

## ORIGINAL PAPER

# Morphological changes during acute experimental short-term hyperthermia

M. VLAD<sup>1)</sup>, N. IONESCU<sup>2)</sup>, AL. TH. ISPAS<sup>3)</sup>,  
ILEANA GIUVĂRĂȘTEANU<sup>1)</sup>, E. UNGUREANU<sup>1)</sup>, CLAUDIA STOICA<sup>1)</sup>

<sup>1)</sup>Department of Clinical Anatomy  
and Surgical Techniques – Chair of Anatomy

<sup>2)</sup>Department of Cell and Molecular Biology

<sup>3)</sup>Department of Anatomy

"Carol Davila" University of Medicine and Pharmacy, Bucharest

### Abstract

Wistar rats have been exposed to progressively higher temperatures for 30 minutes to 40.5 degrees Celsius. The animals were sacrificed 30 minutes after cessation of exposure. Harvested organs (heart, lung, liver, pancreas, kidneys, and adrenal gland) show numerous vascular lesions. Massive red blood cells extravasation and vascular stasis partially fragments the myocardial fibers. Pulmonary capillary dilatation and red blood cells intra-alveolar extravasation cause a hemorrhagic alveolitis that tends to a red hepatization. The liver responds by dilating centrilobular veins, vessels in port area and by granulo-vacuolar dystrophy. Pancreas seems less affected. Vascular hyperemia is discrete while in kidney the vascular spaces are narrowed and the proximal and distal tubules cloudy intumescent appears. In suprarenal gland appear many interstitial capillary dilatation and blood cells extravasation among cell nests of medulla. All these changes induce functional organ failure.

**Keywords:** progressive acute hyperthermia, Wistar rats, visceral lesions, optical microscopy.

### □ Introduction

High-temperature exposure determines for young and, especially older people clinical manifestations, which are the consequence of multiple morphological lesions [1–3]. Depending on their pattern of manifestation, the lesions will have a prognostic, which is unfavorable most of the time, despite the adaptation efforts of the organisms [4–8]. The presentation of the morphological changes, which appear during short-term hyperthermia, may orientate clinical approach of the patients with hyperthermal shock.

### □ Material and Methods

We used healthy Wistar rats, weighing approximately 450 g. The rats were anesthetized with ether and Ketanest 1/10 diluted (1 mL injected into the peritoneum) and then exposed for 30 minutes, in an incubator, to a progressive increase of temperature up to 40.5°C. Some of the animals died immediately after or during the exposure, the rest of them were sacrificed 30 minutes after the anesthesia. Fragments of heart, lung, liver, pancreas, kidney and suprarenal gland were harvested, fixed in formaldehyde, included in paraffin and stained with Hematoxylin–Eosin. The semifine sections embedded in epoxy resins were stained with Thionin. Examination and photography of the sections were performed using a Nikon research microscope.

### □ Results

#### Myocardium

In the myocardium, there is an important vascular hyperemia, vessels are dilated, between the myofibers fascicles there is a massive hematic extravasation. Vascular stasis is significant in large vessels and interfascicular, causing partial fragmentation of the myocardium fibers (Figures 1 and 2).

#### Lung

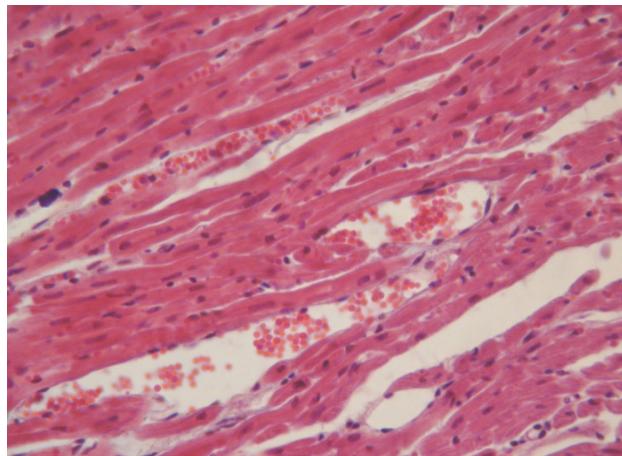
In the lung, there is stasis in the larger peribronchial vessels and capillary hyperemia in the alveolar septa where the capillaries are dilated. Important capillary dilatation in the alveolar septa determines the onset of the hemorrhagic alveolitis. Alveolar septa are thickened through superimposed inflammatory infiltrate. Intra-alveolar hematic extravasations and congestive areas, which evolve towards red hepatization, are a common phenomenon after high temperature exposure (Figures 3–6).

