CHANGES IN THE INTRAMURAL NERVOUS APPARATUS IN COMPENSATORY CARDIAC HYPERTROPHY

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Compensatory cardiac hyperthrophy plays an important part in compensation for organic heart disease, hypertonia, arteriovenous fistulas, and other circulatory disorders.

From detailed investigations into the function, structure and metabolism of the myocardium it has been shown that during prolonged compensatory hyperfunction, the heart passes through three stages: the stage of failure, the stage of relatively stable hyperfunction, and the stage of gradual exhaustion, with progressive cardiosclerosis [4,5,6]. The present work represents a study of the compensatory morphological changes in the intramural cardiac nervous apparatus.

EXPERIMENTAL METHOD

Chronic compensatory hyperfunction was induced in six dogs, by a method which has been described previously [5]; an aortic stenosis which reduced the cross section of the aorta by a factor of 3 was established above the aortic valves. By catherization it was found that the pressure in the left ventricle then varied between 250 and 320 mm mercury, and it was shown by Grol'man's method that the minute volume 10 - 16 days after establishing the stenosis was normal, and compensation had therefore occurred.

The animals were killed 2, 10, 14, 40, and 50 days, and 6 months after the stenosis had been established, i.e. during stages I and II of the compensatory hyperfunction.

The hearts were studied by Nissl's method and by Campos silver impregnation.

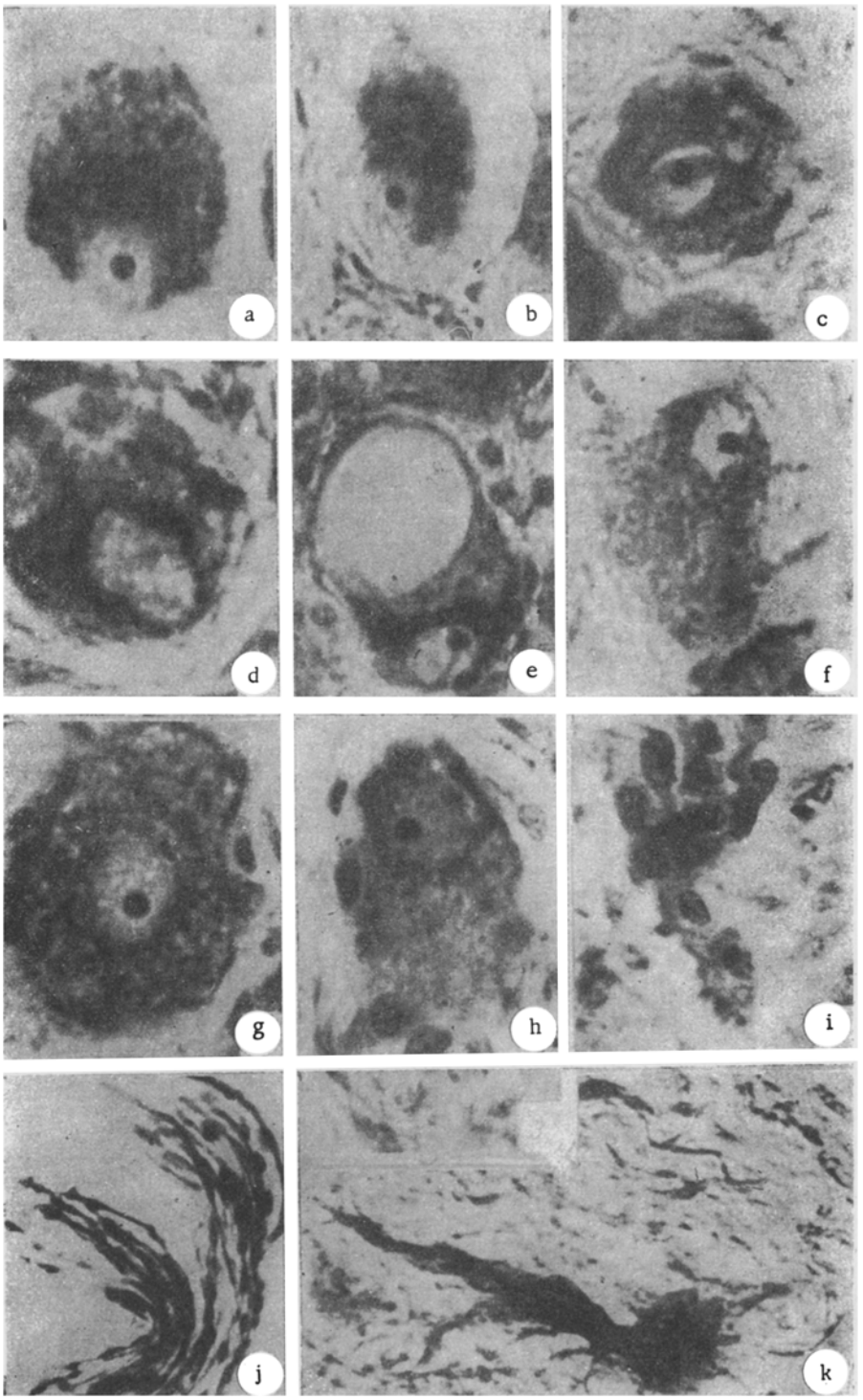
EXPERIMENTAL RESULTS

During the stage of injury, pathological changes occurred in the nerve cells and in the nerve fibers of the intramural cardiac plexus.

