The role of the liver in the regulation of water-electrolyte metabolism

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The role of the liver in the regulation of water-electrolyte metabolism is determined by its hydro-and ion-depositing capacity [2-5,23,32,50,51], participation in the metabolism of renal function regulating hormones [16,29,54,69], hepatic location of specialized osmo-, volume-and ion-receptors [6-8,10,18,20,22,24,28,30,47,61,62,66,67] being the begining of reflectory mechanisms sustaining water-salt homeostasis.

With the help of these reflexes, the liver bordering on the portal system and systemic circulation controls the osmolality and ion concentration in the blood coming from the gastro-intestinal tract and by its action on the kidney provides for internal stability of the organism.

The present paper reviews the reflectory mechanisms that connect the liver and kidney. The first ideas of their existence appeared in 1955 when A. G. Ginetsinsky, basing on the rk of his collaborator L. K. Velikanova, suggested a thesis of osmoregulating reflex [25,63,64]. According to this idea, the internal osmolality is maintained not by direct action of blood or tissue fluid on the Verney hypothalamic centre [68] but in a reflectory way, due to the stimulation of peripheric osmereceptors causing an excitation of the neurons of supraoptic and paraventricular nucleo and changes in the secretion of vasopressin [25,26,68]. Thus, for the first time, a thesis has been suggested of the existence of peripheric osmoreceptors and their associated reflectory mechanisms. These neural devices have been discovered experimentally in 1957-1959 in the liver by L. K. Velikanova and Ya. D. Finkinsthein. In experiments on unanesthetized dogs they have show that an injection into tye portal blood flo of a hypertonic NaCl solution 523 mmol.) and isotonic to it solutions of Na_2SO_4, glucose, mannitol in the amounts providing for a local stimulation of the nervous apparatus of the liver caused a decrease in diuresis [64,67] and, as has been subsequently established, an increase in natriuresis [43]. An infusion of water into the portal system resulted in an opposite effect [15,19,42,66].

A detailed electrophysiological analysis of the hepatic receptive field carried out by many researchers in different year [1,10,13,30,40,58,59,44] has given a convincing evidence of the availability in the organ of not only specific osmo-but also volume-and ion-selective receptors.

Physiological experiments have ascertained that the liver contains receptive formations that are selectively sensitive to changes in portal blood Na, K, and Mg and have shown the existence of the corresponding ion-regulating reflexes in the organism [3,6,8,22,24,30,46,47]. Later electrophysiological studies with records of biopotentials from individual hepatic afferents have demonstrated the existence of four types of fibers selectively responding to an increase of volume, osmolality, sodium or potassium concentrations in the portal-vein system [50,60,62]. The afferent pathways from hepatic osmorecentors pass into the hypothalamic area through the spinal cord. This is confirmed by a considerable disturbance in osmoregulation after the spinal cords has been cut at the Th_5-Th_{12} level, i.e. those segments wich innervate the liver [63]. The same effect is observed in spinal deafferentation at that level [6]. The spinal path of data transmission is also confirmed by impulses appearing in dorsal roots during hepatic osmostimulation [1,9,59,61]. Vagotomy has no essential influence on osmoregulation [6,65], in spite of the fact that vagus nerves contain fibers that carry information from osmoreceptors [13,34,44]. The vagus nerves mainly conduct impulses from Na-,K- and Mg-selective receptors since ion-regulation reflexes disappear in double supradiaphragmatic vagotomy [6,24,47]. The information from the hepatic osmoreceptors is fed to the neurons of supraoptic and paraventricular nuclei, thus causing an increase in their spontaneous activity from 1-3 impulses/min. to 15-20 impulses [40,41,58]. This leads to an increase in vasopressin and oxytocin secretion [10,11,48,49,68] and has been recently shown [14] to a reduction of aldosterone blood concentrarion. Such a hormonal shift results in and inhibition of diuresis and an increase in sodium excretion, i.e. leads to a renal response characteristic for a hyperosmotic shift in the portal vein area [12,39,70]. Apart from neural afferentation, a humoral factor has been described released from the liver during its osmostimulation [17,35,41,52,57,71]. Parallel with direct natriuretic effect on kidneys, it acts directly on the hypophalamic-pituitary system. An estimation of the bioelectrical activity of the hypothalamic supraoptic nucleus after its complete deafferentation made possible to establish that the neural phase plays the role of a pressing but short-term information link while the subsequent humoral phase causes the sustained activation of the central link of the osmoregulating reflex and ADH release [41].

