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OCT 24 1968

DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

#34
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ORGANS OF CIRCULATION

by Karl Löwenthal, Berlin
with 6 illustrations — Trans by C.R. Robins for the Germans

I. Normal Anatomy

a. Morphology

The anatomy of the organs of circulation, which are here described for laboratory animals, show no essential differences between those of man and those of domestic mammals. The heart is somewhat more medially placed than in man in agreement with the more narrowly shaped thorax. The organs concerned are the same as in man. In guinea pigs the pericardium has grown together with the stern in a narrow surface, the same as in rabbits, rats and mice (Schauder). The anterior wall is probably, at least in the rat and mouse, somewhat more arched than in man and the left ventricle forms a proportionately larger part of the latter.

For puncturing the heart, which is of practical importance in guinea pigs (complement production) it is, according to my experience, most suitable to pierce from above, medially and backward into the intercostal space left of the middle of the sternum. Otherwise one will use the peripheral venous system to take blood; in rabbits the veins of the auricle or for larger quantities the external jugular vein which is considerably wider than the internal jugular, in the mouse one must be content with cutting the tail and abstracting the blood from the caudal veins. For injections one most often uses the auricular veins in rabbits, and in the rat and mouse the caudal veins, which one dilates by rubbing with xylol (danger of necrosis!) or, if more frequent injections are necessary, by dipping the tail in warm (not hot) water. Especial topographic data are not necessary for this purpose.

According to Schauder the size of the heart is: rabbits - 3-3.5 cm long and circumference at the base of the heart is 7-8 cm; guinea pigs - 2 and 5-6; rats - 1.2 and 2.5-3; mouse - 0.8 and 2 mm. According to R. Krause the length is 3.5-4 and the base diameter 2.5 cm in rabbits. The weight is given by Schauder as 0.2-0.4 per cent of the body weight for the rabbit. Lucien and Parisot report a heart weight of 9-10 gm in animals of about 3500 gm body weight 8-8.5 gm for 3000 gm and 7-7.5 gm for 2500 gm; Schmidtmann considers hearts of 13.8 gm with 3000 gm body weight as hypertrophied. According to Boissesen and Carlson in guinea pigs which did not vary greatly from a body weight of about 100 gm, a corresponding heart weight averaged 390 mg, those of 200 g corresponded to 450 mg, 300 g to 910 mg, 400 to 1170 mg, 500 to 1420 mg, 600 g to 1670 mg, 700 to 1930 mg, 800 g to 2140 mg. The heart weight of the rat is given by Cameron and Carmichael and Cameron and Sedziah as 350-640 mg in some young animals of 67-160 g body weight or 0.40-0.52 per cent body weight, and as 820-940 mg (0.32-0.37 per cent body weight) in some older individuals with a body weight of 224-289 g. Very detailed figures on the heart size in white rats (Mus norvigicus albinus) are found in Hatai and Donaldson. The weights which are equal for both sexes, is about 0.05 at birth when the body weight is 50 g or is about 1½ months of age 0.28 g with 100 g, or at 2-1/3 months 0.45 g with 200 g or at 5 months almost 0.8 g with 250 g or about 1 g at more than 7 months of age. The data are based, inas far as I could see, on determinations on 36 animals; I have very roughly reduced the data here and the range of variation is not considered.

The topographical relationship of the vascular system requires, as was said, no especial review. Perhaps the presence of a transvicose jugular vein, directly cranoid of the upper border of the sternum and between the two external jugulars is of especial significance for the experiment.

TRACHEA, BRONCHAE, LUNGS AND PLEURA

by A. Lauche, Bonn
with 19 illustrations

I. Normal Anatomy

The most frequent errors which are found in the literature directly concern the interpretation of the conditions of the lungs in small laboratory animals after experimental trials. They require an especially detailed treatment of the normal structure of the rodent lung and a thorough discussion of those kind of conditions which are indeed easily seen to be pathological, but which in the case of extraordinarily large reaction capacity of the lung tissue, chiefly in guinea pigs, are so abundantly found that they actually belong to the normal picture.

a. Windpipe (Trachea)

The windpipe of rabbits runs in the anterior mediastinum as a relatively thin-walled tube which is clearly flattened dorsoventrally. It consists of about 50 almost closed, cartilaginous bodies which are most ossified ventrally and measures (depending on size and age of the animal) about 70 mm in length and 5-7 mm in diameter. The trachea of the guinea pig (about 30 mm long and 2-3 mm in diameter) has relatively thicker walls and is very horseshoe shaped in cross section (laterally somewhat compressed). Also its cartilaginous ring allows only a very slight portion of the dorsal wall to be free so that with the contraction of the musculature they can even overlap. In the rat and mouse the windpipes are relatively thicker walled than that of the rabbit, the latter after all is more nearly equal to that of the guinea pig, probably conforming to the attachment of the musculature. We see as the outstanding difference between the trachea of the old world rodents (rabbits, rat and mouse), on the one hand and that of the new world

guinea pigs on the other hand that in the former group the smooth musculature of the cartilage-free dorsal side attaches outside (dorsal) the ends of the cartilaginous stay while in the guinea pigs it is inserted inside (ventral) the lumen. (see Figure 17).

