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DEPARTMENT OF ANATOMY

November 12, 1958

The Surgical Anatomy of the Pancreas. By Russell T. Woodburne, Professor of Anatomy and Chairman of the Department of Anatomy, The University of Michigan Medical School, Ann Arbor.

The close relationship between surgery and anatomy is never more clearly expressed than in the development of new or more extensive surgical procedures. Current broadened surgical attacks on the pancreas will become proportionately less hazardous as the relationships of the organ and its rich blood supply and drainage are better understood. Posteriorly the gland is related to many large blood vessels: the splenic artery, the splenic vein, the renal arteries and veins, the aorta, and the inferior vena cava. Just medial to the duodenojejunal flexure the splenic vein receives the inferior mesenteric vein and it then combines with the superior mesenteric vein to form the portal vein. The large portal vein ascends against the dorsal surface of the neck of the pancreas. The superior mesenteric artery, arising from the aorta just above the renal arteries, descends behind the neck of the pancreas, and then overlies the uncinate process as it enters the mesentery.

The arteries of the gland are numerous and form a rich inter-connection between the celiac and superior mesenteric arteries. They lie largely on the dorsal surface of the gland and only a few are visible from in front. Nevertheless complete anastomosing arcades of vessels are formed in relation to the head of the pancreas. The gastroduodenal artery divides over the head of the pancreas into the right gastro-epiploic and the anterior superior pancreaticoduodenal arteries. The latter descends near the duodenal groove and connects with the anterior inferior pancreaticoduodenal artery. A posterior superior pancreaticoduodenal artery, arising from the first 2 cm. of the gastroduodenal artery, makes a similar arcade on the dorsum of the head of the pancreas with the posterior inferior pancreaticoduodenal artery. The inferior pancreaticoduodenal arteries usually spring from a common trunk from the superior mesenteric or upper jejunal arteries but may exhibit separate origins from these source vessels. A dorsal pancreatic artery descends posteriorly against the neck of the pancreas and sends its left branch along the dorso-inferior border of the body of the pancreas. This is the constant inferior pancreatic artery. The right branch runs across the head of the pancreas and helps form a prepancreatic arcade. The dorsal pancreatic artery has a variety of sources: splenic, celiac, superior mesenteric, and hepatic arteries. The pancreatica magna artery and caudal pancreatic arteries, along with the inferior pancreatic artery, vascularize the body and tail of the pancreas. The venous drainage of the pancreas corresponds in general pattern to the arterial supply, but the veins are customarily anterior and to the right of the arteries. The posterior superior pancreaticoduodenal artery and vein closely spiral the common bile duct on the dorsum of the pancreas.

R. T. W.
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BIOPHYSICS SEMINAR
November 17, 1958

RIBONUCLEOPROTEIN PARTICLES FROM E. COLI. By James Watson, Harvard University.

RNA forms about 25 per cent of the dry weight of \textit{E. coli}; of this, 10 per cent is low MW "soluble RNA," and 90 per cent occurs in high MW ribonucleoprotein particles. These particles are about 60 per cent RNA; thus the RNP particles make up about 40 per cent of the cells' dry weight.

The RNP particles can be got in four sizes: (i) an irregularly shaped particle sedimenting at 32 S (MW $0.9 \times 10^6$), (ii) a sphere of 51 S (MW $1.8 \times 10^6$), (iii) a larger sphere of 70 S (MW $2.7 \times 10^6$), and (iv) a bispherical particle of 100 S (MW $5.4 \times 10^6$). The relative proportions of these different sizes depends on the Mg$^{++}$ concentration. Only the 32 S and 51 S particles are found at low [Mg$^{++}$]; these combine to form the 70 S at higher concentrations. The 70 S in turn dimerizes into the 100 S particle.

All the particles are electrophoretically mobile and RNAase resistant, suggesting that the protein forms an outer coat over the RNA. The protein is basic, and end group analysis suggests that it is made up of four molecular species. It reacts with formaldehyde, indicating a lack of hydrogen bonding.