In spite of the fact that the question of the existence of

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osmo-volume– and ion-receptors in the portal system has been essentially solved, the problem of their localization, structure and mechanism of stimulation perception remains debatable.

Chronic experiments in dogs with porto-caval venous transposition [23] have shown that hypertonic NaCl infusion thorugh a catheter inserted into vena porta caused no changes in renal function. On the contrary, infusion of the solution into the inferior caval vein from wich the blood in these animals is fed into the liver caused typical osmoregulating response inhibition of diuresis and enhanced sodium excretion. These findings gave evidence of the intraorganic location of osmoreceptors. In all probability, osmo– and ion receptors are located in the interstitial space of the liver as this is precisely the site that provides the best conditions for their stimulation. Chronic experiments in dogs have shown that after absorption of a considerable osmotic load 100-500 mg/kg. NaCl from the digestive tract, the shifts in osmotic concentration are so insufficient that their influence on osmoreceptors seems to be hardly probable. Furthermore, natriuretic responses to infusion of a saline load into the digestive tract takes place in 20-25 minutes on the average while an increase in blood osmolality in vessels is observed already in 5 minutes. At the same time, the hepatic tissue shows a considerable accumulation of sodium [23,51] capable of indluencing the receptory apparatus located in the interstice. The liver acts here as a concentration amplifier creating conditions for excitation of osmo-and ion-receptors [2,23,50].

It can be also supposed that the osmotic gradient in the area of the receptors is developed not only due to accumulation of osmotically active substances in the organ but also by retrograde osmotic water flow which appears from a decrease in hepatic tissue fluid after infusion of hyperosmotic solutions [4,5]. It is believed that an adequate stimulus for ion-selective receptors is an increase in tissue ion concentration without simultaneous water transition in the opposite direction [66]. It is not unlikely that infusion of hypertonic NaCl, KCl, etc. solutions causes stimulation of osmo-and ion-receptors simultaneously. As regards to the structure of osmo-and ion-receptors, for the present it is the subject of pure speculation [21,59,66]. It is believed that osmoreceptors are built of polyglycan clods of the interstitial substance of connective tissue firmly bound th nerve endings. The conformation of molecules of protein-polyglycan complexes under the influence of osmotic and possibly ion stimulation, can change in shape and volume (swelling or unswelling) and can lead to the appearance of signals in their associated nerve endings.

It has been found also that the infusion of hypertonic NaCl solution causes changes in the structure and amount of glycogen in hepatocytes. These transformations seem to lead to the release of water bound to it and effective sodium accumulation [5]. Unfortunately the osmo-and ion receptors discovered by physiological methods have not yet a morphological equivalent for the present. This is what appears to be one of the causes of the publication of papers against the evidecfor hepatic osmoreceptors [27,33,45,53,55]. Their authors arrive at such a conclusion on the basis of observed renal responses of the same type after simultaneous infusion of distilled water, hypo-or hypertonic NaCl solutions into systemic and portal veins. It seems to us, however, that these facts give no sufficient ground for such a flat judgement. Indeed, the volume shifts caused by the solutions used are so considerable (up to 28 %) that osmoregulating responses could either not take place at all or be disguised the volume-regulating ones. Furthermore, the difference could remain undiscovered due to the change in osmolality in general circulation capable of acting on osmoreceptors located in other organs [18-20].

Under natural conditions, the impulses from hepatic osmo-, volume- and ion receptors are integrated in the central nervous system to ensure the biologically expedient renal reaction.

Te pysiological mechanisms described in hepatic pathology are often disturbed.Specifically, the nature of afferent impulses is changed during stimulation of the organic receptors [60], the release of humoral natriuretic factor is blocked [31,38] which leads to changes in renal response and formation of water-salt disorders [36,37,56].

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