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THE ACTION OF PREDNISONE ON THE MORPHOLOGY OF THE VARIOUS ORGANS¹

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In a previous work, the action of cortisone on the morphology of the various organs was studied. The main results were: moderate atrophy of the adrenal cortex, quiescent state of the thyroid, with large follicles and flattened epithelium, episodes of oedema in the islets of Langerhans and diminution of the eosinophil cells in the hypophysis. In the spleen and lymphoid organs, there were histiocytic degeneration with consequent reduction of the lymphoblastic activity and of the lymphocytic contents. The liver showed a progressive enrichment of a cellular glycogen, whilst oedema and glomerular irritation were seen in the kidneys.

It was decided to carry out the same histological researches in order to study the action of a new cortisone-like drug—prednisone (Delta cortene Lepetit, corresponding to delta-1,4-pregnadiene-17 alpha, 21-diol-3,11,20-trione, also known as metacortandracin). This new drug shows, in respect to the previous ones, the property of acting at lower doses, and is without the side-effects of ordinary cortisone therapy (Ferrari et al.).

In histological studies, we examined various organs from

¹ Read before the 2nd International Congress of Allergology, Rio de Janeiro, 1955.

female rats, treated daily with 12.5 mg/kg of prednisone, for a total period of one month, and the results are reported here.

ADRENALS

Even on low magnification, the adrenal glands show a homogeneously thinner cortex. On higher magnification, it can be seen that the glomerular zone consists of a thin layer of cells of reduced surface and with closely packed nuclei. Even the sheath is reduced in width, showing small cells in a state of apparent functional quiescence. The reticular layer is equally reduced in thickness, while the medulla is normal.

THYROID

The gland is shown to be mainly composed of remarkably wide vesicles, with flattened epithelium. The colloid appears dense and compact. All in all, it has the aspect of a thyroid in a state of functional quiescence.

PANCREAS

The exocrine part of the pancreas appears normal everywhere, while large islets of Langerhans are scattered over it. This increase of surface is related to a congested and enlarged state of the intrainsular capillaries. It is sometimes observed that the latter undergo plasmorrhagic extravasation. This plasmorrhagia invests the bordering islets cells, provoking evident signs of degenerative involvement (fibrinoid type).

Furthermore, cytolysis may occasionally be seen due to the abnormal cellular oedema. The most apparent morphological modification is always of oedema-congestion type with occasional signs of cellular damage.

THYMUS

The tissue of the gland is often affected with frequent loss of alveoloform substance. Cellular detritus or cells in various states of degenerative involvement (oedema, pyknosis, etc.) are often seen. These regressive phenomena are more marked in the periphery of the gland, to the point of sometimes considerably altering its normal compactness.

SPLEEN

The splenic parenchyma appears to be moderately congested. The follicles are often the site of degenerative manifestations which particularly affect the histiocytes of the germinative centre. These cells may show signs of oedema, fragmentation and pyknosis, sometimes cells in karyokinesis are even seen. The damaged germinative centres are often filled with fibrinoid patches.

These patches appear to be derived from serous extravasation from capillaries abnormally full of plasma. The pulp is rather poor in cells. These often show abnormal polymorphism with signs of nuclear pyknosis, gigantism, etc.

LIVER

The hepatic parenchyma is morphologically a little different from the normal and any changes are represented by various processes of minute, foamy vacuoles, mainly observed in the cells near the centro-globular veins. These microvacuoles are filled with glycogen. Kupffer's cells are very evident.

HEART

Some preparations may show diffuse congestion, with slight signs of oedema of the muscle fibres.

It is advisable to put forward some considerations by way of comment on this first preliminary histological research. First of all, it must be mentioned that the doses used were much higher than those given therapeutically. The morphological modifications were of the type seen with cortisone. Even prednisone particularly attacks the histiocytes, which usually degenerate through a process of cellular oedema. Involvement of the capillaries was observed peculiarly and these often showed an abnormal serous content with tendency to plasmorrhagia. The plasmorrhagia often appeared to be the cause of the fibrinoid degeneration of the bordering cells.

The action of prednisone on the phenomena of immunological reactivity appears, under the light of this particular study, to be bound up with the biochemical disturbances which this cortisone-like drug brings about in the histiocytes destined for antibody formation. The increased water content of the cells and the probable ionic modifications evidently interfere in the intimate structure of the cells themselves making them incapable of carrying out their reactive function.

Because the cellular damage is limited, the situation is soon brought back to normal, by means of a proliferative effect, as shown by the many cells in karyokinesis.

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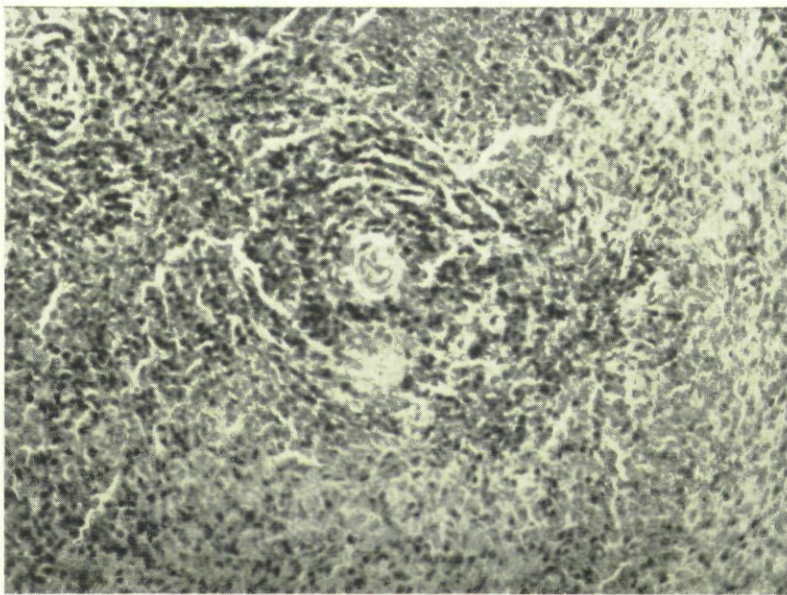


Fig. 1.