The significance of these differences in insertion of tracheal musculature is unknown. Otherwise we find both forms in the animal series. For example the external origin is found in the predecious animals (in all?), the internal origin is found for example in pigs and in man. Here it chiefly interests us that in what appears to be closely related animals such as guinea pigs and rabbits and rats and mice respectively, there are considerable differences in the gross anatomy. We shall see later that these differences are not the only ones but that the old world rodents differ in still other small conditions as for example in the structure of the lung arteries and in the quantity and partition, and also in the ability to react, of the lymphatic tissue. These facts are not only of theoretical interest but are also of practical importance since they require that great caution be used in the transfer of the experimental results, which were obtained in one animal to another, which appears to be closely related. Guinea pigs and rabbits react differently to many stimuli, a fact, which can not be sufficiently emphasized (see also page 39).

In the histological picture we also find some differences in the structure of the trachea in the animals under consideration. Those from the old world show a stronger tendency for calcification of the cartilaginous ring while in the case of the full grown rabbits a calcium ground substance is almost always found in the ventral side, seldom true ossification (Figure 17, Ka). Also in adult rats and mice one frequently finds deposits of

calcium, while I have seen almost no calcium deposits in the tracheal cartilage in guinea pigs. All four rodent species have in common the slight development of the tracheal mucous glands which are found singly, only on the ventral side between the cartilaginous rings. The tracheal epithelium is a several layered, ciliated epithelium which contains goblet cells in the rabbit and guinea pig; in the rat it is two layered and ciliated, in the mouse it is mostly simple and only, at places, two-layered.

b. Bronchiae

The division of the windpipe into the bronchiae in all 4 kinds of animals occurs in the same way into a shorter more horisonal running right principle bronchus and an principle left bronchus which runs steeply downward. The right one give off right away a prominent branch to the right superior lobe which also is noted as the eparterial bronchus since it (as in humans) runs on the upper side of the artpulmonalis, while on the left side, the first bronchus enters the lung underneath the artery. In the larger bronchiae the ciliated epithelium (see Figures 18, 21 and 22), first of all still of several layers, permeated by some goblet (mucous) cells is in well marked longitudinal folds (if the bronchiae are not extended by filling with a fixing fluid). With increasing division of the bronchia the epithelium becomes thinner, first a single layer of high cylindrical cells, then, under decrease of goblet cells it becomes cuboidal and finally unciliated. In the large bronchiae are found in the rabbit, more abundant mucous glands than in the trachea. They decrease rapidly in size and number and are no longer to be found in the trachea. In the guinea pig, mucous glands are also found only sparingly in the larger bronchiae and are entirely absent in the smaller. The same condition is true of the rat and mouse.

While in rabbits and guinea pigs the larger bronchae have cartilaguous plates deposited in its wall, such punctures are absent in the rat and mouse from the point of entrance of the bronchiae into the lung. The smooth musculature which is found in the bronchial wall of all four rodents, shows in guinea pigs an especially strong decline in the concentration of the ring-shaped bundles, between which the muscle fibers only sparingly surround the bronchial wall. One frequently finds this muscular ring strongly contracted in guinea pigs especially in bronchiae which belong to atelectatic conditions (see page 42). As is clearly known from Figure 22, it is then that the ring-shaped bronchial lumen is completely or nearly completely closed, a condition which I never found in the other rodents and which certainly is related to the formation of the atelectasis which will be mentioned later.

