

GALL BLADDER FUNCTION IN ACUTE RADIATION SICKNESS

UDC 616.001.28-07:616.361-008.1-073.75]-092.4/9

P. K. Klimov

I. P. Pavlov Institute of Physiology (Director — Academician V. N. Chernigovskii)
of the AN SSSR, Moscow

(Presented by Academician V. N. Chernigovskii)

Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 57, No. 4,
pp. 46-49, April, 1964

Original article submitted January 23, 1963

It is generally accepted that at times other than during digestion, in physiological conditions bile passes continuously along the hepatic and cystic ducts into the gall bladder, and that the filling of the gall bladder with fresh bile is associated with its concentration [1, 2, 5, 6, 7].

The object of the present investigation was to study the process of filling of the gall bladder and the concentration of bile in the viscus in acute radiation sickness. It was decided to use the roentgenological method of intravenous cholangiocholecystography, which allows the desired object to be attained in chronic experimental conditions without the preliminary formation of a biliary fistula into the bile duct and gall bladder in the animals.

EXPERIMENTAL METHOD

Experiments were conducted on 7 mongrel dogs (3 males and 4 females) weighing from 12 to 17 kg. The animals were kept in ordinary conditions. The last meal was given 14 h before the beginning of the experiment, which allowed the investigation to be made outside a period of digestion. The contrast material (Biligradin, manufactured by Schering), warmed to body temperature, was slowly injected intravenously (0.35 ml/kg). Photographs were taken 5, 10, 15, 20, 30, 45, 60, 75, 90, 105, 120, 150, and 180 min after injection of Biligradin.

All the animals were investigated three times by the method of cholangiocholecystography to study individual variations in the normal process of filling of the gall bladder and of concentration of its contents.

Three dogs were given whole-body irradiation in the form of a single exposure to roentgen rays in a dose of 500 R. Conditions of irradiation: RUM-3 apparatus, tube voltage 190 kV, current 15 mA without tube, filter 0.5 mm copper + 1 mm aluminum, half-value layer 0.8 mm copper, skin-focus distance 150 cm. The other dogs acted as controls.

EXPERIMENTAL RESULTS

The filling of the gall bladder and the concentration of bile in the viscus take place continuously in healthy dogs, with a constant rhythm. Between 5 and 10 min after injection of Biligradin, the hepatic and cystic ducts were filled with iodized bile. Their width on the roentgenograms varied from 1.0 to 1.5 mm. The caliber of the cystic duct close to the neck of the gall bladder reached 2 mm. Bile containing contrast medium appeared practically simultaneously with the cystic duct between the period from 5 to 10 min in the neck of the gall bladder. It moved from the neck to the fundus of the gall bladder at a velocity of approximately 1 mm/min (Fig. 1, 1b). The increase in the concentration of the fresh bile was accompanied by an increase in the intensity of the shadow of that part of the gall bladder into which the iodized bile had penetrated. Meanwhile, the bile present in the gall bladder before the examination, did not mix with the fresh bile for some time, as shown on the roentgenograms by the presence of a distinct boundary line (the phenomenon of "layering of bile"). At 30 min, the amount of bile containing contrast medium was sufficient for it to be seen at the fundus of the gall bladder, where it accumulated in an ever-increasing amount. At this stage the bile present in the gall bladder before the injection of Biligradin appeared on the roentgenograms to be surrounded by a border of fresh bile. Hence, at 30-45 min, the phase of the three-layer or

Changes in the Size of the Gall Bladder in Relation to Stage of Acute Radiation Sickness

Statistical index	Day of acute radiation sickness		
	1st	3rd	13th
M	+ 1.92	+ 2.53	- 1.6
P	< 0.02	< 0.02	< 0.02

multilayer gall bladder began (Fig. 1, 1e). Soon after, at 105-120 min after the injection of Biligrafin, the gall bladder appeared on the roentgenograms as a homogeneous shadow. The intensity of the low-contrast shadow of the gall bladder subsequently increased rapidly, provided that the animal received no food (Fig. 1, 1, i, j).

Clinical observations made after irradiation showed that the animals had developed acute radiation sickness of moderate and severe degrees. On the first days of radiation sickness, i.e., in the stage of the primary reactions of the organism, roentgenograms of all the irradiated dogs showed abnormalities of the filling of the gall bladder: the slowing of the arrival of bile in the gall bladder at the beginning of the experiment alternated with restoration of the filling velocity observed before irradiation. However, this relative acceleration of filling likewise did not remain constant, and within a few minutes it was replaced by a fresh slowing of this process. At 75 min, for example, bile containing contrast medium was only just beginning to fill the fundus of the gall bladder (Fig. 1, IIg). The ability of the gall bladder to concentrate its contents was impaired in the initial period of acute radiation sickness. The width of the bile ducts was often variable (from 3-4 to 1-2 mm in the course of the same experiment), indicating their dystonia. Because of a lowering of the tone of the sphincter of Oddi, bile entered the dudodenum during all 3-4 h of the experiment.