Spleen. Splenic follicle with partial deterioration of its external zone.

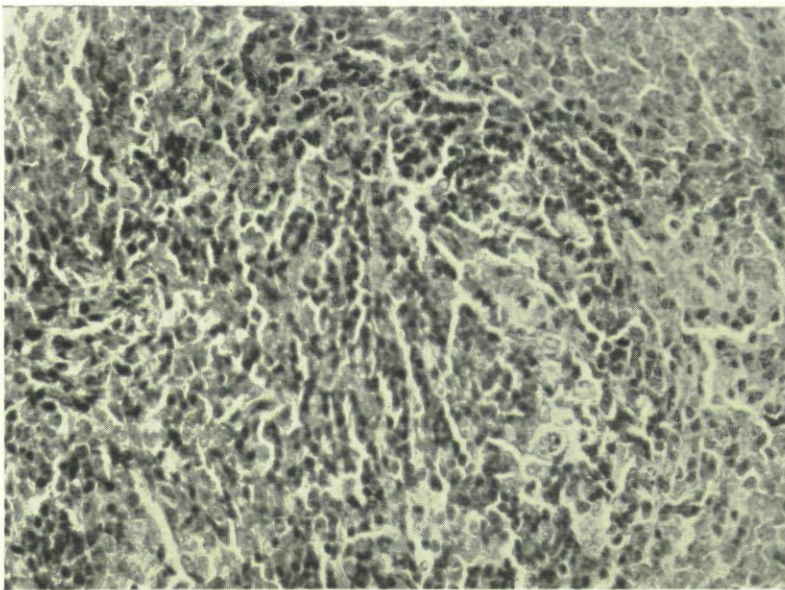


Fig. 2.

Spleen. Partial oedema of the follicular areas with degenerative cellular oedema.

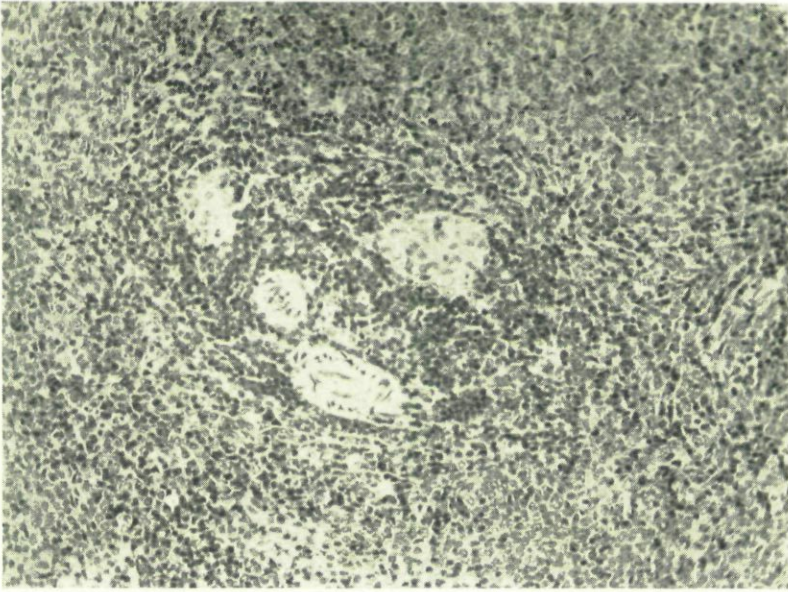


Fig. 3.

Spleen. Follicle showing presence of intraparenchymatous serous lacunae.

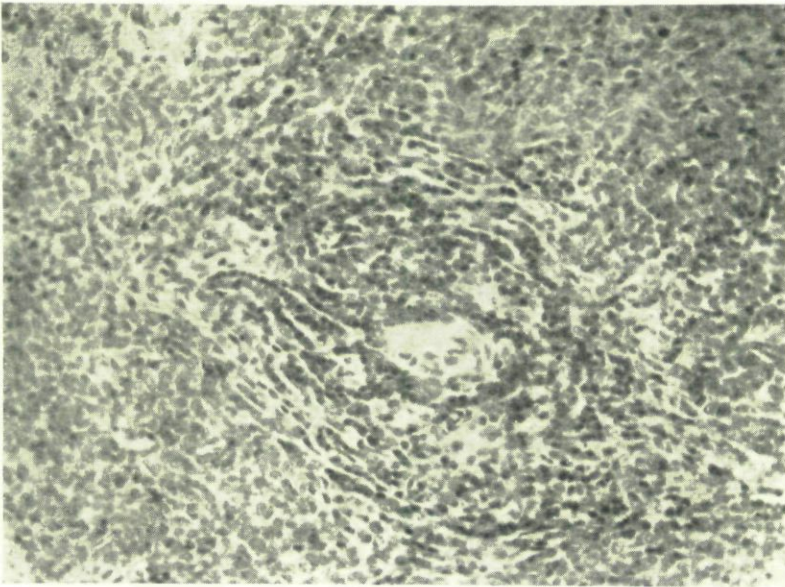


Fig. 4.

Spleen. Splenic follicle with serous lacunar areolas. Corresponding to these areas signs of cellular involvement are more marked.

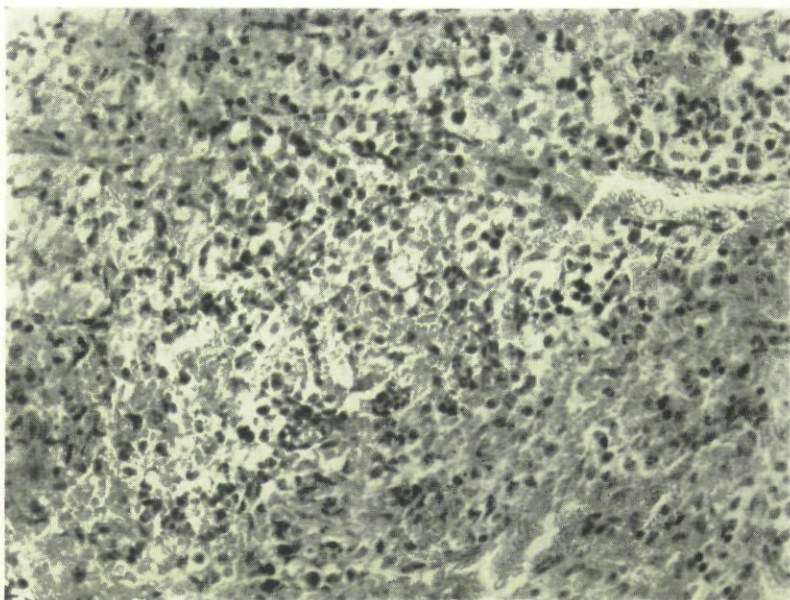


Fig. 5.