After as little as two days, various degrees of edema could be seen in most of the nerve cells, and there was a gradual dissolution of the Nissl substance.

In the initial stage of the edema of the neurones the nucleus was displaced from the center, and there were grains of Nissl substance in the peripheral parts of the neuroplasm (Fig. a). Later, after 10 - 14 days, the edema in some of the neurones increased. Fluid collected beneath the capsule of the cells (see Fig. b), and in the perinuclear space, displacing the nucleus and nucleolus (see Fig. c). In many of the nerve cells the nuclei themselves were edematous, and vacuoles appeared in the cytoplasm (see Fig. d). Small vacuoles occurring in the cytoplasm increased in size as more fluid accumulated in them, and stretched the cells. Such neurones had an annular appearance (see Fig. e). In some neurones there might be a diffuse solution of the Nissl substance: only a small number of the fine grains of this substance remained around the nucleus, which had been displaced towards the periphery of the cell (Fig. f). The glial and connective tissue cells of the stroma were also edematous and weakly basophil.

During the stage of relatively stable hyperfunction, 40 - 50 days after the operation, two kinds of histological changes occurred in the neurones: in most of them the edema disappeared, and various stages of reformation of the



Changes in the neurones of the intracardiac apparatus during compensatory hyperfunction. Explanation in text.

Nissl substance occurred, it once more became basophil, collected into clumps, and became evenly distributed throughout the cytoplasm. The nuclei and nucleoli then once more occupied a central position in the cell (see Fig. g).

A small proportion of the nerve cells underwent further irreversible change. The glial cells became ameboid, and collected beneath the capsule of the necrotic neurones. Phagocytosis of the neurones could then be observed (see Fig. h). Clusters of glial cells and histiocytes accumulated at the site previously occupied by the neurones (see Fig. i). There was then a focal proliferation of connective tissue cells in the myocardium and in the stroma of the nerve ganglia.

During the relatively stable hyperfunction, changes in the nerve cells could be observed which were characteristic of chronic stimulation of the nervous system.

The shape of the cells changed, and cytoplasmic outgrowths resembling pseudopodia were formed (see Fig. k); there was an excessive growth of nervous processes, so that the neurones became "shaggy".

In the stage of damage, betwen the 10th and the 14th days, there was also edema of the nerve fibers which make up the intracardiac plexus. There were vacuolized varicosities of various sizes, and the neurofibrils within them separated into strands. A small number of nerve fibers suffered Wallerian degeneration (see Figure j).

During the stage of relatively stable hyperfunction, pinshaped swellings were found along the course of the nerve fibers and in the cell processes.

We may now compare the morphological changes occurring in the cardiac nervous apparatus with those in the myocardium. In the stage of damage, when the glycogen and phosphocreatin content of the myocardium fell rapidly, the muscle fibers swelled, signs of protein distrophy [4, 5, 6] occurred, and in the neurones of the intracardiac ganglia there was an edema, and the Nissl substance dissolved. During the stage of relatively stable hyperfunction, when the myocardium hypertrophied, the glycogen and phosphocreatin content was normal, there was an increased amount of lactic acid, but there were also early signs of cardiosclerosis; in the neurones, besides a return to normal of the structure of the Nissl substance, there were indications of chronic nervous excitation, as shown by an excessive development of the nervous processes.

E. M. Krokhin [1] also observed indications of chronic stimulation in the hearts of human patients suffering from angina pectoris, who had died from repeated myocardial infarcts.

It appears that under conditions of our experiments, the chronic stimulus to the nerve cells was due both to metabolic changes associated with compensatory hyperfunction and hypertrophy, and to necrosis of some of the neurones. It is highly probable that the growth and the formation of new nervous processes resulted from the compensatory hyperfunction of the neurones, which took over the function of the dead nerve cells to supply the innervation of the increased mass of myocardium.

Because the majority of the pre-ganglionic nerve fibers of the vagus terminate in neurones of the intracardiac ganglia [2, 3, 7], it appears probable that the histopathological changes of the intracardiac neurones and of the nerve fibers, as described above, play some part in the reduction of the vagal reflexes observed by F. Z. Meerson [5] in experimental angina.

The results obtained allow us to draw the conclusion that during compensatory cardiac hyperfunction, changes in the intracardiac nervous apparatus run parallel with changes in function, metabolism, and the structure of the myocardium.

SUMMARY

Changes in the intramural nerve ganglia and in the myocardium caused by experimentally induced compensatory cardiac hyperfunction followed a definite pattern. During the first stage there was an edema of the neurones, various stages of diffuse lysis of the Nissl substance, and vacuolization of the processes of the nerve cell. The second stage was one of relatively stable hyperfunction, during which the edema disappeared from most of the neurones. A small proportion of the neurones were irreversibly damaged, and died.

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