#### Liver

Liver lobulation is preserved. Intralobular capillaries are dilated with hematic microthrombi. Establish a granulo-vacuolar hepatocyte dystrophic process. Centrilobular vein is dilated. Portal-biliary vessels are also dilated (Figures 7–10).

### Pancreas

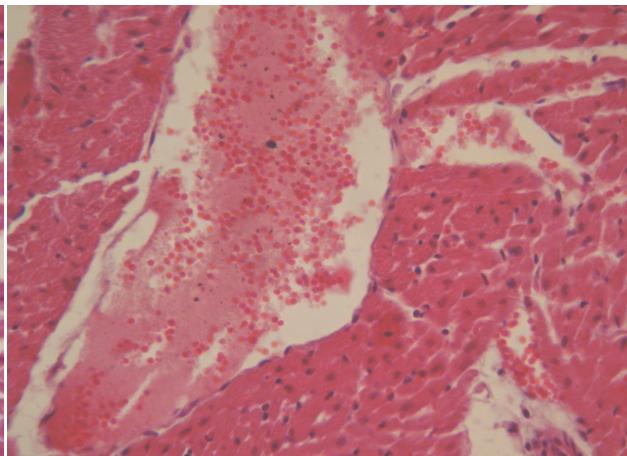
In pancreas prevails the vascular stasis, intra- and inter-lobular. Around the exocrine acini there is a discrete vascular hyperemia as around Langerhans islets among the endocrine cells. There are no acinar lesions (Figures 11 and 12).



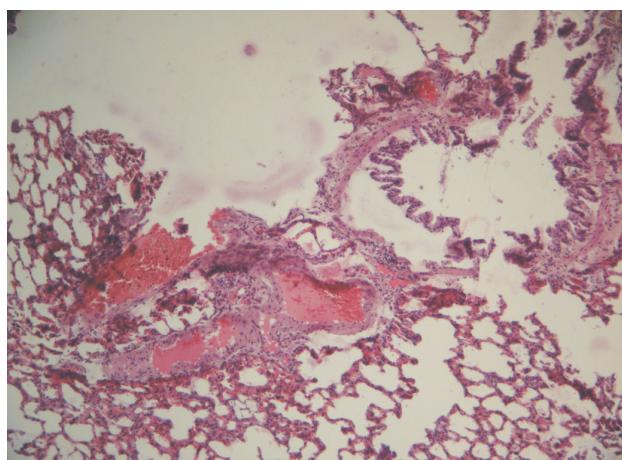
**Figure 1 – Blood extravasation among bundles of cardiac muscle cells (HE stain, ob.  $\times 20$ ).**

### Kidney

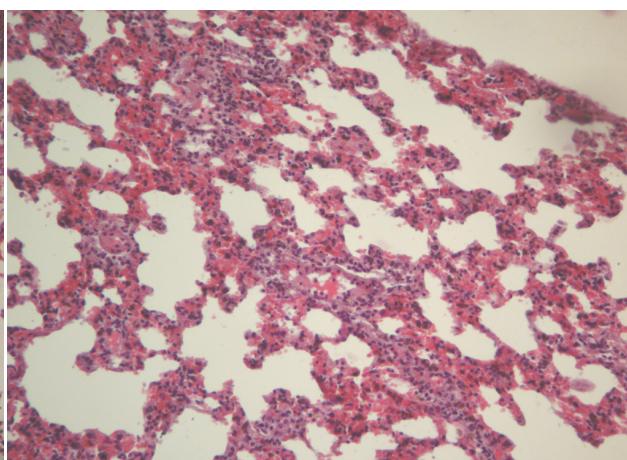
Vascular stasis in the kidneys is common in large vessels of the cortico-medullary and glomeruli vessels. Glomeruli have dilated capillaries; the urinary spaces are narrowed by mesangial cell proliferation.