Spleen. The splenic vessels and the parenchyma in general appear rich of granulocytes.

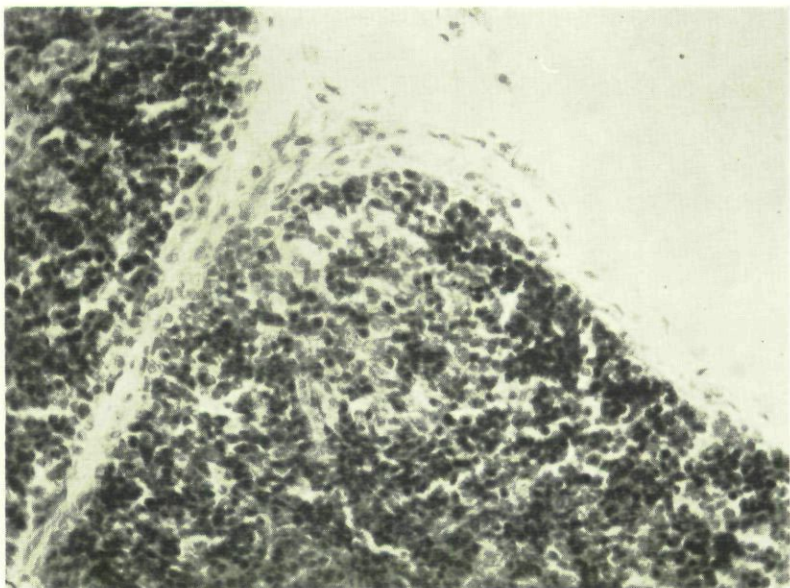


Fig. 6.

Thymus. Areas of cellular rarefaction caused by degeneration of the structural elements.

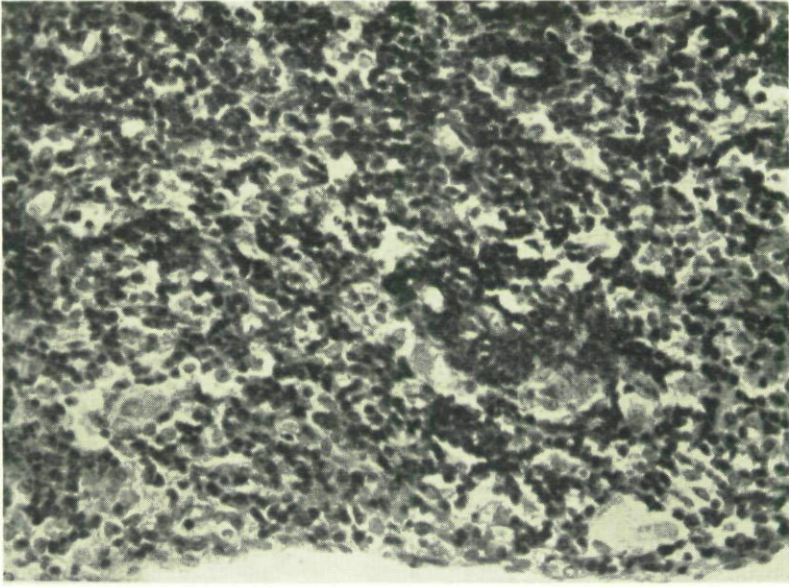


Fig. 7.

Thymus. Marked signs of parenchymal involvement, with areolae of cellular degeneration. Pyknosis and other nuclear damages are evident here and there.

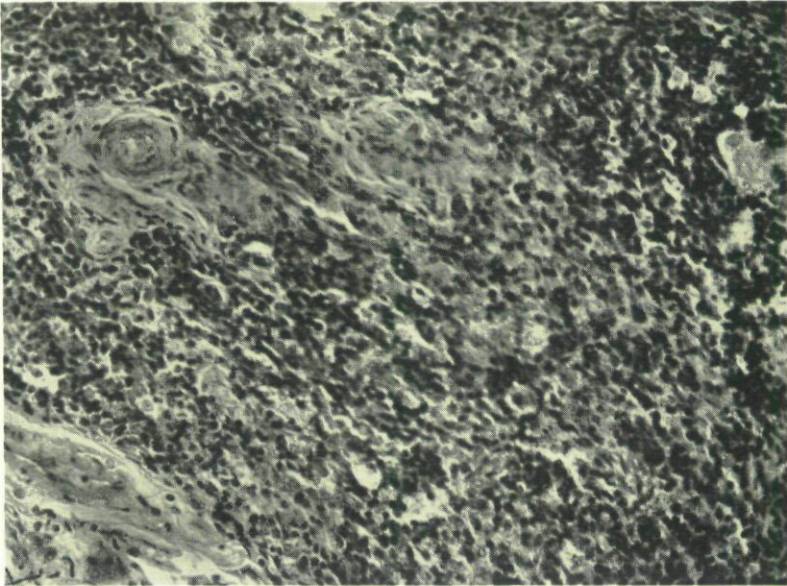


Fig. 8.

Thymus. The parenchyma very frequently shows signs of cellular involvement with oedema, pyknosis, nuclear fragmentation, etc.

