ORIGIN, DISTRIBUTION AND FUNCTION OF THE ACIDIC MUCOPOLYSACCHARIDES OF WHARTON'S JELLY IN THE HUMAN UMBILICAL CORD

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The umbilical cord is one of the more important organs of the embryo, the development and viability of which are largely determined on the condition of this organ. It is hence understandable that particular attention has been paid by research workers to the detailed study of its anatomical and histological features.

In the Russian literature, the fullest report of the histogenesis and microscopic structure of the umbilical cord and its Wharton's jelly is to be found in the papers published by M.Ia. Levina [6, 7, 8, 9]. A.V. Vikulov [2, 3, 4] has described an extravascular channel in the umbilical cord which seems to play some part in the development of certain diseases of the fetus during intra-uterine life, being a possible channel for the passage of infection from the maternal to the fetal circulation. This observation has obliged us to re-assess the function of the jelly of Wharton, which has heretofore been regarded as being only a protective covering for the umbilical vessels. It was of particular interest to institute a new approach to the study of the histogenesis of the umbilical cord and of Wharton's jelly, and, in particular, to the investigation of the origin, distribution, and functions of such physiologically active substances as are the acidic mucopolysaccharides, large amounts of which are deposited in the tissues of the umbilical cord.

EXPERIMENTAL METHOD

Umbilical cords taken from newborn babies and from fetuses (from the sixth to seventh week of development to full term) were fixed in 0.5% lead solution in 12% formalin. Paraffin sections were treated by the usual histological procedures. The acidic mucopolysaccharides were stained by means of histochemical methods, such as that of Hale, or the PAS reaction, as modified by McManus, Hotchkiss, and Gastaldi, staining with toluidine blue, with a parallel testicular hyaluronidase-treated control section for each of these procedures.

EXPERIMENTAL RESULTS

Umbilical tissue is little differentiated in the six–seven-week fetus. Wharton's jelly appears as a fibroblastic syncytium, still retaining certain mesenchymal features. The most characteristic feature of this stage of development is the copious secretion of jelly by the fibroblasts. The process of synthesis of mucopolysaccharides leads to accumulation of granules of mucoid substance within the cytoplasm of the fibroblasts, and these granules undergo displacement towards the surface layers of the cytoplasm, and are secreted by the cells. The processes of synthesis and secretion proceed in all the fibroblasts, but most actively in the cells of the perivascular zones. The fibroblasts are loaded with mucopolysaccharides in the form of granules of different sizes, from the smallest to grains the size of the nucleus, or even larger (Figure 1). The secreted granules absorb water to form a jelly-like substance in which filamentous structures subsequently make their appearance. The total amount of jelly is still small at this stage, however.

Fig. 1. Secretion of jelly-like substance by the fibroblasts of Wharton's jelly. Umbilical cord of a human embryo of 6-7 weeks development. Stained with toluidine blue. Objective imm. 90. Gomal 6.

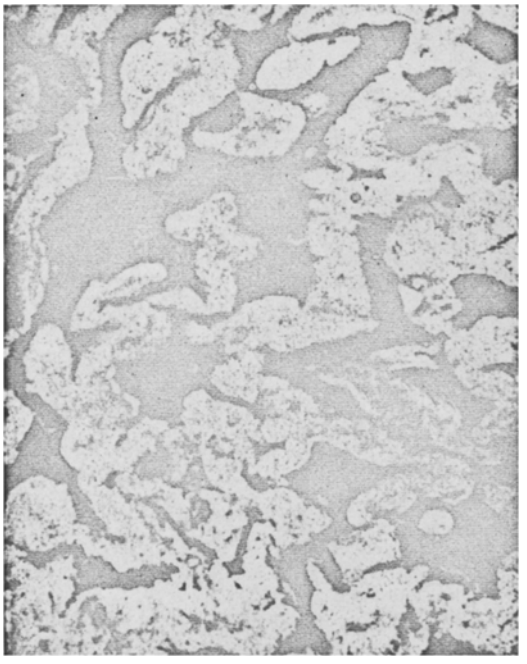

Fig. 2. Wharton's jelly of the umbilical cord of a newborn baby. Stained according to Hale. Objective x8. Gomal 6.

Rapid accumulation of mucoid substance takes place as a result of the process of active secretion, and this, in conjunction with accelerated differentiation of the tissues leads by the 9th-10th week to the formation of the umbilical vessels and of Wharton's jelly. Large bundles of fibers are formed, in particular in the subamniotic region. The characteristic appearance of Wharton's jelly now begins to appear: a reticular structure of bundles of fibers, in which are included elements of the fibroblastic syncytium and aggregations of the jelly-like substance. A considerable slackening off of secretory activity of the fibroblasts is seen at this stage. The falling off of synthesis and secretion of mucopolysaccharides is most marked in the central regions, which have been saturated with the jelly-like secretion. The secretory processes still remain fairly active in the peripheral parts of Wharton's jelly. The impression is received that the secretory process is of a zonal nature; side by side with groups of actively secreting fibroblasts can be seen zones giving no evidence of secretory activity. It is conceivable that this picture is the result of alternation of periods of secretory activity with periods of relative inactivity. At later stages of embryogenesis, and owing to the continuing differentiation of the fibroblasts, they progressively lose their powers of synthesis and secretion of mucopolysaccharides. Granules of mucopolysaccharides are still to be distinguished within their cytoplasm, but they do not attain the size seen at earlier stages.

