AN INVESTIGATION OF THE ORIGIN OF THE COLOSTRUM CELLS*

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There are conflicting views on the origin of the cellular elements of the colostrum. The opinion most commonly held is that the large and small colostrum cells originate from mesenchyme and enter the colostrum by diapedesis through the epithelium of the breast alveoli and ducts. This view was supported, among other authors, by Bizzozero & Vassale (1887) and Varrier-Jones (1924). On the other hand, Wallich & Levaditi (1905) held that both wandering cells and epithelial cells may be present in the colostrum. Grégoire (1930), among others, goes further, and suggests that the majority of the cells are epithelial in origin.

There are very few histological data on the changes in the epithelium of the human breast between late pregnancy and the early post-parturitional stages. Most of such investigations of the colostrum cells have been carried out on lactating animals such as the guinea-pig and cat.

The present investigation deals especially with the histological changes in the human breast in the early post-parturitional stage, and supports the view that the majority of the colostrum cells are epithelial in origin.

MATERIAL AND METHOD

Sections from fifty-eight breasts were examined. Forty-five of these came from women who died in the first few days after delivery, three came from women who died during parturition and ten others in the resting stage or in different menstrual phases were used for comparison. The ages of the subjects varied from 12 to 40 years.

All the breasts were fixed in 10% formalin and the sections stained with haematoxylin and eosin. Sagittal sections of the whole breast were cut at a thickness of 100μ. With such sections it was possible to compare different areas in the same breast and also to obtain a three-dimensional picture of the glands. Some thin sections (10μ) were used to obtain a clear picture of the cellular structure, but thin sections did not give such a complete idea of the structure in depth and in them the glandular elements were seen in disconnected fragments. Smear preparations of colostrum were also examined.

RESULTS

The resting breast. There are so many factors affecting the histology of the adult breast that separate descriptions are needed of the different phases.

Breasts of young women who died of chronic diseases, especially tuberculosis, were chosen. In cases of this kind, menstruation usually ceases and the mammary

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gland can be assumed to be in the resting stage. Figs. 1 and 2 show characteristic features of what may be classified as the resting breast. Histological examination showed clusters of alveoli at the periphery (Pl. 1, fig. 1), whereas ducts with few alveoli were characteristic of the centre of the corpus mammae (Pl. 1, fig. 2).

There were many variations in the glandular elements, not only in the relative abundance of glandular elements in different breasts, but also in the relative abundance and degree of cellular differentiation within a section of the same breast. The varying amounts of glandular tissue in the breasts of different women has been described in a previous paper (Engel, 1941), but the striking variations in different parts of one and the same breast are now emphasized by means of whole sections of breasts used in this investigation. This variation in alveolar structure is best shown by studying different sites in the same section of a whole breast. Pl. 1, fig. 3, shows a section of the whole breast from a girl aged 17 years. The arrows show the sites from which the photographs in Pl. 1, figs. 4 and 5, and Pl. 2, fig. 6, were taken. Well-marked ducts with few budding alveoli are seen in Pl. 1, fig. 4. The alveolar pattern has become more complex in Pl. 1, fig. 5; marked proliferation of the alveoli is shown in Pl. 2, fig. 6. This extensive proliferation was most frequently seen at the basal periphery, and may be sufficiently well marked as to give an appearance of changes due to pregnancy.

The epithelium lining the budding alveoli in these non-lactating breasts has a double layer of cells. The external cells are small and inconspicuous in the resting breast (Pl. 3, fig. 14) but become much more distinct as soon as the breast is under increased hormonal stimulation (Pl. 2, fig. 10). The two layers are distinct from the outer myoepithelium which does not directly concern this investigation. The generally accepted view that there is only one layer of cells lining the alveoli cannot be confirmed.

The breast during menstruation

Detailed histological changes during menstruation were described by Rosenburg (1922). There is no general agreement, but proliferation is believed to occur during the first phase of the cycle, followed by regression in the second phase. Dieckmann (1925) is of the opinion that the mammary gland does not respond at all in the menstrual cycle. The correlation of clinical experience with the findings of this investigation suggests that the response depends on the proportion of the glandular and fibrous content.