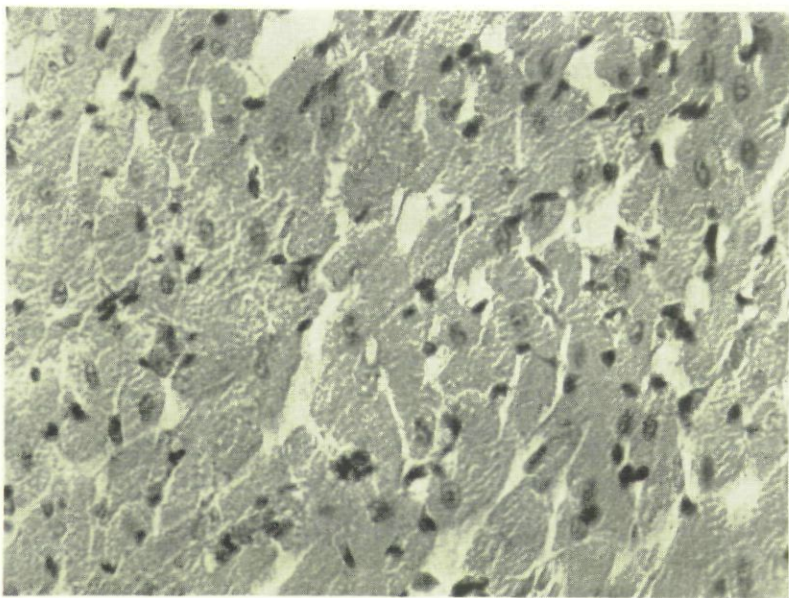


Fig. 9.

Heart. The muscular parenchyma here appears to be substantially of normal structure.

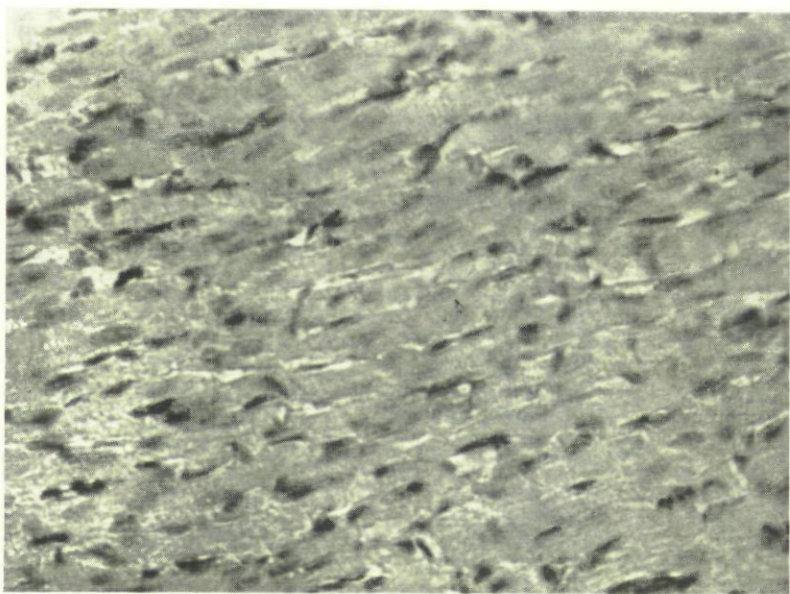


Fig. 10.

Heart. The cardiac muscle shows some oedematous arcles along the fibres.
The rest is normal.

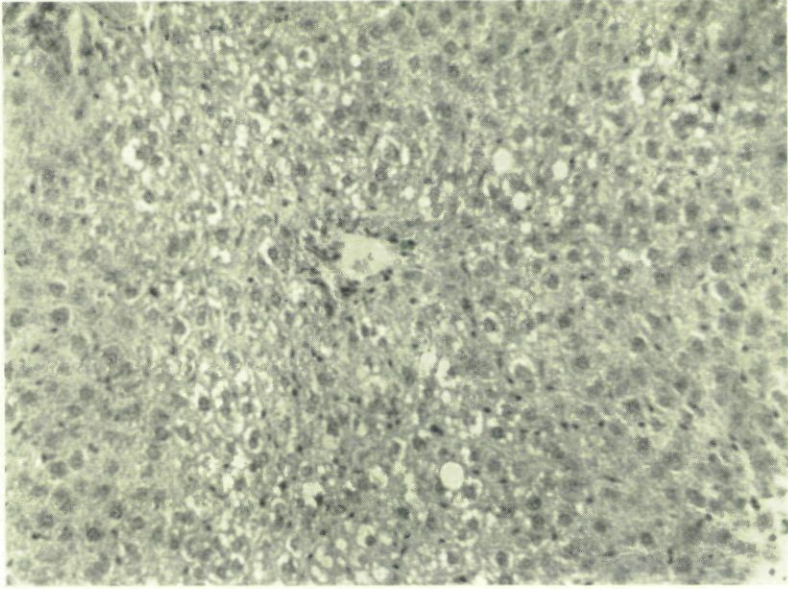


Fig. 11.

Liver. Glycogenic-type areolar structure of the parenchyma.

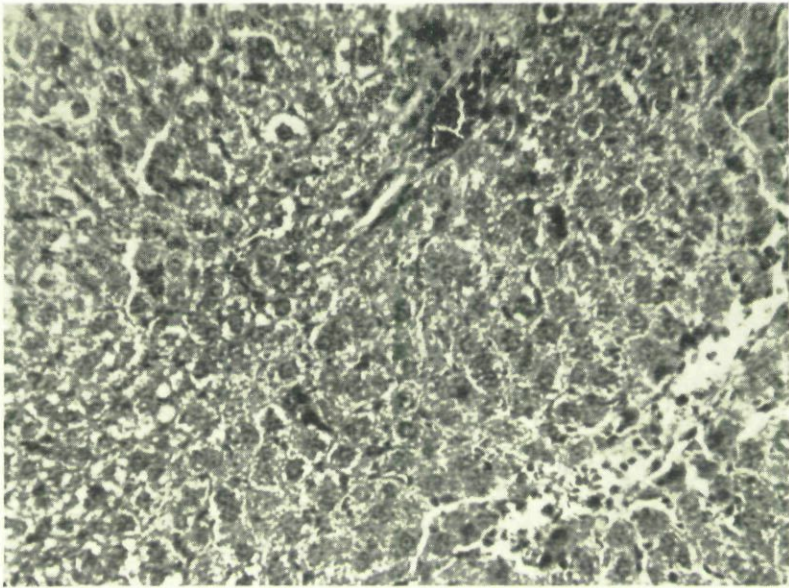


Fig. 12.