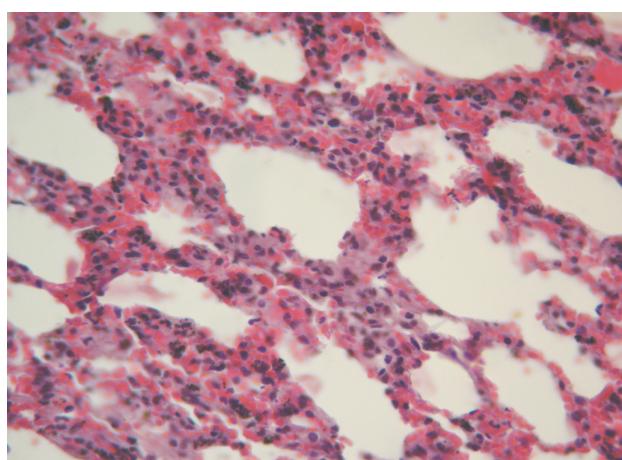
**Figure 2 – Massive vascular dilatation of large vessels of interstitial cardiac fibers space (HE stain, ob.  $\times 20$ ).**



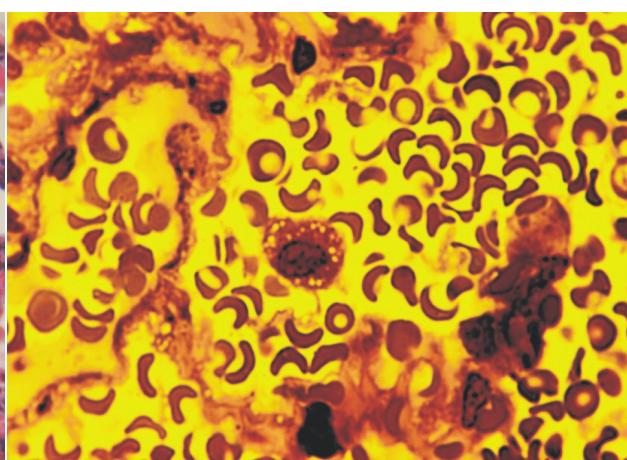
**Figure 3 – Peribronchial vessels with marked vascular stasis, adjacent alveolar septa to the capillary dilation, dysplastic bronchial epithelium (HE stain, ob.  $\times 10$ ).**



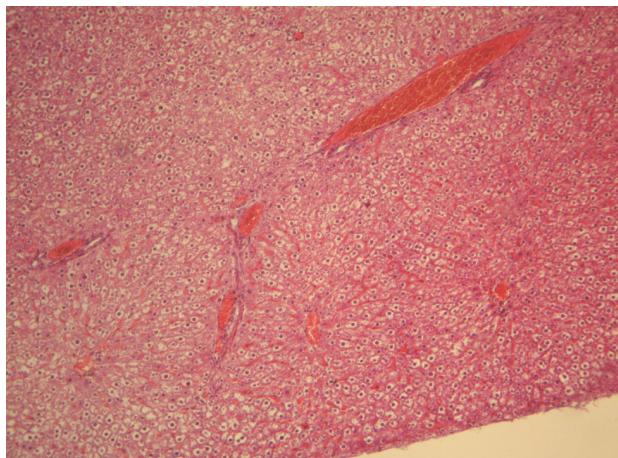
**Figure 4 – Thickening of the alveolar wall with discrete inflammatory infiltrate and capillary stasis in the alveolar wall (HE stain, ob.  $\times 10$ ).**