At the point of division of the bronchiae, but also located elsewhere in the wall, are found very numerous lymph nodes whose size and number varies greatly not only in different animals but also in the same animals according to the condition of excitation. With stronge. development these lymph nodes extent through all sections of the bronchial wall. The palisade layer (of epithelium) is often clearly reduced and flat in that it forms a semi cellular projection against the bronchial lumen. Also the elastic fibers which occur abundantly in the bronchial wall are interrupted at the place of occurrence of the lymph nodes. Under conditions of excitation the lymph nodes can in time unit in the form of a continuous lymphatic ring and cover (see (Figure 21).

c. Lungs

The lungs of rabbits, guinea pigs and rats are placed next to each other in Figure 19, after removal of the heart. They are equally reduced in size (2/3 natural size) and projected in ventral view. It also shows again that in gross nature the rabbit, rat and mouse belong closely together while the guinea pig lung is much more divergent. In the rabbit, rat and mouse the right lung far exceeds the left in size while in the guinea pig this is not the case. The number and arrangement of the lobes of the lung can be seen in Figure 19. It should be noted in individuals that the small right medial inferior lobe (Heart lobe) lays broadly on the esophagous and is separated by the inferior vena cava of the lateral inferior lobe from the actual lower lobes. In all four animals there is always found a ligamentum pulmonale (L.P.), which extends from the diaphragm to both lower lobes as a fine membrane, and it must not be confused with an inflamed adhesion. By further pleural doubling a special pleural sack is formed for right medial inferior lobe or the heart lobe. The guinea pig lung is different from the three old world rodents also in that the right side of the inferior medial or accessory (Schaffner) lobe does not lie in a special pleural sack. While the normal number of lobes in the rabbit on the right side is 4 and on the left side is 2, it occasionally happens that a median lobe is formed on the left side if the upper lobe is deeply cut by an indentation (see Figure 19). Also in the guinea pig, the left upper lobe is occassionally split further by an incisure so that one finds 4 lobes on both the right and left sides. The right medial inferior lobe can be a depper indentation of the fissure which is always present can even be divided into 2 small lobes. In the rat and mouse there is usually only one left lobe present since the fissure (S.I.) which is sometimes deeper, usually runs only the surface of the right lobe. Therefore one frequently finds a

further division of the right upper lobe by a deep cut of the fissive S.2 visible in Figure 19, [illegible]e to this the disparity of the right to the left lung is still marked, 5:1 lobes.

The histological structure of the lungs has already been given for the larger bronchiae. The further smaller branching of the bronchiae show no essential differences. Similar to man, the bronchioles divide into 2 (seldom 3?) Bronchioli terminals, which go into the Bronchioli respiration. These are already situated in individual alveoli and indeed on the side which lies opposite the accompanying pulmonary arteries. The alveolar canals (Ductusel-vectares) which are mostly known as the Atrium attach to the respiratory bronchioli, the alveolar sack or infundibula arise from the alveolar canal. The alveolar canals are relatively shorter in the rabbit than in the three other rodents (Oppel). From Figure 24 one sees (inthrax) the division of a terminal bronchioli of a guinea pig into the alveoli under the pleura.

On the nature of the cells which line the alveoli these have recently been expressed differences of opinion on the basis of storage studies and the results of tissue culture in which some researchers, chiefly Policaid, represent the concept that the alveoli are cavities in the inside of the connective tissue and that the lining cells are of mesendrymal origin.

In thin sections which are treated with the usual staining methods, the alveolar epithelium can be hardly demonstrated. For this purpose one silver thicker sections. One discerns then that the alveolar epithelium and the "Unucleated plate" sets directly on the capillary wall. With the removal of the bronchial tree the groups of epithelia are reduced in size and number of cells so that they often lay individually in the alveoli of the normal lung and indeed in the interstices of the capillaries. According to more recent investigations, chiefly by Seemann, the so-called "Unucleated plate"

never appears to exist in the form of a cellular unnucleated structure. On the other hand we are probably dealing with a noncellular membrane (basal membrane) from which the epithelium was removed. According to this interpretation the cappillary looks in the alveoli border directly, the alveolar lumen so that the assumption of a respiratory epithia in the form of an "unnucleated plate" would be weak. Also in recognition of this interpretation afxihi however, one can not say that the alveolar spaces is in the connective tissue since they are bordered through these membranes sharply by mesenchyne. This can be especially clearly demonstrated by the results of the silver studies of Seemann which were undertaken once in the bronchial tree and another time in the system of canals (vessels?). For explanation see Figures 2 and 3 on plate X in Seemar. The alveolar walls of the rodents are relatively thicker than those in man. In part this thickening is only an apparent one since the diameter of the capillaries is greater in relation to the alveolar diameter. In part, however, the thickening also is due to the fact that there are numerous lymphoid and leucocyte cells situated in the alveolar wall in rodents (Gerlach and Finkeldey). Also the quantity of elastic fibres is larger in rabbits and guinea pigs than in man; in the rat and mouse the picture is about comparable/that of man. In the removed lung the elastic fibers always run in a winding way. They increase with age and appear, with reference to the degree of their development, to have a certain correlation with the mode of life, chiefly the degree of mobility of the animal. Their development, considered from the narrow sense, is first established in extra uterine life (Linser).

