pathway provides the energy required for the many biochemical processes relating to cellular function and body 'work'.

Since the recognition of the pentose phosphate pathway in animal tissue, studies have revealed that the reaction sequence of glucose breakdown *via* this route provides the pentose sugars required for the synthesis of nucleic acids; it also contributes notably towards the formation

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of TPNH, an essential coenzyme for fat synthesis. Thus, the metabolism of glucose *via* this pathway can be expected to be augmented in response to conditions necessitating an increased production of the substances which directly or indirectly result from its utilization.

In the resting gastric wall, there was evidence of glucose breakdown only *via* the glycolytic route; during digestion, however, the pentose phosphate pathway was found to be extensively utilized, its intermediates being necessary for the biosynthesis and replacement of pepsin, renin and lipase. In the blood vessels, metabolic activity *via* the pentose phosphate pathway increased in proportion to the type and severity of the injury inflicted. Under normal conditions, the breakdown of glucose in the veins occurs only via the glycolytic route[1]; the demands of the response to injury are thus evidently met by added metabolic activity *via* the pentose phosphate route.

In the artery, where both the glycolytic and direct oxidative pathways are normally engaged in glucose metabolism, the latter route is shown to be considerably more utilized after injury. This has also been observed to occur (though to a lesser degree) in vessels undergoing atherosclerotic changes[13].

In physiological or pathological processes, the metabolic response of the affected tissues, whether detrimental (as in atherosclerosis) or beneficial (as in repair), must involve increased utilization of the pentose phosphate pathway if biosynthesis of RNA and DNA for protein production and cell proliferation, as well as of various coenzymes and nucleotides, is required.

From the medical point of view, three interesting observations made by other investigators are worthy of note.

During wound healing, OHKUBO et al.[14] found that in granulation tissue the glycolytic pathway is partially blocked. It would appear that this holds true only for the granulation tissue itself. Some of our studies (not yet completed) of the metabolic pattern of the *whole* of the injured area indicate that, in the process of inflammation and repair, metabolic activity *via* the Embden-Meyerhoff route alters little or actually increases with the increase in the shunt. Histologic examination of the slices cut across the injured area suggests that the pentose shunt represents the sum of the metabolic activity *via* this route produced both by regeneration of the injured tissue itself and that of the numerous cells infiltrating the area as a normal response to the healing process.

Studies on the local reaction to the infectious process in plants by several investigators[15–19] suggest that the shunt may play a role in localizing the lesion. It would be of interest to see whether the same holds true in animal tissue, in which event this pathway could also be considered as part of the body's defense mechanism.

In a recent communication, LABORIT et al.[20] discuss at some length the possible alterations in the pathways of glucose metabolism consequent to changes in the environmental factors influencing the functional activity of the body, thus attempting to relate biochemical data to physiological phenomena.

Extensive and continuous studies are being conducted in the field of cell metabolism but little clinical application has, as yet, materialized from this accumulation of knowledge. This is probably largely due to the fact that most research clinicians are not sufficiently familiar with the advances in biochemical knowledge and techniques; and the biochemist, on the other hand, does not appreciate the practical application because of his lack of biological orientation.

Production of $^{14}CO_2$ from glucose-1-^{14}C and glucose-6-^{14}C

Tissue	Type of process, injury or irritant	$^{14}CO_2$ production in c.p.m. less background per 100 mg of tissue (wet weight)[a]		Ratio
		Glucose-1-^{14}C	Glucose-6-^{14}C	
Stomach	At rest	1681	1480	1.1
Stomach	At rest	1813	1880	1.0
Stomach upper half	Digestion	12310	1836	6.7
Stomach upper half	Digestion	10403	1931	5.4
Stomach upper half	Digestion	14042	1622	8.6
Stomach lower half	Digestion	12288	4780	2.6
Stomach lower half	Digestion	9762	3725	2.6
Artery	Normal	270	95	3.0
Artery	Normal	324	103	3.0
Artery	Phenol 1%	2750	134	20.5
Artery	Phenol 1%	1532	298	5.1
Artery	Alcohol 50%	1030	196	5.3
Artery	Alcohol 50%	863	251	3.4
Artery	Anastomosis	911	122	7.4
Artery	Anastomosis	1121	256	4.4
Artery	Crushed	1003	186	5.4
Vein	Normal	158	142	1.1
Vein	Normal	108	74	1.5
Vein	Phenol 1%	1036	193	5.4
Vein	Phenol 1%	911	104	8.7

[a] Each value represents the mean of three separate determinations; incubation was for 120 min at 37°C in 95% O_2 and 5% CO_2.

Résumé. On a constaté dans le métabolisme de glucose une augmentation de l'utilisation de la voie oxydative directe dans la paroi de l'estomac durant la digestion, et dans celle des vaisseaux sanguins pendant inflammation, réparation et reconstruction. Les resultats ont été analysés en fonction de leur intérêt pour les problèmes cliniques.

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