The proliferation of the alveoli during the first phase of the menstrual cycle is shown in Pl. 2, fig. 7, and in fig. 8 the two layers of cells are more marked than in the resting breast. The outer or basal layer of cells consists of large, pale cells with small nuclei. The cytoplasm has been shown to contain neither glycogen nor fat droplets. The internal layer is composed of small, closely packed cells, almost filled by the nucleus, hence their dark staining.

Chronic mastitis

Chronic mastitis, or mastopathia, occurs in many women, particularly in those over 35 years of age. It is now generally accepted that the condition is not inflammatory but due to hormonal imbalance. Many cases show the effect of hormonal

stimulation on the secretory basal cells. Pl. 2, fig. 10, shows the large, clear basal cells and the smaller and darker internal layer from such a case. The dark nuclei of the inner layer make a sharp contrast with the pale outer layer.

The histological changes in the breast during parturition

Three of the breasts examined were from women who died during delivery and were therefore in the colostral stage. The specimens were most useful in the elucidation of the different nature of the two cell layers. Pl. 2, fig. 9, and Pl. 3, fig. 11, show alveoli from two of these cases. Pl. 2, fig. 9, shows alveoli now lined with a single layer of cells and containing desquamated cells in the lumen that have probably been shed from the internal epithelial layer. Pl. 3, fig. 11, shows, in one alveolus, a complete internal layer coming away from an intact basal layer. In examination of many sections of these breasts all stages have been seen, from the intact internal layer still partly adherent to the basal layer, that is, in the act of desquamation, to the debris in the lumen of an alveolus now lined with a single layer of epithelium. This debris can be seen collected in the small alveolar ducts illustrated in Pl. 3, fig. 13, which shows a small alveolar duct packed with cellular debris, although its own epithelial lining is intact.

Some indication of the fate of the duct epithelium is given by Pl. 3, fig. 16. This part of the wall of a glandular duct shows epithelial proliferation and hydropic degeneration. These cells are large, their nucleus is small and the pale cytoplasm contains neither glycogen nor fat droplets demonstrable by Best's glycogen stain or Sharlach R. These hydropic cells are very similar to the large colostrum cells. It is possible that some of the desquamated cells retain fat droplets or fat may be ingested after desquamation.

A colostrum smear (Pl. 3, fig. 15) illustrates a typical large colostral cell probably derived from hydropic duct cells and short chains and coherent clusters of small darkly staining cells. Floating freely in the colostrum, the cells are spherical, and it is suggested that they come from the internal epithelial layer of the alveoli.

Wandering cells abound in the tissues supporting the alveoli, but only a few polymorphonuclear cells were seen in the colostral smears.

DISCUSSION

The fact that the alveoli of the non-lactating breast are lined by two rows of epithelium is stressed because it bears on the origin of the small colostral cells. The present position in regard to the origin of the colostral cells can best be summed up by quoting Saner (1950): '...cells from the periductal stroma reach the alveolar lumen by passing through the basement membrane; these entering cells are chiefly lymphoid, but there are also numerous eosinophil cells, plasma cells, monocytes and polymorphonuclear leucocytes. Many of these cells contain fatty debris.'

The evidence presented here does not support the above statement, but suggests that the small colostral cells are in fact derived from the internal layer of the double layer of cells lining the alveoli, in the non-lactating breast, and that this inner layer of cells is shed into the lumen at the time of onset of parturition. The majority of the so-called lymphocytes are probably of this epithelial origin. Occasional poly-

morphonuclear cells can easily be recognized, but other members of the family of wandering cells could not be distinguished with any certainty.

The alveoli of the lactating breast are lined with a single layer of cells. The material examined indicates that in non-pregnant women the alveoli have two layers of epithelium. In the resting stage the basal layer is inconspicuous but under increased hormonal stimulation, as in some breasts during menstruation, and in chronic mastitis, the two layers become more clearly defined.