Thus when the histological picture of the rodent lung (in an unexpanded condition) frequently makes a more firm impression than the comparable picture obtained of the human lung, the compaction (best for elastic preparation)

is to be more precisely studied and without delay to study more precisely the inflammed thickening of the septa or of the pneumonic center in citile-static cases. This has frequently appeared since the differentiating of atelstatis from hypostasis and pneumonia here is still more difficult than often is the case in man, chiefly in children. Also the oxydasis reaction is used to advantage since already normally the capacity of the lung capil-laries and septa for oxydase-positive cells is larger than in man (Gerlach and Finkeldey). In my opinion, the size relationships of the lung (absolute value, as well as the relation of the lung size to the bronchial-, alveolar-, and capillary-diameters respectively) plays a larger role for the form, propogation and extension of the different diseases, especially of the in-flammation, than one has heretofore ascribed to it. Similar size relationships are surely a basis - perhaps not the least important - thus many times the picture of lung inflammation of the small laboratory animals agrees only in principle mit with the findings in small human children and infants. On the other hand the size relations, which differ thus, whould provide a basis for especial caution when one is to compare the experimentally produced lung diseases of the small laboratory animals with the relations in the adult human lung.

As in man, pores are found also in the alveolar walls of the rodent lung (Muller) through which they connect adjacent, alveoli, which at the same time do not pertain to the bronchiolus. Whether such "windows" are also found in the interlobiar septa as Loeschek supposes for man, I can not establish. The clear cut lobular border of certain atelectasic areas in guinea pigs in any case supports the fact that this kind of window could exist as in very slight development at best.

In the lungs of pregnant guinea pigs, Motta found innumerable lipoid-containing cells in the alveolar spets. He derived then from the alveolar epithelium and correlated their increase during pregnancy with the variation in lipoid substances which increased during this period. However, we are probably dealing here with derivatives of the reticulo-endothelium.

Of greater significance for the researcher who is working experimentally, is the knowledge of the conditions of the lymphatic tissue in the rodent lung. It not only often exists in proportionately much larger quantities but also shows, especially in guinea pigs, an unusually larger capacity of reaction to the most different stimuli. One can differentiate two forms of behavior (Cuerissi - Pellisier, Klein): (1) compact, more or less sharply defined nodes which are embedded in the more coarse connective tissue reticulium, thus peribronchially and perivascularly rich (Figure 21) and (2) completely diffuse, very variable, strongly developed, lymphatic heaps in the delicate septa often independent of bronchiae and vessels (Figure 20). As follows especially from the thorough investigations of Gerlach and Finkeldey, these variable, strongly developed, "lymphoid nodes" belong to the normal picture of the guinea pig lungs from 5 weeks of extra-uterine life on. They are found sometimes especially frequently under the pleura (Arnold). Since these nodes are increased and spread out by insignificant, stimuli, not only bacterial but also mechanical, their condition after any given interference is evaluated with the greatest caution. The center shwwn in Figure 20, I found in the lung of a guinea pig which died suddenly without other lung variations. In this strong development they often can no longer be differentiated from the perivascular nodes. In composition the small pneumonic centers, together with the perivascular lymph nodes are often enormously developed and form broad lymphatic bands and rings around

the vessels and bronchiae. Also in the rabbit, rat and mouse one often finds an - compared to man - enormous proliferation of lymphatic tissue in the course of chronic inflammation processes (see Figure 21). It is thus not suitable to study the small rodents in whose utilization the expansion and mass of the lymphatic tissue plays a somewhat important role. Numerous errors in the literature sufficiently demonstrate this (see Gerlach and Finkeldey on this matter). Which stimuli lead to an especially strong lymphatic reaction is still little known. Doubtless in the case of guinea pigs even mechanical stimuli will suffice (for example, rock dust). On the other hand a stronger lymphatic reaction does not follow every chronic infection. A comparison of Figures 21 and 28 clearly demonstrates this. In Figure 21 one sees the enormous proliferation of lymphatic tissue in the wall of the bronchiae, which is not essentially changed, whereas in the case of Figure 28 the inflammation of the bronchiae which has already long existed has not been followed by any hyperplasia of the lymphatic apparatus at all. Probably, there had previously developed an extraordinary high degree of bronchiostasis and all bronchiae were filled with pus. In the entire section which the greater part of the lower lobes, a relatively small lymph node with a "germ center" is found only at L in the bronchial wall.

In addition the cell mass which consists predominately of lymphocytes, Gerlach and Finkeldey describe adventitious cell masses in the normal picture of the lung of the guinea pig which consists of lymphoid cells and numerous polymorphonuclear leucocytes with eosinophilic and pseudoeosinophilic granations. The structure of this center in general parallels the "lymphoid nodes" except that it is already found in very young animals.