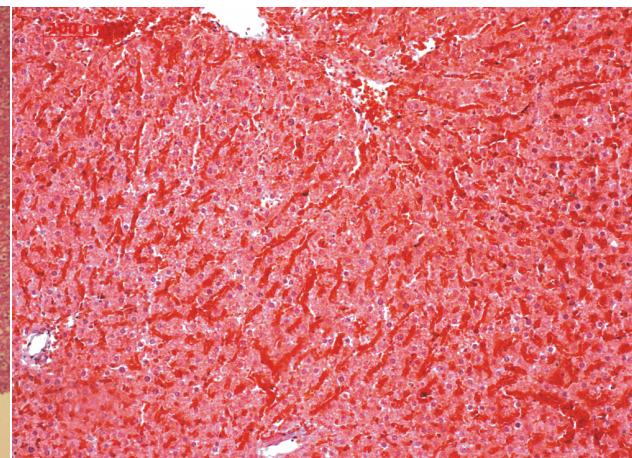
**Figure 5 – Thickened alveolar septa with inflammatory infiltrate and increased capillary hyperemia (HE stain, ob.  $\times 20$ ).**



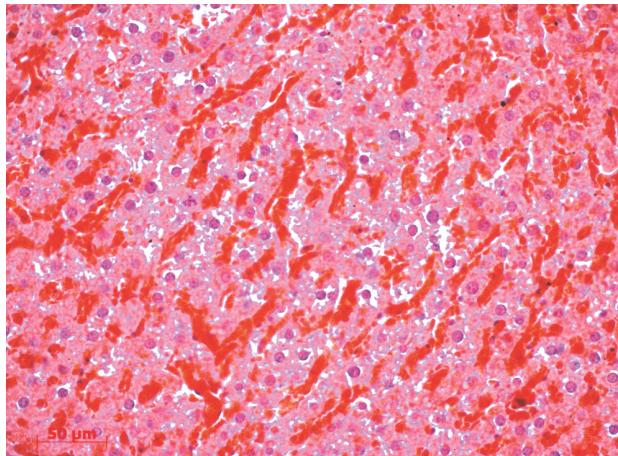
**Figure 6 – Intra-alveolar extravasated blood, intra-alveolar macrophages and desquamated epithelial cells of alveolar wall (HE stain, ob.  $\times 40$ ).**



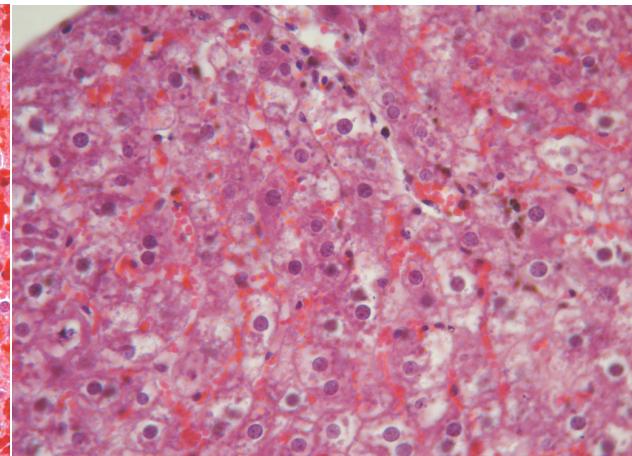
**Figure 7 – Preserved lobulation. Hepatocyte granulo-vacuolar dystrophic process. Dilation of large vessels in porto-biliary and centrilobular areas (HE stain, ob.  $\times 10$ ).**