Liver. Slight diffusion of glycogenic-type areolae.

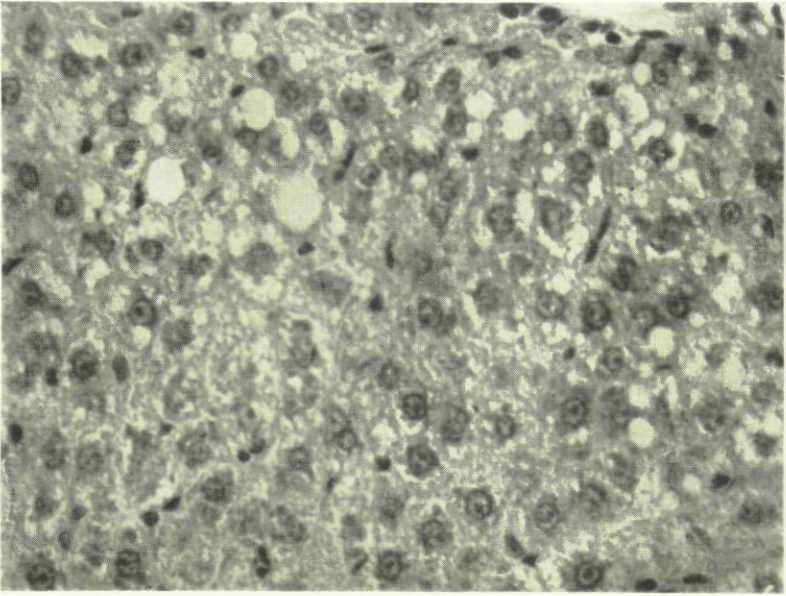


Fig. 13.

A detail (higher magnification) showing the areolar formations in the hepatic parenchyma.

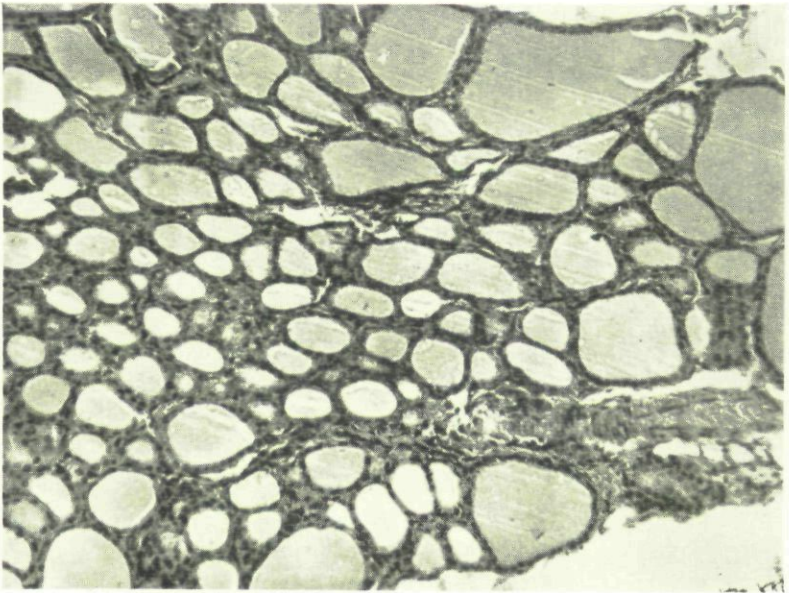


Fig. 14.

Thyroid. Glandular parenchyma with presence of numerous follicles with wide diameter. Glandular epithelium of average height.

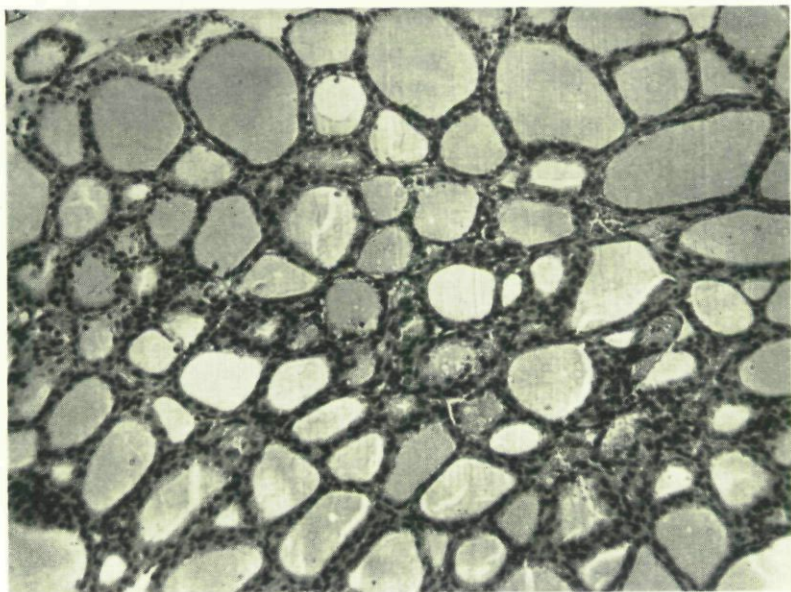


Fig. 15.

Thyroid. Gland with follicles with wide diameter and epithelium of average height.

