ENDOMETRIAL GLYCOGEN IN STERILITY

by

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Introduction

For the proper implantation and subsequent growth and development of the fertilised ovum in the uterus, it is necessary that adequate amounts of carbohydrate in general and glycogen in particular be present in the glandular secretions of the endometrium (Zondek and Shapino, 1942; Hughes *et al* 1950). The high glycogen content of these glandular secretions serves as a major source of engery for the maturing embryo.

Endometria which have undergone inadequate secretory transformation contain less than normal amounts of glycogen in intracellular vacuoles and intraluminal secretions when stained with periodic acid Schiff (PAS). This lack or deficiency of glycogen makes such endometria unfavourable for continuation of pregnancy. This may lead to sterility or habitual abortion.

Patients and Methods

Endometrium from 136 females were studied. They were in the following groups:

Group A: One hundred and five endometria from females who reported with sterility. Their age ranged between 18-24 years (mean 20.5 years). Ninety were cases of primary sterility and 15 were that of secondary sterility.

Group B: A set of 31 endometria from normal age matched females formed the control for this study.

Detailed clinical history, physical examination and laboratory investigations were carried out on both the partners to detect any obvious cause for inability to conceive.

Endometria from the body of the uterus during the second half of the menstrual cycle was collected in 10% buffered formal saline. It was processed for histopathological examination by the standard technique. All sections were stained with haematoxylin and eosin, and periodic acid Schiff (PAS), Mcmanus (1972). Stainable material digested by 0.1% malt diastase, in 0.02 M phosphate buffer, at pH 6.0 was taken as glycogen. The amount of glycogen in each specimen was estimated visually and graded as 1 plus, 2 plus, 3 plus and 4 plus. (Figs. 1, 2, 3).

Endometrial dating was carried out by the method of Noyes (1971) using the changes in the endometrial glands and stroma as the guidelines for labelling progressive steps in secretory differentiation. The phase of cycle in each specimen was estimated by histological examination and

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checked as to whether histology corresponded to the expected maturity of the menstrual cycle.

Results

A total of 408 sections from 136 endometria were studied. They were divided in normal and abnormal endometrium based upon the histological dating (Table). In those labelled normal, histological maturity corresponded with the clinical or chronological maturity expected of the endometrium irrespective of the glycogen content.

Of 105 endometria from group-A, 75 were called normal based on histological grounds. Sixty of them were cases of primary sterility. In these, glycogen was present in small amount (1 plus) during the early secretory phase. It was present in small granules/particles in the infranuclear and perinuclear location. It did not necessarily localise in the region of cytoplasmic vacoulation but also extended towards the luminal margin of the cell more than the cytoplasmic vacoule. With the maturation of the cell, glycogen moved along with the vacoule towards the supranuclear position in the midsecretory phase. Particles tended to increase in size and became blob like and appeared in the lumina of glands during late secretory phase. Small amount of PAS positive material was also seen in the stroma, mostly localised in the periglandular region. In general, the appearance of glycogen followed the pattern seen in the controls (group-B) but the glycogen content was considered less than normal control date wise.

The remaining 12 of group-A which were called histologically normal were cases of secondary sterility (Table). Despite adequate histological maturity, the glycogen content was markedly low. In

TABLE

Pattern of Histological Maturity and Glycogen Content in Endometrium of Patients with Sterility (Group—A) and in Normals (Group—B)

Group	A (n-105)				B (n-31)	
	Normal (n-75)		Abnormal (n-20)			
	Number (%)	Glycogen	Number (%)	Glycogen	Number (%)	Glycogen
Primary sterility						
Proliferative phase	—	—	6 (20%)	—	6 (20%)	+
Secretory phase						
Early	12 (16%)	+	8 (26.7%)	—	8 (26.7%)	++
Mid	25 (33.3%)	++	8 (26.7%)	+	9 (26.7%)	+++
Late	26 (34.7%)	+++	5 (16.7%)	—	8 (26.7%)	+++
Secondary sterility						
Proliferative	—	—	0 —	—	—	
Secretory phase						
Early	4 (5.3%)	—	2 (6.7%)	—		
Mid	3 (4%)	+				
Late	5 (6.7%)	+	1 (3.2%)	—		

these cases very slight amount of glycogen appeared during the midsecretory phase in the perinuclear region. It was mostly seen as diffuse haziness. The PAS positive material in the periglandular area appeared normal. No increase in glycogen was seen with the advancing age of the gland. In these cases the glycogen appeared late and remained deficient.

Thirty endometria out of 105 of group-A (Table) were labelled abnormal as their histological maturity did not correspond with the expected maturity. Of these, 27 were cases of primary sterility and 3 of secondary sterility. Six (20%) of these were in proliferative phase, while remaining 24 were in the secretory phase. Glycogen content was grossly deficient in the primary sterility cases and was negligible or almost absent in the secondary sterility patients. No glycogen could be demonstrated either in the glandular lumina or in the cell cytoplasm. The stromal periglandular PAS positive material however did not show any abnormality.

Discussion

Endometrium in 30 (28.5%) out of 105 patients who presented with infertility showed gross histological abnormalities and marked reduction in glandular glycogen. Majority of these (27 out of 30) reported with primary sterility. Those who showed normal histological maturity as expected from menstrual history also showed glycopenic endometrium but all these cases belonged to the secondary sterility group. Our findings attribute an important role to normal glycogen content in the glandular cells for proper implantation of the fertilized ovum. Maximum glycogen deficiency was noted in the secondary sterility group. This appears to have developed subsequent to the previous pregnancy and hence acquired and needs further elucidation. No attempt has been made to draw a conclusive mechanism for its occurrence from this data, as only few cases belonged to this group in the present study. This forms an interesting avenue for further investigation. Even in the primary sterility group, glycopenic endometrium was seen in 21 secretory phase endometria and further highlights its importance.

The importance of adequate glycogen in the endometrial glands has been recognised from early days (Zondek and Stein, 1940). But data available is limited and controversial. Earlier studies have stressed the importance of the presence of sufficient glycogen at the time of implantation of ovum and for its continued growth (Hughes *et al* 1950).

Baveja *et al* (1972) reported a retarded endometrium in terms of glycogen in 72.7% of habitual abortion patients. Disturbed carbohydrate metabolism has also been noted in many cases of toxaemia of pregnancy (Roy Chowdury, 1979; Mardikar *et al* 1980). Though no follow up study is available in these patients but many are bound to end up with secondary sterility. The importance of the late proliferative or preparative stage requires more elucidation. It is likely that an endometrium which is not fully developed morphologically and histochemically in the secretory phase was probably inadequate in the late proliferative phase also. This possibly points to a local defect at the glandular level. In some cases even though the histological picture presented synchronous development of the gland and the stroma, relatively normal amounts of glycogen in the stromal cells and small amount in the glandular epithelium point towards derangement at the level of glands.

The exact mechanism of glycopenic

endometrium is not well understood but appears to be a relative refractoriness of glands to hormones. For some unknown reason this is more in the secondary sterility endometrium but is also seen in primary sterility cases. Proper evaluation and understanding of the data requires further longterm controlled studies especially directed towards ellucidation of role the local factors might play on the endometrium—hormonal interaction.

Summary

Endometria from 105 (group A) cases comprising of 90 cases of primary sterility and 15 cases of secondary sterility were studied. A group of 31 normal (group B) endometria formed the control group. On the bases of histological dating it was called 'normal' or 'abnormal'. Estimation of low endometrial glycogen in cases of secondary sterility and in 'abnormal' endometria of primary sterility was observed. Significance of the finding is discussed.

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See Figs. on Art Paper I