The lung vessels merit special discussion since they also readily show a condition of far reaching variation in their structure from that found in man. The veins of the lung of all four rodent species are surrounded from the heart out with cross-striated musculature which, however, extends for a different distance in the various species. In rabbits and guinea pigs it surrounds only the short extrapulmonary portion in the form of a circular longitudinal layer. The rat has only a circular layer of fibers which, however, also surround the larger pulmonary branches. In the mouse, according to Streda, bundles of this kind of cross striated muscle are found even in the walls of the small veins. These bundles are said to make up almost the entire outer wall. As yet I have not been able to convince myself of this. According to Arnstein these cross striated muscle fibers around the veins of the lung of the rat and mouse exhibit all the characteristics of cardiac musculature. They are said to serve in assisting the removal of the lung to the heart. The lung arteries of the rabbit, rat and mouse exhibit a very thick musculature in comparison with that in man, which starts the pressure that assists to a great extent the action of the heart. The lung arteries of the guinea pig show perfectly remarkable relations which according to my knowledge of the literature, have been unobserved heretofore. They do not possess a musculature comparable to that in the rodents previously discussed; a section of the wall is often partitioned into muscle prominences which are arranged together like a string of pearls. These prominences are already strongly developed in the new born. The lumen of the artery is - compared with the thickness of the musculature - usually disproportionately narrow, since, in most cases, the arteries are contracted in histological preparations. The ratio can be clearly seen in Figure 22. Here the arterial branch is shown with the

corresponding bronchus with elastic staining. The cushion of muscles (p) is clearly seen along with the elastica interna (which runs undeviatingly in a straight line) of the vessels which are here probably little contracted. In a literature survey of reports of similar relations in other animals, I have found to date only the statement by Oppel that, according to Plana, the small lung arteries of the cow, sheep, and pig contain muscle rings around the lumina of the vessels. They probably retain to the job of restraining the velocity of the blood stream entering the capillaries thus the opposite problem, which appears to follow from the comparatively strongly developed muscularis of rabbits, rats and mice. Which explanation is correct must remain open. Yet another interpretation must be considered in the guinea pig which also must bear in mind the muscle-ring structure around the bronchiae which has already been mentioned. As already discussed, I relate the atelectatic region, which is part of the normal lung picture of the guinea pig according to Gerlach and Finkeldey, to contraction of individual bronchiae (see Figure 24). Therefore we can now advance the idea that the contraction of the bronchus is accompanied by a contraction of the corresponding branches of the lung arteries so that the region cut off from the air supply will also be supplied with less blood. The experimental interpretation is supported chiefly by the results of research by Ceelen, as yet unpublished, on the lungs of guinea pigs, the dust-inhalation studies were suspended. It follows from this that the guinea pigs reacted only very slightly to the dust inhalation, since they are apparently in a position to close off a large section of the lung by contraction of the bronchiae, whereas rabbits always suffer badly from dust inhalation. Thus both rodent species are not adapted for such studies, on opposite grounds, however; the guinea

pig reacts too little, the rabbit to strongly. Also the studies recently conducted by Schults-Brauns in the Bonner Institute with "Nitrose" gases (trans note: Nitrose sometimes means nitrosylsulphuric acid) yielded important differences in the reactions by rabbits and guinea pigs. These differences also could be related to the ease with which guinea pigs close off large sections of the lungs by contraction of the bronchiae.

The lymph vessels of the lungs are very well developed, as in man. They surround the bronchiae and the vessels on all sides and have their origin in the alveolar walls. In the normal lung they are not prominent and in this section they can not be found with certainty in the surrounding connective tissue since their walls are superimposed. In acutely inflammed lungs they are often very apparent and in such cases surround, as greatly expanded spaces, the vessels whose lumina they greatly exceed.

Probably the vessels, like the bronchial ramification of the lung, are provided with a great number of nerves, on whose supression in individuals we have learned from the works of Berkley for the rat and Larsell for the rabbit.