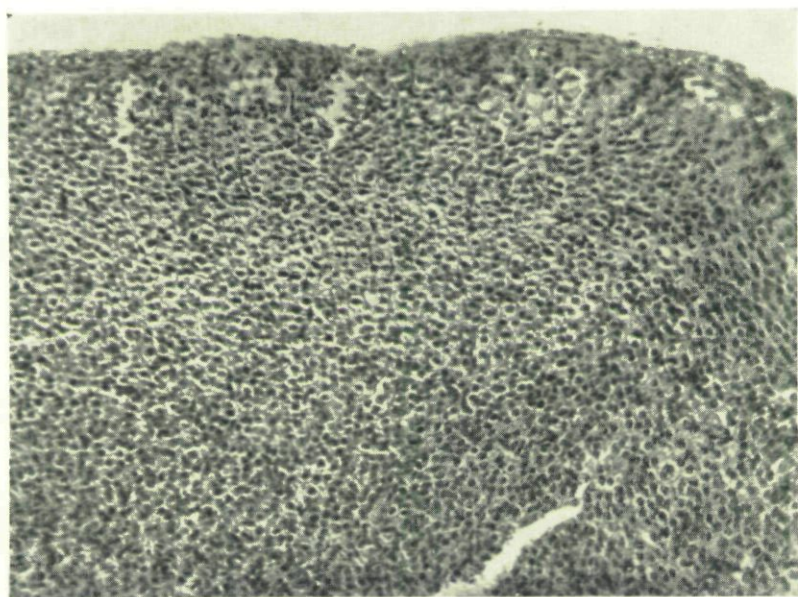


Fig. 16.

Adrenals. Compact gland, with cells showing a small surface, on the whole reduced in height. Morphological appearance of relative functional quiescence.

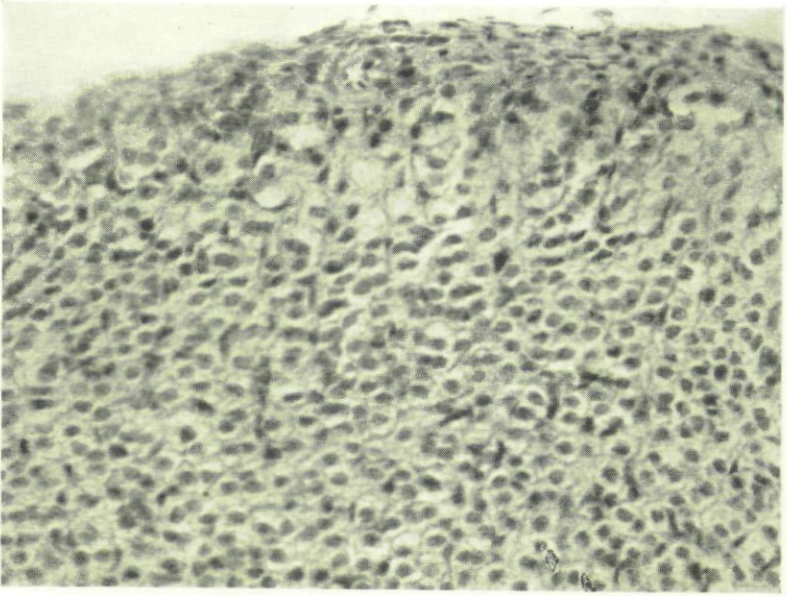


Fig. 17.

Adrenals. Detail of the previous. Thin glomerular layer. Cells of the fascicular layer mainly small and clustered together.

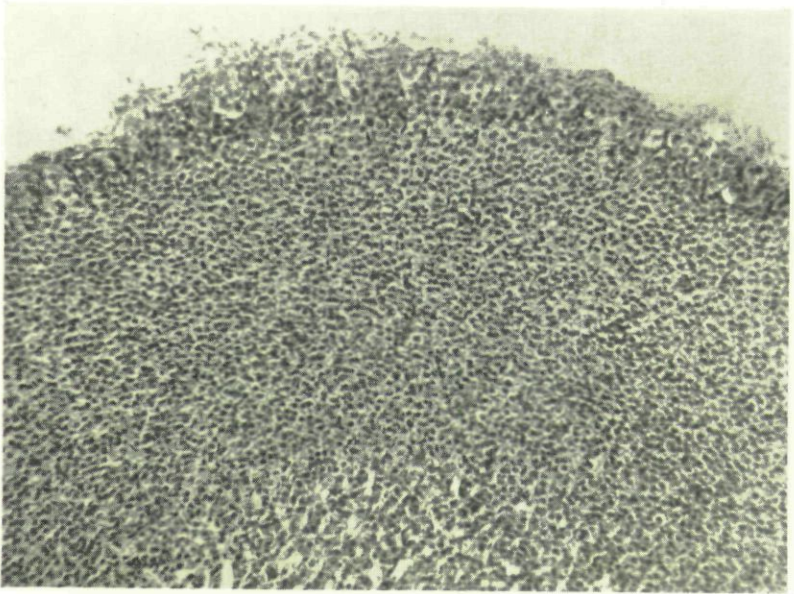


Fig. 18.

Adrenals. Gland slightly reduced in thickness, particularly in regard to fascicular layer.

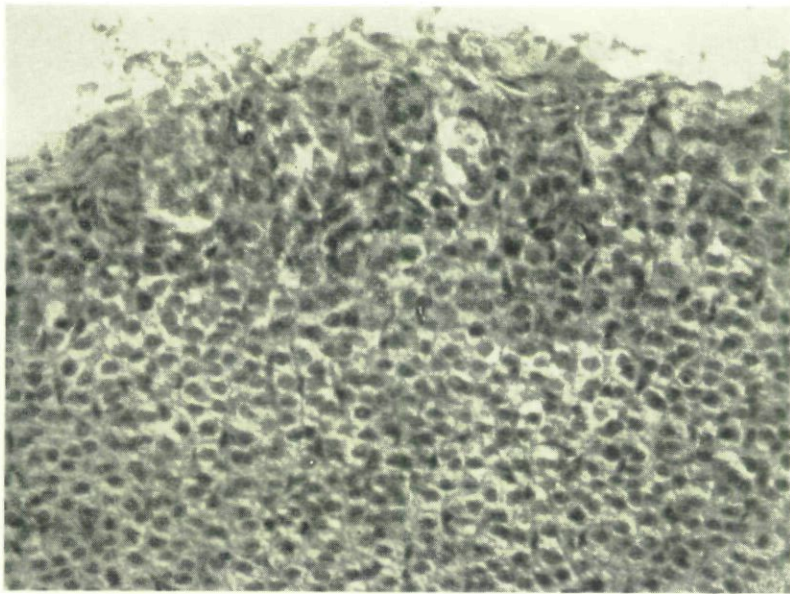


Fig. 19.