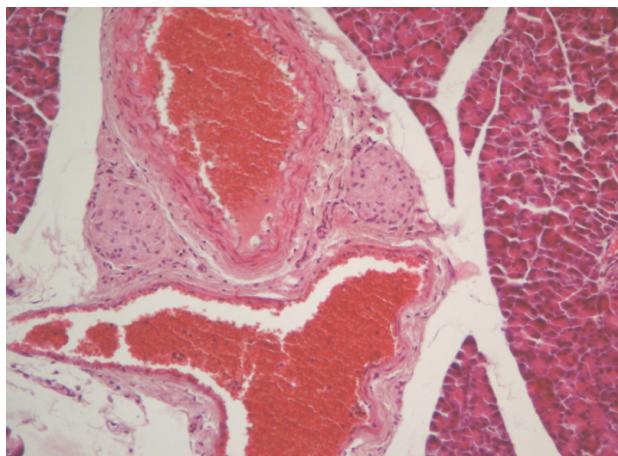
**Figure 8 – Hepatic sinusoids dilated with thrombi in the hepatic lobule (HE stain, ob.  $\times 20$ ).**



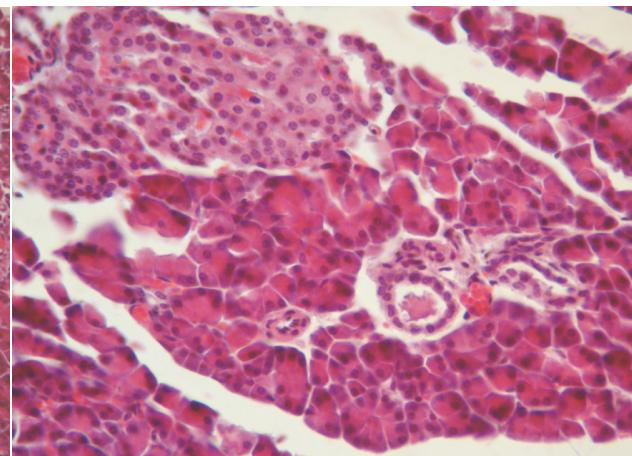
**Figure 9 – Dilated sinusoids with confluent hematic thrombi (HE stain, ob.  $\times 40$ ).**



**Figure 10 – Intense granulo-vacuolar dystrophic process and pronounced sinus capillary stasis (HE stain, ob.  $\times 40$ ).**



**Figure 11 – Marked vascular stasis in the interlobular space (HE stain, ob.  $\times 10$ ).**



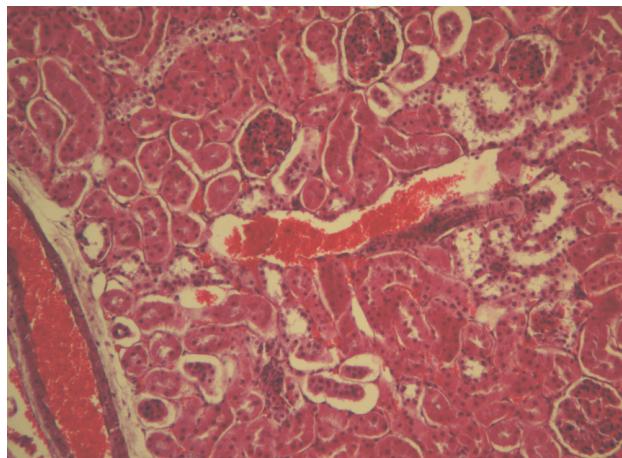
**Figure 12 – Discrete vascular stasis among glandular acini and Langerhans islets (HE stain, ob.  $\times 20$ ).**

In proximal and distal tubules, there are phenomena of turbid degeneration, possible tubular-glomerular nephropathy.