The bacterial contents of the normal lung is very small. Probably bacteria are completely lacking in the alveoli. This follows from the fact that tissue culture of lung tissue always remain sterile if one uses the peripheral portion of the organ for the culture. Also according to the bacteriological investigations of Arlo (guinea pigs) Jones (rabbits, guinea pigs, rats and mice) the lung tissue itself is almost completely sterile whereas the lymph nodes can be infected up to 50%. One finds in them (according to the statements of the above named researchers) chiefly streptotrix, Bacillus subtilis and various cocci, all microbes which can also be found in the dust from hay and straw. In all probability they are harmless, only under especially unfavorable conditions might they evolve

pathogenic properties (see p. 55, necrobacillosis).

d. Pleura

With reference to the pleura, its composition in humans who did not possess a Ligamento pulmonalos was already referred to (p 32) and we also mentioned the special plmural sach for the heart lobes. Histologically the pleura consists of a thin layer of tight (compact? - trans.) connective tissues with an elastic boundary lamella. On the surface it contains a stratified layer of flat "cortical" cells about whose nature (whether epithelial or endothelial) equal differences of opinion exist as in the nature of the alveolar epithelia (see p. 33). The cortical cells are very deciduous so that one can demonstrate them only with very careful handling of the lung. Frequently one gets to see when the pleura is covered by a fibrinose exudate under which they often swell and often, by adiposis assume a cubical shape.

B. The Esophagus and Stomach

by Walter Lenkeit, Berlin
with 5 illustrations

The position of the esophagus both in the neck as well as in the thorax is about the same in all animals. Measured from the pharynx the length amounts to 12-15 cm in the rabbit, 8-10 cm in the guinea pig, about 7-8 cm in the rat and about 3½ cm in the mouse.

The mucous membrane in the case of the guinea pig, shows x ledge-shaped elevations, whose height increases from the upper part of the esophagus to the lower portion. In the rabbit mucous glands are found only in the uppermost section about at the level of the center of the larynx (R. Krause). In the other rodents they are completely lacking (Oppel). The muscularis mucisae is formed clearly only in the lower third of the esophagus of the rabbit. The tunica muscularis consists of cross striatis muscle fibers which extend to the region of the cardium in the rabbit and to the cardium in the guinea pig, rat and mouse. The physiological study of the make up of the esophagus as regards both kinds of muscles in the animals in question shows typical fast contractions for the cross striated musculature.(E. Mangold, Inacka). Only in young rabbits is the slowly rising and falling course of the contraction curve indicated from participation of smooth musculature (Inoaka). The smooth musculature accordingly would contract in the case of the rabbit in the course of the folding of the esophagus. Exhaustive morphological comparable to the physiological studies on this are still to be made.

II. STOMACH

a. Normal Anatomy

1. Morphology

The stomach of the rabbit has the shape of a retort. Left of the cardium the large and small curvatures meet to form a large, dorsally directed blind sac, the stomach - fundus. To the right the stomach contracts gradually, to form an enlargement before the Pylorus, the Antrum pylori. According to Schauder, the capacity amounts to approximately 40-50 cc.

The musculature is weakly developed; only at the antrum pylori is it especially thick. The mucous membrane appears microscopically to be almost homogenous. It is especially in the Fundus, placed in a more or less superficially; whitish ring-like folds exist on the cardium. The color of the mucous membrane is gray-red in the gastric portion, gray-yellow in the pyloric portion. The stomach lacunae are clearly seen, with a magnifying glass, in the fundus portion, less well in the pylorus (R. Krause).

Position. In the filled condition (as is almost always the case) the stomach lies ventrally to the abdominal wall, while cranially the lesser curvature lies next to the liver. To the left the blind sac of the stomach can rest on the lateral abdominal wall in the region of the last two ribs. On the right lying between the stomach and the abdominal wall is the ventrally diagonal portion of the caecum (Schauder).

C. SPLEEN

by E. Landa and Ph. Regek, Vienna
with 6 illustrations

1. Normal Anatomy

a. Morphology

1. Mouse

Weight about 0.2 gms; according to Martin the spleen measures 1.5 x 0.3 x 0.2 cm. We found figures significantly above and below that of the means listed above. The smallest spleen seen by us in the animals which we used was 0.7 x 0.55 x 0.3 cm. On the basis of the average values, given above, the drawn out configuration of the mouse spleen varies from this condition in the case of abnormally small proportions to a bean-shaped structure. The color of the spleen is red-brown, its consistency somewhat higher than that of the liver. The abundant microscopic visibly vitheous transparencies of the Parenchyma are due to the follicle layer.

In cross-section the spleen is triangular. The angles of the triangle correspond to the caudal, cranial and dorsal borders. The caudal wall is somewhat shaper than the others; the mesentery inserts in the dorsal border. The three edges of the spleen meet above and below the pole; thus the under side is more rounded and bluntly angle while the upper is more sharp.

The caudal region of the spleen, when the abdominal cavity is opened, is visible chiefly from in front. The main portion lies lateral to and behind the stomach and, when broadly expanded it lies against the veribral column.