If the bacteria are grown in the presence of chloramphenicol (which inhibits protein but not nucleic acid synthesis), there is a vast reduction in the number of the above four particles accompanied by the appearance of new smaller particles. The smaller particles are 75 per cent RNA, and are RNAase sensitive. At low [Mg$^{++}$] a 15 S particle is found, which combines into 24 S and 31 S particles at higher concentrations. By comparison of RNP fractions got by growing cells on P$^{32}$ both before and after chloramphenicol treatment, it was found that most but not all of the smaller particles are newly synthesized, rather than breakdown products of the normal particles. Chloramphenicol grown cells also show an increase in the soluble RNA fraction.

The evidence cited points to a considerable similarity between the bacterial RNP particles and the microsomes of other organisms.

F. M. W.

ARTHRITE STUDY UNIT
November 20, 1958

THE PHYSICAL CHEMISTRY OF ANTIGEN-ANTIBODY REACTIONS. By Dr. S. J. Singer, Associate Professor of Chemistry, Yale University.

The number of sites involved in antigen-antibody bonding, the forces and chemical groups active, and the bond strengths of various combinations were investigated, using rabbit antibodies against proteins combined with the respective antigens in solution.
It is well known that when antigen is added to a mixture of antibody and antigen at their “equivalence” point (i.e., where all the antigen has precipitated with all the antibody), the precipitate dissolves. The reason for this is that at high concentrations of antigen the species, G-Ab-G (where G represents antigen and Ab, antibody) with a ratio of 2 G: 1 Ab and the species, G-Ab-G-Ab-G, which has a 3:2 ratio of antigen to antibody, are favored over larger aggregates in which the ratio of G:Ab is smaller. Fragmentation of the precipitate with the formation of such small species occurs upon addition of the antigen, as determined by ultra-centrifugation patterns. On the other hand, in the zone of antibody excess, such forms as:

\[
\frac{\text{Ab}}{\text{Ab-G-Ab}}
\]

predominate and are of such a chemical nature and large size that they too are insoluble.

Bound antigen can be calculated by subtracting free antigen from total antigen, both of which can be determined by means of ultracentrifugation or electrophoresis. Plotting bound \(\frac{G}{Ab}\) versus the per cent of total antigen in a solution gives a curve which may be extrapolated to 100 per cent total antigen (infinite antigen excess), at which point the bound \(\frac{G}{Ab}\) ratio is found to be 2:1. In other words, rabbit precipitating antibodies are divalent. Any deviation from this ratio of 2:1 in solutions at less than infinite antigen excess is an indication of the weakness of the bonding strength.

A more precise study of binding energies may be undertaken by determining the free energy change (\(\Delta F^o\)) of the reaction, recalling that \(\Delta F^o = -RT \ln K\), where \(R\) is the universal gas constant, \(T\) is the temperature in Absolute units, and \(K\) is the equilibrium constant of the reaction, which may be determined experimentally. Such work has shown that the total binding energy of a protein antigen is not significantly different from that of a hapten, with their respective antibodies. Bond energies for all antigen-antibody combinations are uniformly small, which would satisfy the requirements of a template theory, where the antibody must separate from the determining antigen after formation.

Dissociation of Ab-G combinations occurs at acid and at alkaline pH’s. Perhaps in one molecule’s reactive sites, one or more carboxyl groups in the charged state is needed to interact with oppositely charged groups in the complementary sites for bond stability to be maximal. Experimental results on the variation of \(K\) with pH at acid pH’s are consistent with this concept. At alkaline pH’s an intramolecular configurational change in the antibody molecule may be involved, causing a dissociation. Intermolecular electrostatic forces are probably not significantly involved in many Ab-G combinations, because the magnitude of \(K\) shows no correlation with the product of the net charges on the antigen and antibody molecules.

M. S. M.
YALE MEDICAL SOCIETY
December 5, 1958

PERIPHERAL CIRCULATION. By Nicholas M. Greene, Departments of Surgery and Pharmacology.