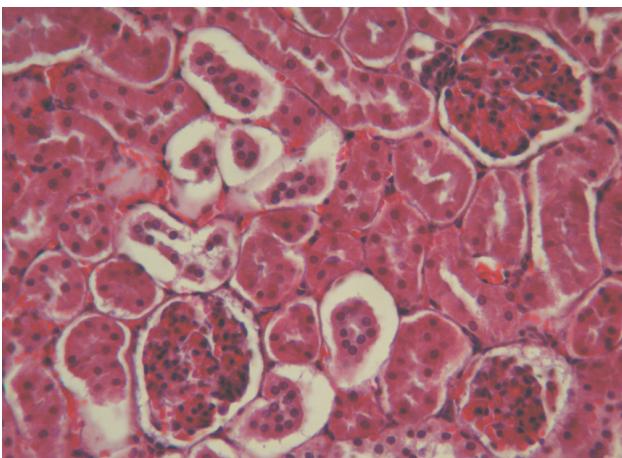
Cortical-medullar interstices are hemorrhagic, either diffuse, either focally. In some areas of the cortex, small

outbreaks occur periglomerular bleeding and between tubes, marked vascular stasis. The tubular-glomerular nephropathy is incipient.

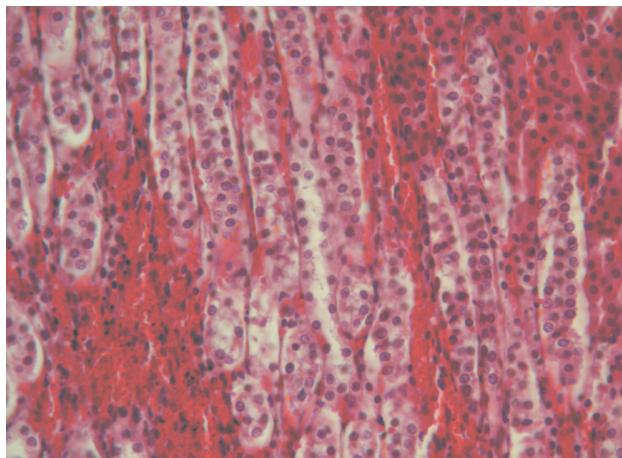
The vascular stasis is present even in large vessels of perirenal fat tissue (Figures 13–16).



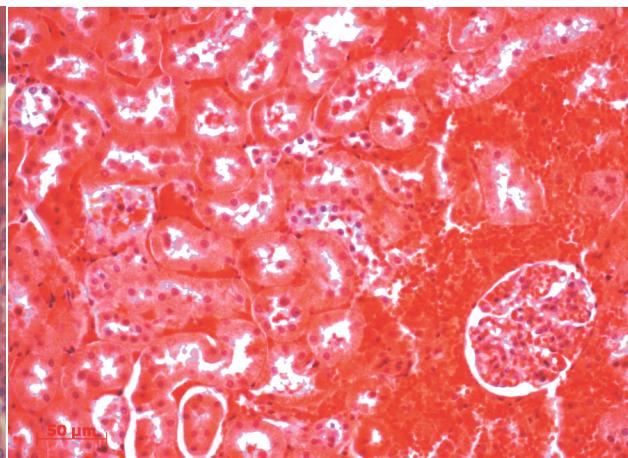
**Figure 13 – Vascular stasis in glomeruli and large vessels of renal cortical (HE stain, ob.  $\times 20$ ).**



**Figure 14 – Glomerulus with dilated capillaries. Cloudy intumescence in proximal and distal tubules (incipient tubulo-glomerular nephropathy) (HE stain, ob.  $\times 40$ ).**