Not until the 13th-14th week do separate mast cells appear in the tissues of Wharton's jelly. They arise from free, relatively undifferentiated cells located in the tunica adventitia of the umbilical vessels. We cannot exclude the possibility that they may originate from subendothelial elements of the umbilical vessels, but this possibility would require additional, very thorough verification. The mast cells synthesize and store granules of mucopolysaccharides. The number of mast cells increases, as a result not only of their new formation, but also of mitotic and amitotic division of already-formed cells, which migrate from the perivascular regions to the peripheral parts of Wharton's jelly, where they release their accumulation of mucopolysaccharide granules.

As the fibroblasts progressively lose their power of synthesis and secretion of mucoid substance, the function of production of mucopolysaccharides is taken over by the mast cells. Only a few scattered fibroblasts continue to produce mucopolysaccharides, up to the termination of pregnancy. Mucopolysaccharides are secreted almost exclusively by the mast cells during the latter months of pregnancy. The mast cells are not, however, fully able to compensate for the loss of the secretory function of the fibroblasts, and for this reason the relative concentration of acid mucopolysaccharides in Wharton's jelly falls perceptibly during the second half of pregnancy.

Wharton's jelly takes on a characteristic structure towards the end of pregnancy. It then takes on the form of a reticulum made up of well developed bundles of collagen fibers. Highly differentiated fibroblasts, retaining their syncytial connections, are to be seen, fused or trapped within the bundles. Very frequently, small amounts of mucopolysaccharides may be seen in the immediate vicinity of such fibroblast inclusions into the collagen bundles, affording evidence of the residual secretory activity of these fibroblasts. The meshes of the reticulum are filled with jelly, being a viscous aqueous solution of compounds of protein with acid mucopolysaccharides, of the type of hyaluronic or chondroitinsulfuric acid (Figure 2). The jelly is often traversed by strands of fibers.

The structure of Wharton's jelly varies greatly from one umbilical cord to another, as well as from one location to another in the same cord; the size and number of collagen fibers differ, as well as the size and shape of the meshes. The meshes filled with jelly, are in general stretched along the axis of the cord, and since they intercommunicate they constitute something of the nature of the continuous extravascular channel described by A.V. Vikulov. The meshes become particularly fine in the central perivascular zone, and between the vessels they appear in transverse sections as narrow slit-like spaces (Figure 3). The meshes become larger towards the periphery of the cord; the outermost subamniotic layer does not, however, usually contain mucopolysaccharides, but consists of a dense tissue, rich in collagen fibers. This subamniotic layer does not, as a rule, extend over the whole of the outer surface of the umbilical cord. In places, meshes containing jelly are situated immediately below the basal membranes of the amniotic epithelium.

Fig.3. Intervascular region of Wharton's jelly in the umbilical cord of a newborn baby. Stained according to Hale. Objective x8. Gomal 2.

We have as yet been unable to find a satisfactory explanation of the existence of such variations in the mutual relations of the jelly and the amniotic epithelium. In some cases the acid mucopolysaccharides fill only the peripheral meshes of Wharton's jelly, where they form considerable deposits. The meshes of the central parts of the cord contain a substance which, when treated by the ordinary procedures, resembles that of the peripheral zones, but which does not give a reaction for acid mucopolysaccharides. It might be supposed that this effect may be due to secretion and accumulation in the central regions of the cord of products of incomplete synthesis of mucopolysaccharide, but the explanation of this phenomenon remains obscure.

The conjunction of the thick bundles of collagen fibers with aggregations of jelly-like substance confers considerable strength and elasticity on Wharton's jelly, necessary for its undoubted role as a protective layer for the umbilical vessels. We believe, however, that this is not the sole, or even the most important function of Wharton's jelly. Papers published during the past few years have drawn attention to the importance of the biological protective function of substances of the type of the acid mucopolysaccharides, which are able to suppress the vital activities of a number of bacteria and viruses, and to inactivate their toxins [5, 10, 11, 12]. Evidence has been published [1] that secretion by the fibroblasts of Wharton's jelly is regulated by nervous impulses proceeding from the fetus.

A consideration of published data and of the results of our histochemical investigation of the umbilical cord, in conjunction with A.V. Vikulov's description of an extravascular channel, leads to a somewhat different approach to the evaluation of the functions of Wharton's jelly. According to Vikulov, the extravascular channel of the umbilical cord is made up of a system of intercommunicating cells filled with a "proteinic fluid" which flows towards the fetus. But this "proteinic fluid" is a very viscous jelly-like substance, and we think it highly improbable that it could circulate freely. The accumulation within the tissues of Wharton's jelly of enormous amounts of such biologically active material as are the acid mucopolysaccharides, the production of which is

probably regulated by the fetus, affords a basis for the assumption that Wharton's jelly functions as a kind of barrier to the spread of infection from the maternal to the fetal organisms.

SUMMARY

Acid mucopolysaccharides of Wharton's jelly were studied in umbilical cords of the newborns and in human embryos at various periods of pregnancy. The fibroblasts of Wharton's jelly synthesize and secrete acid mucopolysaccharides only during the first months of pregnancy (up to the fifth or sixth months). Mast cells begin to appear in the Wharton's jelly from the 13th-14th week and take over the function of synthesis and secretion of acid mucopolysaccharides. It may be assumed that the Wharton's jelly serves as a kind of protective barrier to the possible spread of infection from the mother to the fetus.

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