The mesentery, which inserts on the vertral margin, consists of two membranes. The anterior membrane is the Ligamentum gastroliensle which is

thin in cross-section and contains but few vessles. After separating away this membrane one meets the posterior one, which corresponds, in the rodents, to the free mesenteric portion in which the Pancreas is embedded. The caudal portion of the pancreas almost reaches the spleen. The important mesenteric portion, just mentioned is not directly connected to the stomach and it is erroneous to denote the splenic mesentery as the Ligamentum gastrolinicle as generally happens. A splenic hilium is lacking. Most of the splenic vessels are found in the posterior membrane of the described double mesentery.

The anterior and posterior mesenteric membranes unite above the spleen poles to a ligament which extends from the stomach and the upper spleen pole cranially to the diaphragm (the ligamentum phrenicolienale).

2. Rat

Weight approximately 1 gm. The size of the rat spleen is extraordinarily variable. In most case animals infected with Bartonella but otherwise healthy, have immense spleens (see Lauda, Sorge, Cannon and others cited in the Literature on p 248). Martin gives as average measurements 3.5 - 4.5 cm length, 0.8-1.0 cm width and 0.5-0.6 cm thickness. The other relations are all analogous to that found in the mouse (see above). In external configuration it differs only in the condition that the lower splenic pole also generally appears accumuate and that the caudal mxx contour of the spleen, in contrast to the ventral countour which runs in a straight line is often irregularly curved so that the width of the spleen can vary somewhat in different regions. Also the mesenteric relations differ in no way from those described for the mouse.

3. Guinea pig

Weight about 0.5 grams. The spleen of the guinea pig is a flattened

organ which differs considerably from the spleens of the other animals in that it is disc-shaped. According to Martin the measurements in the animals used are as follows: Length 2.5-3.0 cm, width 0.8-1.0 cm, thickness 0.3-0.4 cm, numbers which we could confirm. Since the thickness is a small dimension the triangular form of the cross-section although it exists is nevertheless obscured. The ventral edge which forces the stomach and to which the mesentery attaches, is on the same basis strongly rounded and is occasionally completely lost in the caudal region of the spleen. The upper and lower bodies are clearly rounded.

The relations of the mesenteries are analogous to those described earlier for the other animals. They differ, however, in so far as the interior and posterior membranes of the double mesentery are extraordinarily short so that the spleen appears to be almost directly attached to the stomach. A delicate Ligamentum phrenicolienale is present.

The surface of the spleen is smooth when the organ is well filled with blood and clearly granulation when the spleen is contracted.

4. Rabbit

According to Martin the relatively small spleen in the animals used for the study is approximately of the following proportions (young animals have a somewhat larger spleen): length 5 cm, width 1 cm and thickness 3 mm. Weight about 0.1-0.3 % of the body weight according to Wall. According to Martin the spleen lies in the region of the 10-11 rib, 1-2 cm farther caudal if the stomach is very full, and indeed caudalaterally from the left portion of the greater curvature with which it is connected via the Ligamentum gastrolienale. The dark red-brown organ exhibits a soft consistency. The cranial edge is rounded whereas the other edges are sharp. The ligamentum lienules are not present.

Spleen

b. Histology

1. General

With every similarity in the structure of the spleen in the mouse, rat, guinea pig and rabbit, an exacting study of the anatomy with respect to histology yields nonetheless real, characteristic differences whose knowledge is not only of interest from the standpoint of comparative anatomy but also is very significant for the animal experimentator for avoiding error in special problems. Before we point out the differences in the spleen structure in the laboratory animals in question it is deemed necessary for easier understanding to describe the structure of the animal spleen in general since only the most important features have been emphasized in previous books. It should be assumed (1) that the mystery surrounding the structure of the normal spleen has to a great extent been clarified thanks to intensive work especially in recent years (2) that in particular every since the open questions of the open vs closed blood channel in the spleen in addition the problem of the make up of the sinus and of the arrangement of the reticulium can be regarded as settled, but since only a precise theoretical knowledge of the histology of the spleen can correctly give the investigator the various details of the microscopic picture and especially since the various details can be grasped with little experience only by fixed techniques. The recognition of the splenic sinus and the sinus wall structure respectively can only be used for demonstration in well-washed preparations. In the usual sections of spleen even the experienced have difficulty in recognizing it.