**Figure 15 – Hemorrhagic medullary interstitium (HE stain, ob.  $\times 20$ ).**

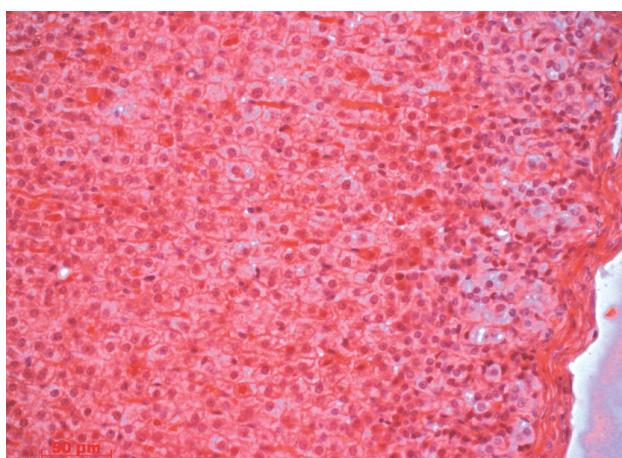


**Figure 16 – Periglomerular hemorrhagic foci. Peritubular interstitial vascular stasis (HE stain, ob.  $\times 20$ ).**

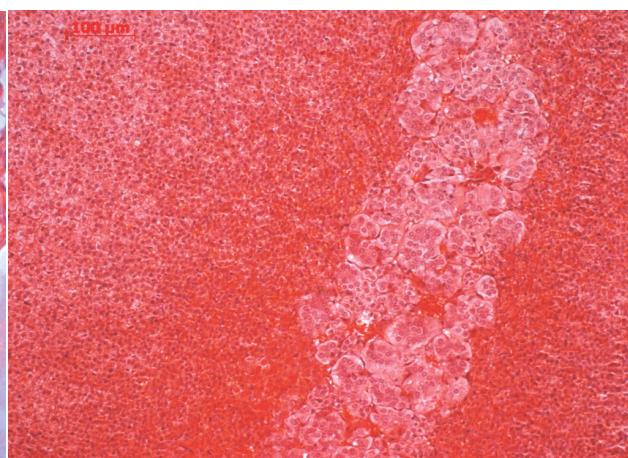
### Suprarenal gland

Capillaries dilatations are also found in the suprarenal gland, in the cortical-medullary interstices. Zona glomerulosa and zona fasciculata of the suprarenal cortex present significant interstitial capillaries dilatations, suggesting marked stasis. Vascular dilatations are

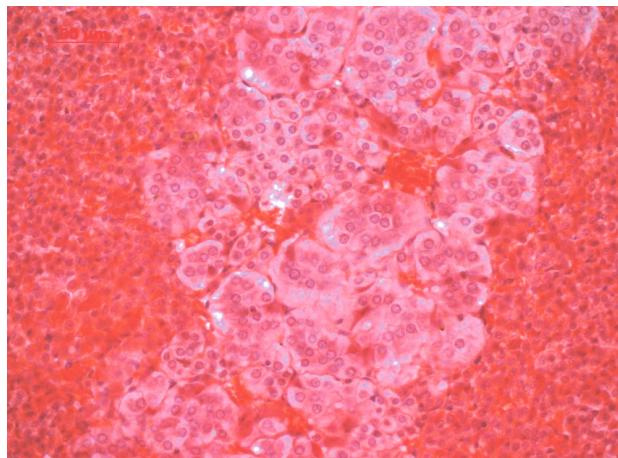
attended by interstitial blood extravasations inside the zona reticularis and between the cells nests of the adrenal medulla. In the adrenal medulla there are also cellular alterations, and vascular dilatations are larger than those recorded in the adrenal cortex (Figures 17–20).



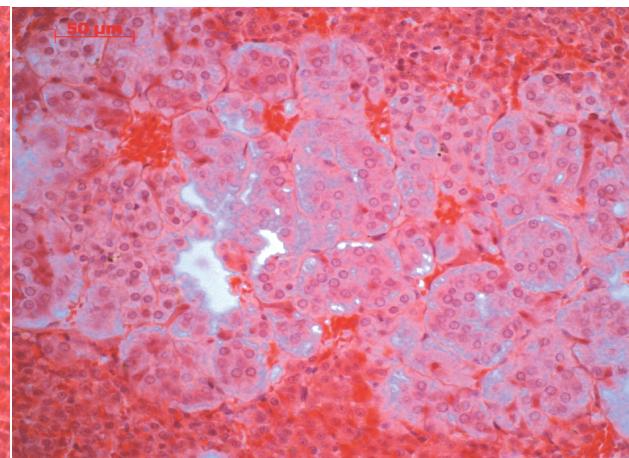
**Figure 17 – Cortical area with glomeruli and fasciculi. Intense interstitial capillary dilation (HE stain, ob.  $\times 10$ ).**