The two layers have already been shown by Berka (1912) and Dawson (1934). In Dawson's paper, fig. 15 shows the two layers of cells, and her fig. 26 on p. 672 shows the 'vacuolated' basal cells in a breast during the intermenstrual phase. Dawson is quite definite about the two epithelial layers in the alveoli of the non-lactating breasts. No explanation of the difference and of the loss of the one layer in pregnancy is brought forward. Berka is also definite about the two layers of epithelium. His description is not quite clear as he maintains that the non-lactating breast only contains ducts. His illustrations, however, show typical glandular clusters situated in loose connective tissue contrasting to the dense fibrous tissue of the mammary body.

As regards the large colostral cells, the position presents itself as follows: the idea that these cells are chiefly or exclusively wandering cells has never been convincingly proved. The fat laden colostrum cells in the writer's preparations were so similar to the proliferating cells in the ducts that these hydropic cells may well be the forerunners of the large colostrum cells. Both these cells are characterized by their large cytoplasm and small nucleus. Whether they contain fat debris or not is dependent on their past history.

The so-called colostrum bodies are probably small agglomerations of fat droplets and not cells (Forsell, 1939).

The conclusion arrived at is that the majority of the colostrum cells is of epithelial origin; wandering cells form only a small minority. This conclusion is particularly supported by the examination of material from parturient women.

SUMMARY

1. The alveoli of the non-lactating mammary gland are lined by a double row of cells. The basal layer is best recognized when the breast is under increased hormonal stimulation.

2. The basal layer is composed of the secretory cells, whereas the internal layer protects the former and is cast off as soon as the breast functions. The cast-off cells of the internal layer appear as small colostrum cells.

3. The large colostrum cells take their origin from proliferated and degenerated cells of the ducts. It is concluded that the majority of colostrum cells is epithelial in nature; a small minority belongs to the family of wandering cells.

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EXPLANATION OF PLATES

PLATE 1

Fig. 1. Virgin aged 19 years, died of nephritis. Breast shows several lobules of glandular tissue with well-marked budding alveoli. The picture is taken from the basal periphery. ×26.

Fig. 2. Virgin, aged 40 years. The breast shows a few ducts with poorly developed alveoli. ×100.

Fig. 3. Contact print of section from which figs. 4–6 are taken. The places from which figs. 4–6 are taken are marked by arrows.

PLATE 2

Figs. 4–6. Various places of one and the same section (fig. 3), showing primitive (fig. 4), more developed (fig. 5) and greatly proliferated glands (fig. 6). ×90. (Figs. 4 and 5 are on Pl. 1.)

Figs. 7, 8. Virgin, aged 19 years. Effect of beginning hormonal stimulation (proliferative phase of the cycle). Enlargement of the external layer of cells (fig. 8) (×245); lobular proliferation (fig. 7) (×70).

Fig. 9. Woman died intra partum, aged 26 years. There are many desquamated cells in the alveoli, the external (secreting) layer being intact. ×200.

Fig. 10. Mastopathia (biopsy) showing the two rows of cells lining the alveoli. ×160.

PLATE 3

Fig. 11. Woman died in delivery. Desquamated but coherent internal cellular layer (arrow). ×180.

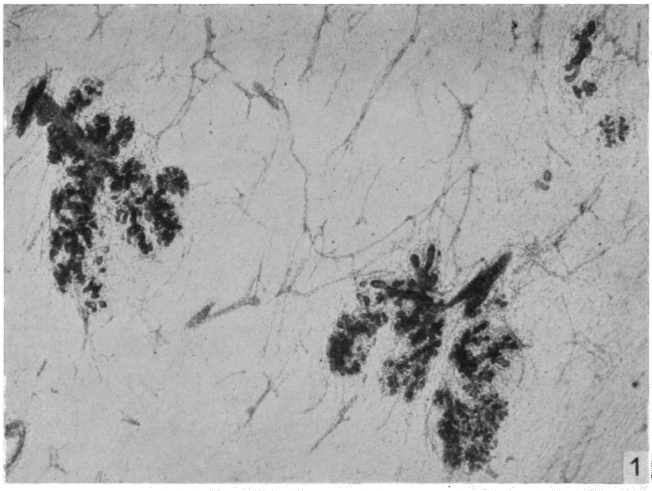
Fig. 12. Distended alveoli in fibrous portion of a colostral breast. Woman died in delivery. ×135.