My colleagues and I have undertaken a project to show the precise way in which anaesthetic drugs alter the oxygen requirement, peripheral circulation, and respiration of the animal or individual to whom the drug is given. As preparation for our work we had to consider the complex interrelationships of blood flow, blood pressure, and oxygen tension in post-arterial peripheral circulation. Post-arterial circulation varies in its characteristics, depending upon the organ or part of the body one studies; but if we use the circulation in the skin as our prototype, our system will have the following components: an arteriole, a metarteriole, and arteriovenous shunt extending from the metarteriole to the venule, several capillaries also extending from the metarteriole to the venule, a venule, and various sphincters which can occlude the capillaries at their metarteriolar end or diminish the diameter of the metarteriole. Depending upon the spontaneous vasomotion of the system the precapillary sphincters may operate whereby either a few or a great many red cells pass through the capillaries, and the rest of the cells will pass directly into the venule through the arteriovenous shunt. If the preponderance of the circulation is through the shunt, the oxygen tension in the venous end of the system obviously does not reflect with accuracy the utilization of oxygen by the tissue. Furthermore, the pressure and flow relationships of the system will change, depending upon the vasomotion of each or all of the components of the system. For example, the pressure in the capillary will fall if either the metarteriolar pressure is reduced due to constriction of the metarteriole (as seen in Reynaud's disease), or if the venous backpressure is increased. Conversely, vasodilatation and increased blood flow (seen as hyperemia) may arise from exercise, heat, trauma, or vasodilatory drugs, such as histamine. Since the tissue oxygen tension is related to the rate of blood flow, when the velocity of the blood rises and oxygen utilization is unchanged, the oxygen tension at the venous end of the system will rise; conversely, tissue oxygen tension will fall with a decrease in velocity though oxygen utilization is unchanged. Other assumptions further utilized the equation (Ohm's law) that Flow = Pressure/Resistance, so we assumed that with a constant arteriolar pressure an increased resistance would produce a decline in flow, and a decreased resistance would produce a greater flow.

The studies I wish to report on today were to determine the effects of sympathetic denervation on skin oxygen consumption in patients. Our measurements involved the use of a platinum electrode of fixed voltage; the electrode reduced any molecular oxygen present, and a galvanometric deflection indicated directly the amount of oxygen reduced and therefore originally present. Some of our data were as follows: (i) During a period of "denitrogenation" of a nonsympathectomized patient (during which the patient breathed only oxygen), an increase of 300 per cent in the skin tension was seen (ii) with a temporary sympathetic block (spinal anesthesia or para-
vertebral block) skin oxygen tension may fall precipitously or only slightly. In interpreting our results it was concluded that oxygen tension of the skin during sympathetic denervation was related solely to the oxygen supplied the tissue. Oxygen supply depends upon three factors: the coefficient of oxygen diffusion, the oxygen tension in the entering arterial blood, and the rate at which the oxygen is brought to the tissue by capillary blood flow. Only the latter factor is altered by sympathetic block. The results suggest that criteria of the adequacy of capillary blood flow based upon either skin temperature determinations or blood flow in terms of cc. (blood)/100 gm. (tissue)/minute may be misleading under certain circumstances because they do not take into account the fact that in the hyperemic state the velocity of capillary blood flow may become inadequate to maintain normal tissue oxygen tensions.

In studying the physiological significance of changes in tissue oxygen tensions, biochemical indices such as changes in serum lactate, pyruvate, and potassium may be used. Care must, however, be taken to differentiate the metabolic response due to reflex epinephrine release occasioned by the hypoxia from the metabolic response to hypoxia per se. In experimental animals, data were obtained indicating that about one-third of the metabolic response to hypoxia may be ascribed to the release of epinephrine and not to the hypoxia itself. Preliminary data in patients with a complete sympathetic block indicate that the decreases in skin oxygen tension observed during limited sympathetic denervation are not associated with significant metabolic evidences of hypoxia.

H. J. L.