**Figure 18 – Accentuated vascular dilation process with interstitial blood extravasation in the reticular area and among cell nest of medulla (HE stain, ob.  $\times 10$ ).**



**Figure 19 – Accentuated vascular dilatation process of vascular dilation and blood extravasation in the reticular area and among medulla cells nests (HE stain, ob.  $\times 40$ ).**



**Figure 20 – Marked vascular dilatation of medullar and reticular area. Partial cell destruction in medulla (HE stain, ob.  $\times 40$ ).**

## Discussion

Acute experimental short-term hyperthermia is realized by increasing the central temperature to  $40.5^{\circ}\text{C}$  [3]. Exposure of the animal to an environment warmed up progressively for a short period of time determines the installation of the hyperthermic shock with immediate reactions which are especially vascular – vascular dilatations and stasis, mainly in the cardiac, pulmonary, hepatic and renal parenchyma. Because of the hemodynamic disturbances, these organs present morphological irreversible injuries owing to the hypoxia [2]. Hemodynamic modifications in acute experimental hyperthermia appear rapidly after high temperature exposure. Heart, lung, liver and kidneys present irreversible morphological lesions immediately after the exposure, producing functional organ failure [2, 4]. In our experiment the organ least involved was the pancreas, where structural modifications were less obvious.

During hyperthermia, myocardium responds rapidly through vascular dilatations, interfascicular vascular stasis and extravasated between myofibril, which caused contractility disorders [9]. Disturbance of the systemic microcirculation in the lung in acute experimental hyperthermia consists of capillaries dilatation inside the alveolar septa, peribronchial vessels stasis, thickening of the septa through inflammatory infiltrate and hemorrhagic alveolitis. All these disturb the gas exchange, and determine functional organ failure [10]. Hepatic reaction to experimental hyperthermia is also vascular [11]. Centrolobular vein stasis, sinusoid capillaries stasis is complicated by the apparition of intra-capillary hematic thrombi, and granular-vacuolar dystrophy.

Early kidney response to high temperature exposure is also vascular [12]. Capillaries dilate, glomerular stasis is marked, and urinary spaces narrow through stasis and possible mesangial proliferation. Medullar interstices are hemorrhagic. Also, there is a turbid degeneration in proximal and distal tubules, suggesting the development of a tubular-glomerular nephropathy.

Vascular dilatations and hematic extravasations insude the cortical zona reticularis and adrenal medullar are

accompanied by partial medullar destructions. Pancreas response to hyperthermia is a vascular adaptation reaction with discrete peri-acinar vascular hyperemia but without injuries of the acini or the islets, which is probably explained by anatomical disposition of the pancreas in rats. Animals exposed to high temperatures undergo a process of hypoxia and anoxia due to the slow of blood circulation and the lack of oxygen in dead tissues. The organism itself reacts in hyperthermic stress by rapid release of a group of shock proteins PSH [13], which decrease the pancreatic injuries and improve the survival in necrotic pancreatitis [14]. There is a group of shock proteins PSH 27, PSH 32, PSH 60, and PSH 70, with protecting role in inflammation and pulmonary injuries [13]. In this context, experiments should be repeated for variable conditions of time and temperature in order to evaluate the protecting role of PSH and to correlate the appearance of morphological injuries with organism response as a whole.

## Conclusions

The exposure of experimental animals to high temperature environments results in multiorgan disturbances of the microcirculation, which determines functional organ failure and compromises the vitality of the tissues and the whole organism.

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**Corresponding author**

M. Vlad, MD, PhD, Department of Clinical Anatomy and Surgical Techniques – Chair of Anatomy, “Carol Davila” University of Medicine and Pharmacy, 8 Eroilor Sanitari Avenue, 050474 Bucharest, Romania; Phone +4021–317 23 27, e-mail: vlad\_marius@hotmail.com

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