Fig. 13. Woman died intra partum. Duct contains many desquamated cells while its lining is intact. ×220.

Fig. 14. Beginning alveolar proliferation to show the basal cells. ×180.

Fig. 15. Colostral smear showing rows and clusters of small cells. The cell in the centre is vacuolated, indicating the position of fat droplets dissolved out during fixation. ×250.

Fig. 16. Woman died intra partum. Proliferated and degenerated cells originating from the epithelium of a duct. ×260.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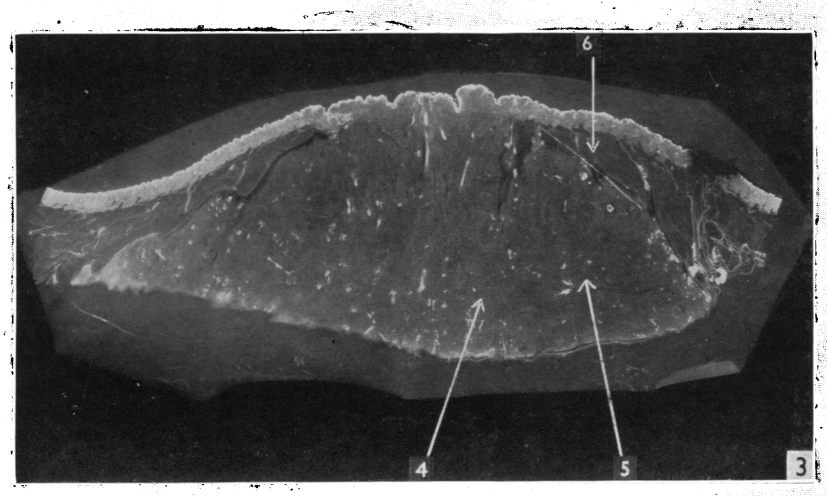