Adrenals. Detail of the previous. Cells of the external layer showing a reduced surface. Functional vacuolation almost absent.

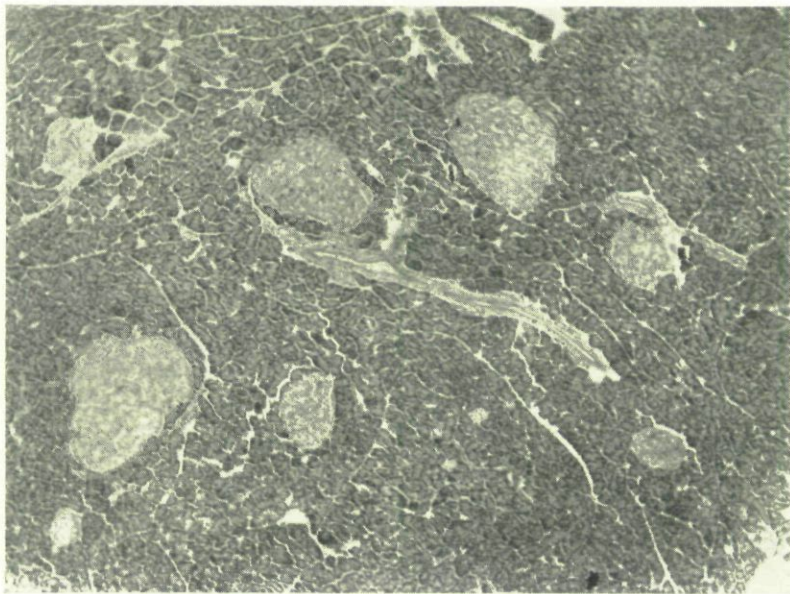


Fig. 20.

Pancreas. The gland, slightly magnified, is normal.

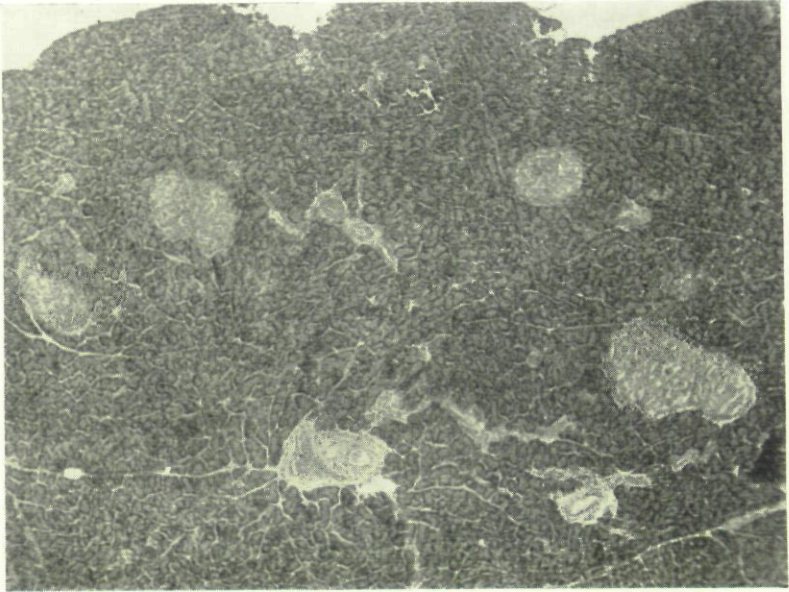


Fig. 21.

Pancreas. Another detail of the gland, here free from any particular structural alterations.

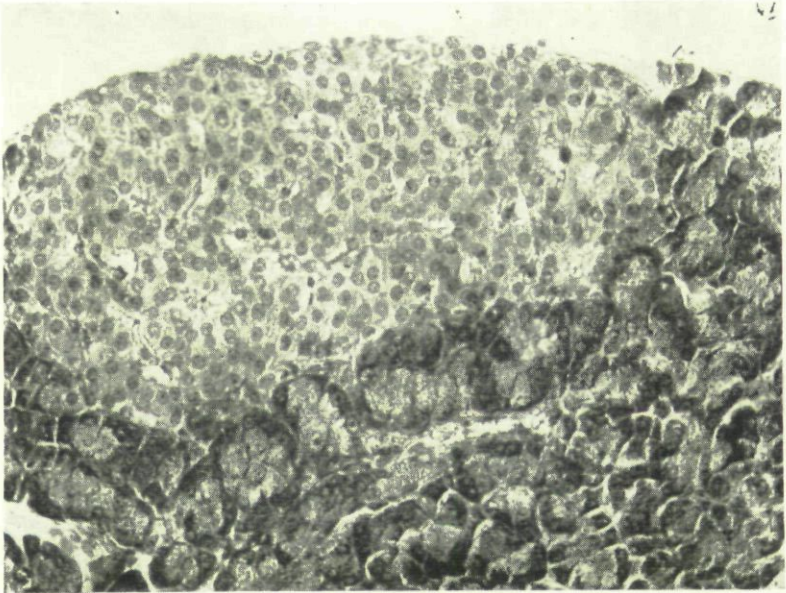


Fig. 22.

Pancreas. Islets of Langerhans showing substantially normal structure, except for a few small areas of cellular rarefaction.

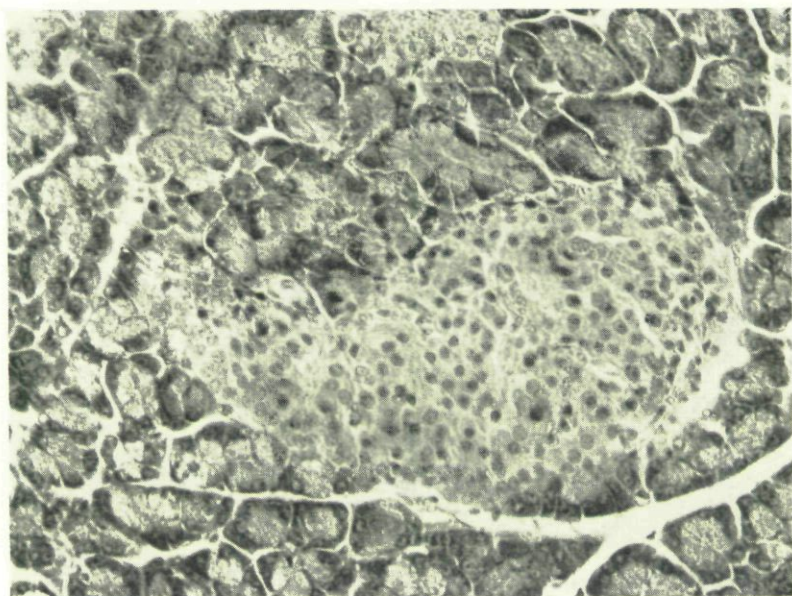


Fig. 23.