In stage II of acute radiation sickness (the stage of relative fitness) the disturbances of the activity of the biliary apparatus established in stage I of the disease persisted. In all the animals the gall bladder was larger than before the disease (see table). This fact, previously observed in man [3] and animals [4], indicates a disturbance of the tone of the viscus. The bile ducts, which were dilated in the first few minutes of cholangio-cholecystography, became constricted at 30-45 min and were again dilated at 60-75 min. This showed the existence of a state of dystonia and dyskinesia of the ducts. The intensity of the gall bladder shadow remained weak throughout many hours of observation (6-7 h), indicating a lowering of the concentrating power of the bile duct. Often the roentgenogram taken before the beginning of the second cholangio-cholecystography revealed a gall bladder shadow of low intensity (Fig. 2, IIIa). The fact that iodized bile had stayed several days in the gall bladder indicated a disturbance of the evacuatory power of the gall bladder, or hypotonia of the viscus.

In the stage of frank radiation sickness, starting with the 6th-8th day after irradiation, the most marked abnormalities of the filling of the gall bladder with bile and of its concentration were observed. Fresh bile entered the gall bladder in small amounts and was held up for a long time near its neck. The typical stages of "layering" of bile were not seen on the roentgenograms; gradually and much sooner than in normal conditions - at 45-60 min - the gall bladder formed a homogeneous shadow. However, the contrast of the gall bladder shadow remained low, and its outlines were not clearly distinguishable against the background of the soft tissues of the abdomen. The dystonia of the bile ducts was intensified and constriction was predominant. Often the outlines of the ducts was beaded, because of their irregular filling with bile containing contrast medium. The sphincter of Oddi was either spastically contracted for several hours or relaxed for an equally long period. The gall bladder was smaller in size than before irradiation (see table).

In two cases which ended in recovery of the animals, the filling and concentration of bile returned, with considerable fluctuations, to its initial state on the 45th-60th day, but in the stage of recovery, as a result of a temporary worsening of the animals' state of health, the filling process was depressed, although this gave way on the following days to normalization of the bile secretion. The periods of normal activity of the biliary system had become more constant 2 months after irradiation; as a rule they coincided with other clinical and laboratory evidence of an improvement in the state of the animals' health.

A roentgenological investigation of the activity of the biliary apparatus of the control animals was carried out at the same times as in the irradiated animals. Prolonged observations showed the absence of changes in the filling function of the gall bladder and in its ability to concentrate its contents.