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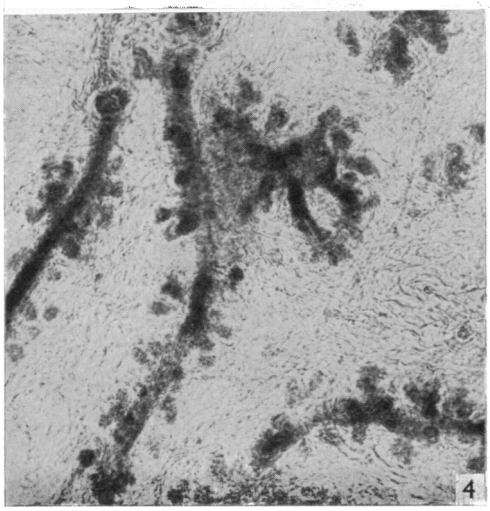
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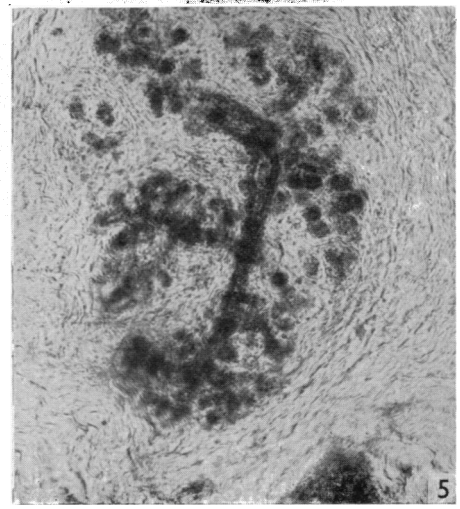
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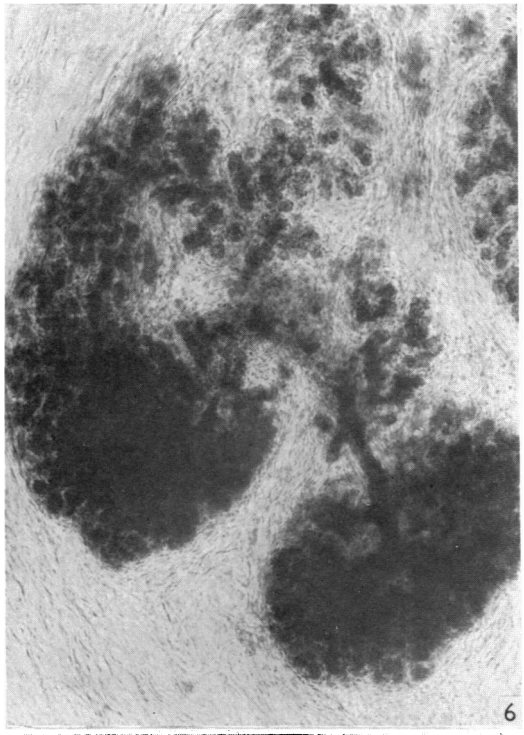
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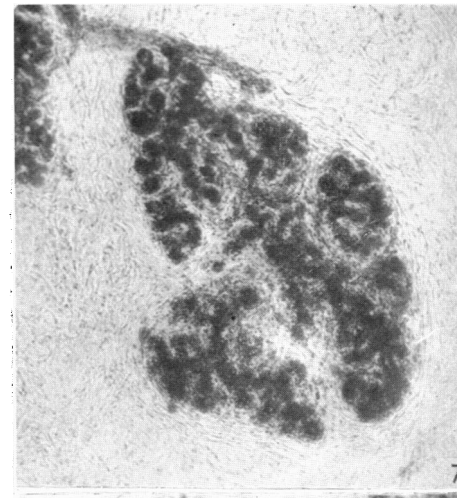
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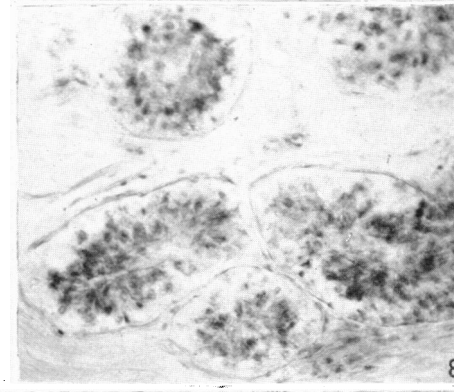
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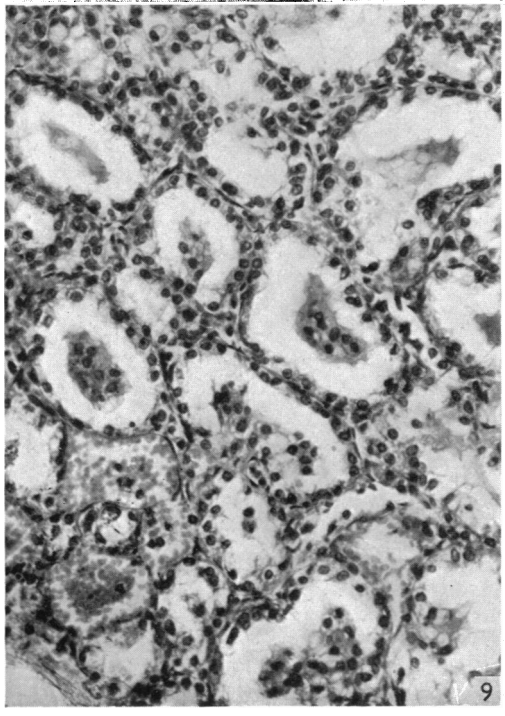