Pancreas. An islet of Langerhans showing marked vessel congestion. Abnormal plasma extravasation of the dilated capillaries, with involvement of the bordering cells.

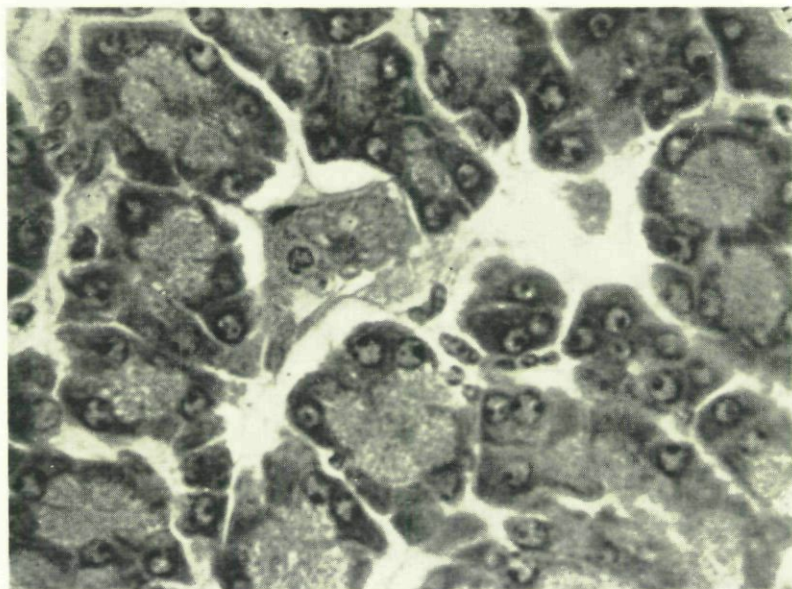


Fig. 24.

Pancreas. Small, markedly congested vessel with bordering serous patch.

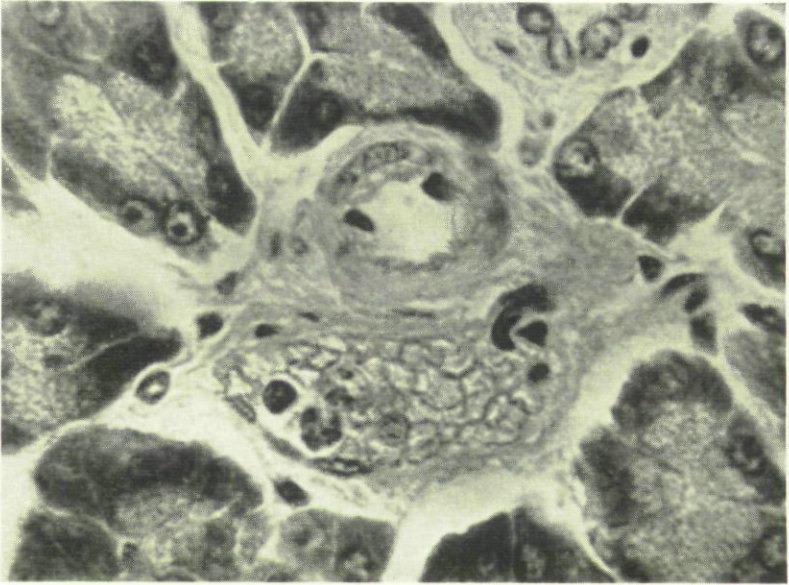


Fig. 25.

Pancreas. Markedly congested interstitial vessel. Capillary with oedematous walls and peripheral halo.

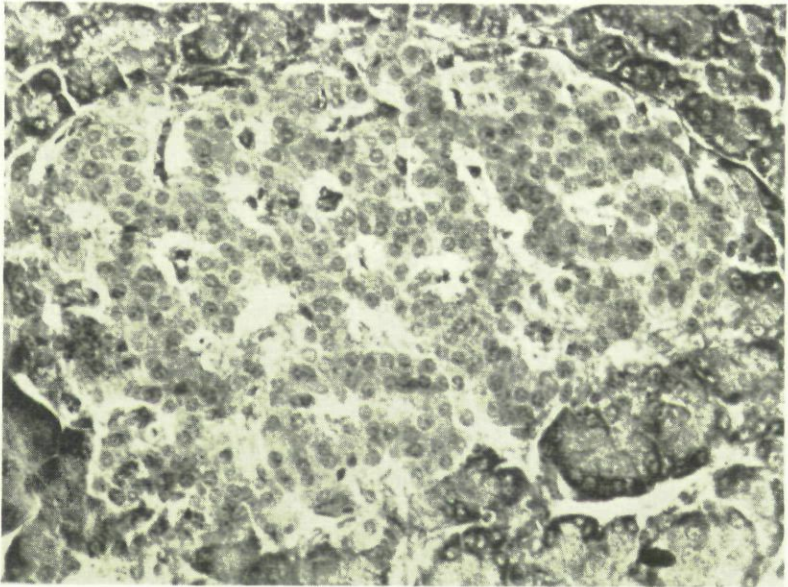


Fig. 26.

Pancreas. Islet of Langerhans with marked congestion and vascular dilatation. The alteration of the capillaries produces the plasmorrhagia and the oedema which, in turn, are responsible of the cytologic involvement and therefore of the hyperglycemic functional disturbance.

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