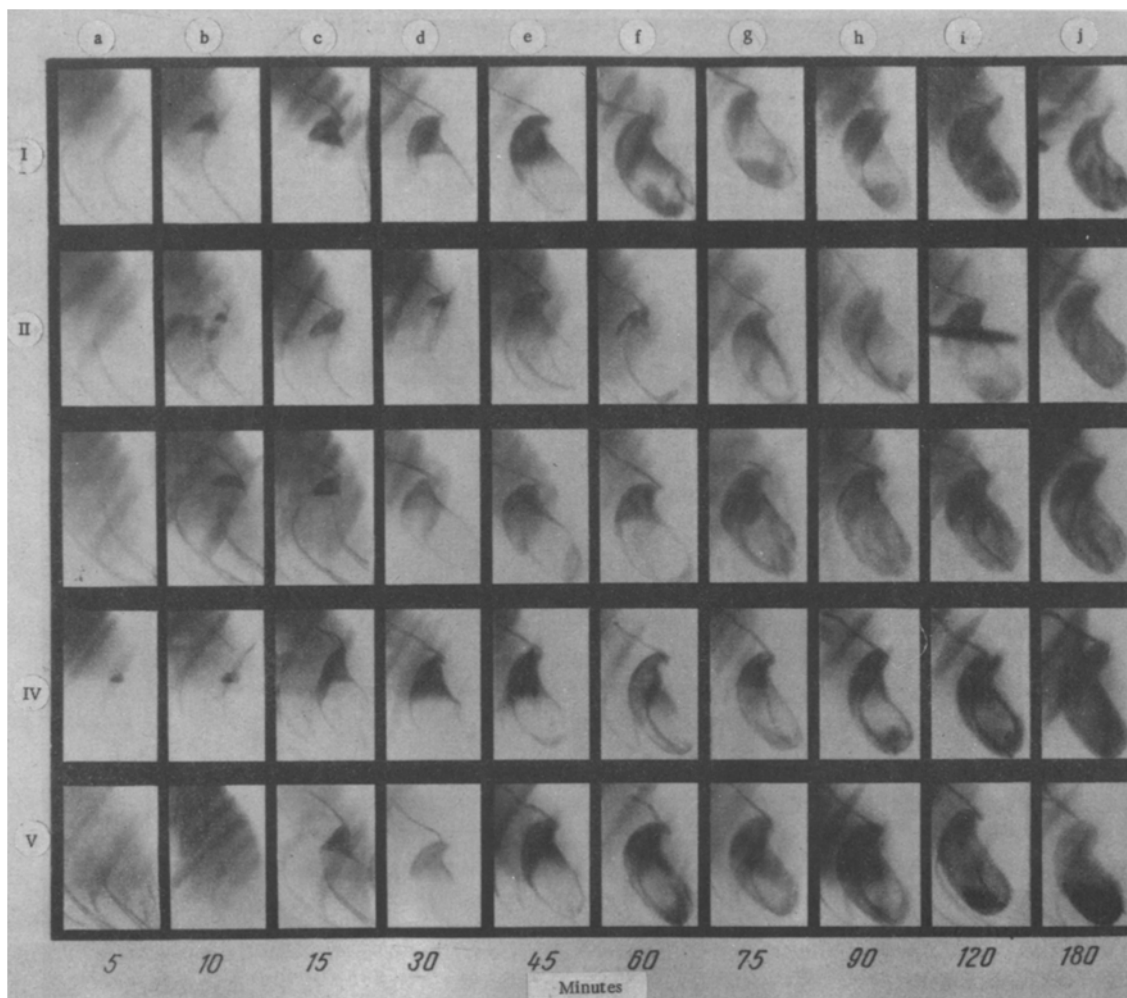


Fig. 1. Filling of the gall bladder and concentration of bile before and during acute radiation sickness in the dog Dolya. I) Roentgenograms of the gall bladder and bile ducts of a healthy animal; II) filling of gall bladder on 1st day; III) on 3rd day; IV) on 10th day; V) on 15th day after irradiation. a) Roentgenograms of the region of the liver, gall bladder, and bile ducts 5 min; b) 10 min; c) 15 min; d) 30 min; e) 45 min; f) 60 min; g) 75 min; h) 90 min; i) 120 min and j) 180 min after injection of Biligradin.

Hence, in acute radiation sickness, the process of entry of bile into the gall bladder is disturbed, the tone of the viscus is modified, and the smooth working of the sphincteric mechanisms of the gall bladder and bile ducts is impaired. These functional changes in the activity of the biliary apparatus are revealed by the stimulation or depression of bile secretion, depending on the stage of the disease. In addition, dyskinesia and dystonia of the gall bladder and bile ducts appear. Bile enters the gall bladder irregularly: slowing alternates with a period of faster filling, followed again by slowing; not until the end of the stage of recovery does the rate of filling of the gall bladder become constant.

Preliminary experiments in which adrenalin, carbachol, chlorpromazine, and atropine were given showed that the disorganization of the natural synergism of the sympathetic and parasympathetic divisions of the autonomic nervous system creates a roentgenological picture of functional disturbances of the biliary apparatus very similar to the disturbance of the activity of the gall bladder and bile ducts in acute radiation sickness. This suggests that an important factor in the mechanism of the development of the disturbances of the function of the biliary system in acute radiation sickness may be a disturbance of its neuro-humoral regulation.