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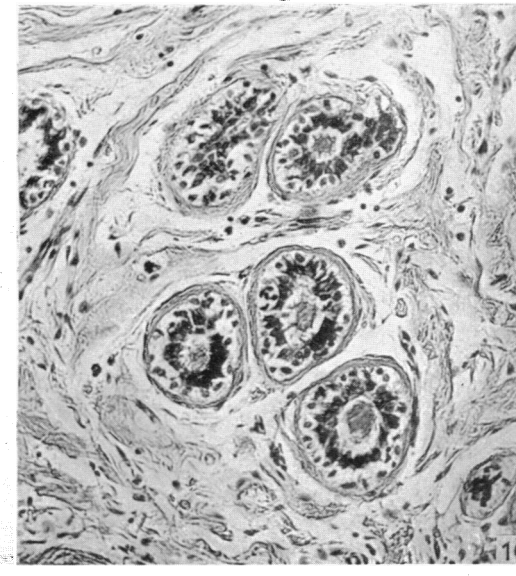
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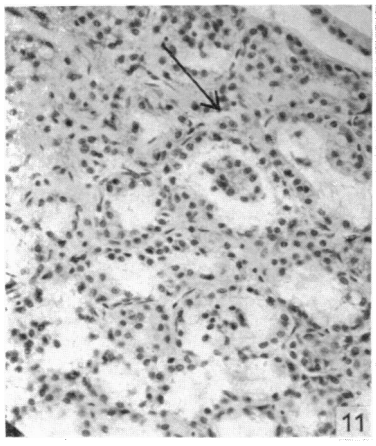
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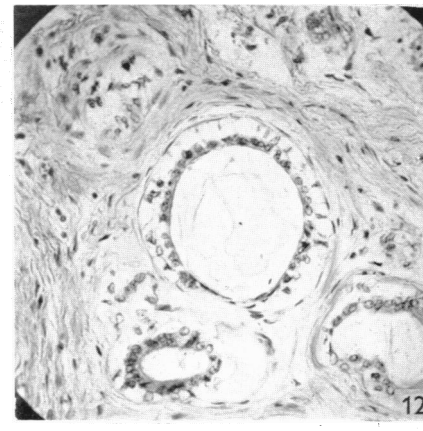
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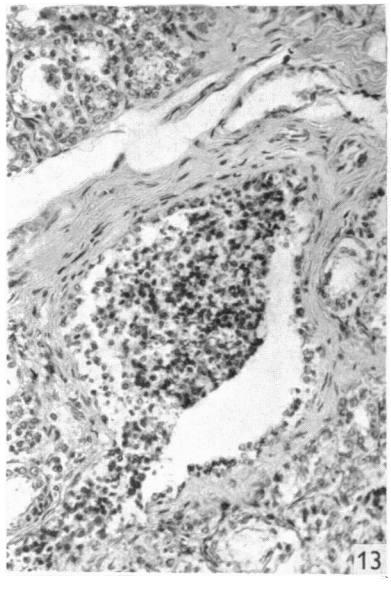
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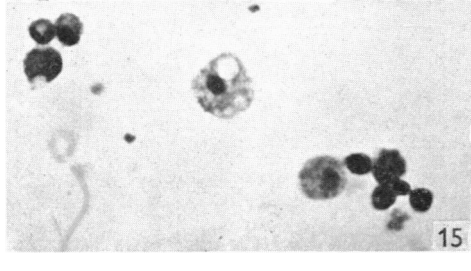
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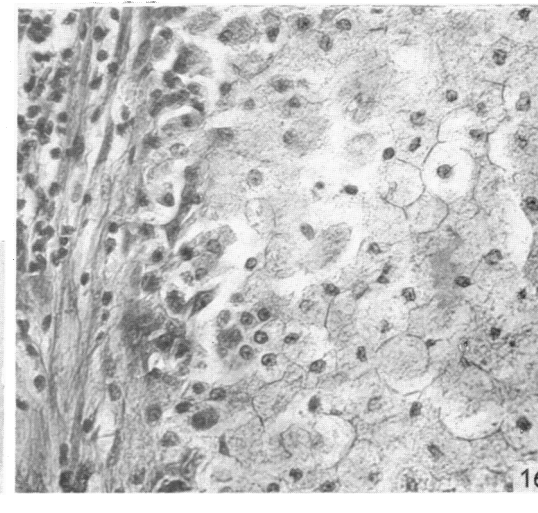
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