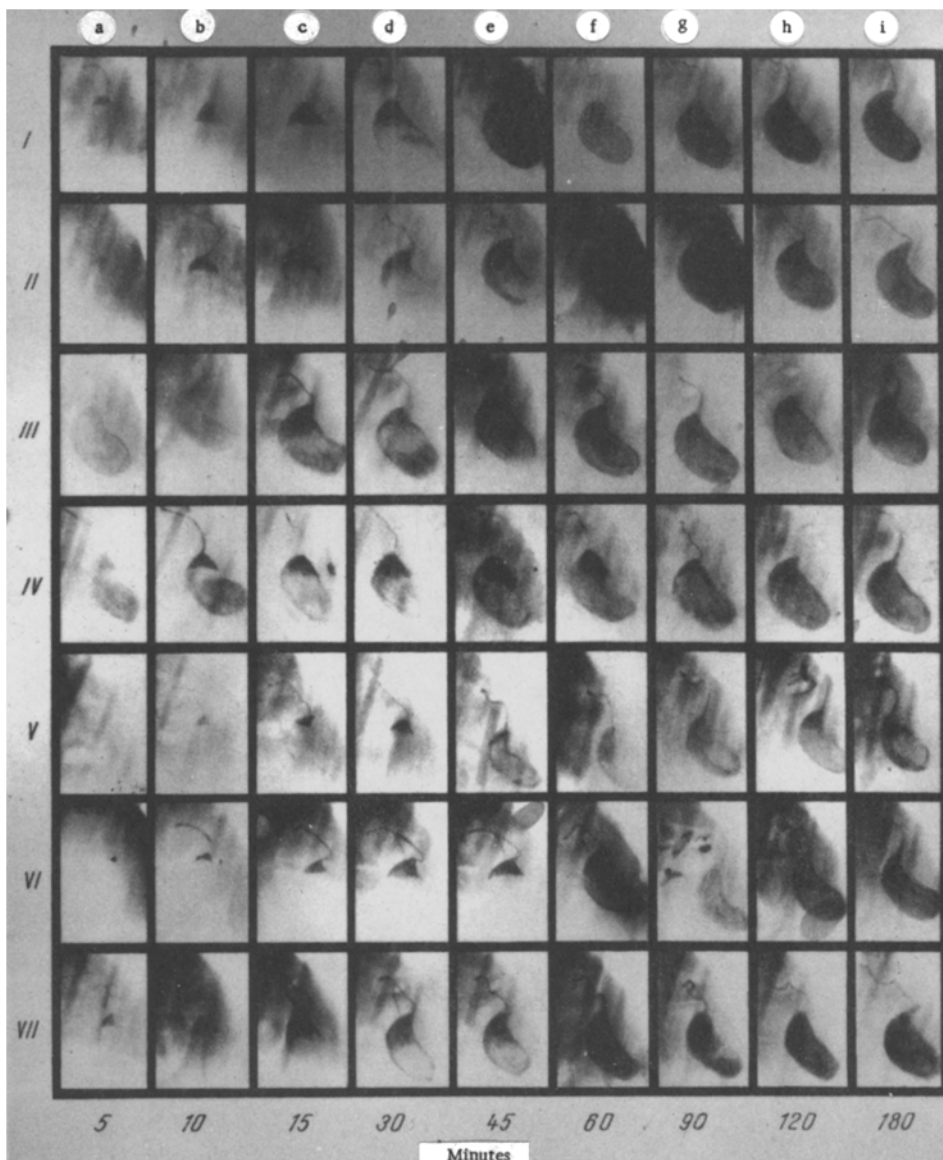


Fig. 2. Roentgenograms showing the filling of the gall bladder and concentration of bile before and during radiation sickness in the dog Tarzik. I) In the healthy animal; II) on the 1st day, III) 3rd day; IV) 7th day, V) 13th day, VI) 21st day; VII) 38th day after irradiation. a) 5 min; b) 10 min; c) 15 min; d) 30 min; e) 45 min; f) 60 min; g) 90 min; h) 120 min; i) 180 min after injection of Biligradin.

SUMMARY

A roentgenological study was made of gall bladder filling with fresh bile and of its concentration in the interval between digestion in healthy dogs and dogs irradiated with roentgen rays.

In acute radiation sickness disturbance of gall bladder filling and of bile concentration were functional and depended on the stage of the disease. Dystonia of the gall bladder (mainly of hypotonic character) and dyskinesia of the bile ducts were found.

LITERATURE CITED

1. N. I. Bogolyubov, Carbon Dioxide in the Bile. Data on the Physiology of the Liver. Doctorate dissertation, Kazan' (1872).
2. A. M. Dokhman, Data Relating to the Study of Bile. Absorption in the Gall Bladder, B. M. 189....
3. G. A. Zedgenidze, I. S. Amosov, and L. F. Sinenko, Med. radiol., 2, 3 (1958).
4. P. K. Klimov, M. M. Popov, and N. A. Solov'ev, Transactions of the I. P. Pavlov Institute of Physiology [in Russian], Vol. 9, Moscow-Leningrad (1960), p. 232.
5. L. D. Lindenbraten. Vestn. rentgenol., 5, 3 (1960).
6. A. Fischer, The Physiology and Experimental Pathology of the Liver [in Russian], Budapest (1961).
7. H. Tera, Stratification of Human Gall Bladder Bile in vivo. Stockholm (1960).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.