Two components of spleen tissue which above all allows a superficial orientation of the complicatedly built organ, are the connective tissue framework and the vessels which moreover mutually exist in a definite

relationship. The connective tissue stroma consists of the extensive fibrous capsule of the organ and the trabecular system. The capsule of the spleen is very differently developed in the various animals. It consists of thick connective tissue fibers whose smooth muscle fibers and elastic elements could be interposed. From them the splenic trabeculae receive their starting point, which is always more reduced pulled in from the capsule in the connective tissue of the spleen and thus the coarse fibrous stroma of the splenic parenchyma is demonstrated. These trabiculae also consist of connective tissue, elastic fibers and muscular elements. The coarser splenic plus rabiculae contain in their center, excurrent and incurrent vessels but in the case of the smaller trabiculae this relation to the vessels is lacking. As Hartmann and Bennet could show recently, in as much as a uniformity in the stroma of the trabecular system has come to light, like the more coarse trabeculae, the spleen comes apart in a kind of "loculos", during which , of course it cannot be told by a sharp mutual separation in the latter. The results were reproduced best with the schame of the authors in question from which it follows that the trabeculae are multiply flattened and thus represent a partition-like structure. Concerning the question whether these "loculos" can function as "flood locks" will not be treated here, it is emphasized only that with the contraction of the spleen without doubt must lead to a shortening of the trabeculae and under various changes of shape to a lessening in size of the locules. The parallein with a sponge (Huech and others) is certainly proving correcty. Between the larger and smaller traticulae spanz the fibrious reticulum which pentetrates deeply the spleen pulp and which connects to the adventitious sheaths of the vessels and to the sinus venosus. We will come back to these details later.

The greatest difficulty that is encountered in the study of the distribution of vessels in the spleen concerns especially the question about the open and closed blood path, has remained the subject of intense discussion for a long time. These very difficult questions are also being solved chiefly due to the excellent description of the results which were clarified by Hueck, whose methods should be referred to in the German Society of Internal Medicine, 1928.

The splenic artery enters into the organ at the splenic hilus in most cases having already split into several branches. The individual branches, after entering the parenchyma of the spleen, lie, as previously mentioned, in the thick connective tissue sheaths which represent the splenic trabiculae, in which they branch futher. The artery is accompanied by the vein. The artery leaves its fibrious casing and divides off from the veins when the diameter of the vessels has decreased to a certain size (in humans, according to Heuck, at a diameter of 0.2 mm) and now enters the pulp where lymphatic cells infiltrate into the media and Adventitra of the vessels. These produce the well-known lymphatic sheath. At the points of separation the artery, the lymphatic sheath increases in size to form nodules. The Malpighian corpuscles which usually contain the artery somewhat assymnatricly. A more precise description of this is given later. Between the branchings off of smaller arterise branches inside of the nodule capillaries, this so-called central artery of the lymph follicle narrows and finally after completely losing the lymphatic sheath it leaves the nodules in order to immediately divide in the pulp into a greater number of smaller vessels, the pneicillar ~~xxxxx~~ vessels. For the latter it is characteristic that they, at least usually, are immediately supplied with a thickened wall which marks these small

arterial branches to a short distance as capsule arteries. These capsules consist of connective tissue fibers which run parallel to the axis of the vessels, between which isolated or even several nuclei come to be. The entire structure usually has an elliptical form (Ellipsoid of the English and American literature). In unwashed sections which were treated with connective tissue dye, these capsules are not readily found; in the case of Azan or Mallory's Dye they appear as dark blue in the section, probably circumscribed, depending on whether the surface of the direction of the cut is oblong or else roundish with longitudinal striatium in whose center the small arterial capillaries can be found. The latter consists of an endothelial covering whose nuclei project conspicuously into the lumen of the vessels and which appear to be on a small membrane. Muscular elements are no longer observed in the capsular arteries. Whether one denotes the capsule artery or only its continuation after the loss of the capsule as the capillary, different views are found in the literature, is of little importance. Also the question of the function of this characteristic thickening of the wall of the splenic artery and capillary respectively will here be only briefly touched upon. Many talk of a valve which hinders the entrance of a larger blood valve under larger pressure into the parenchyma of the spleen, many discover in it an apparatus designed to prevent the backflow of blood from the pulp in the arterial system (Oberniedermyer-backflow valves). According to Miles the capsules are lacking in the rabbit.

The arterial leg of the splenic circulation can thus be followed to the following points.

1. The penicilli vessels, which represent the continuation of the central artery ⟶ the capsular capillaries ⟶ the arterial capillaries.

2. The penicilli vessels which end in the border zone of the region of the follicles.

3. The follicle capillaries which in part also reach the border zone.

The main excurrent canal for the venous blood represents the already mentioned trabecular veins; it should be added that its small branches are not in the trabeculae but adhere closely to them. The trabecular veins collect the blood from the sinus. The latter represents the blood space whose entrance, thanks to the peculiar construction of its wall, is filled by erythrocytes in the pulp and from the pulp respectively. They are generally tubes which anastromose with each other.

Mollier was the first to recognize the characteristic perforated construction of the sinus.

We have earlier noted that the pulp is tranversed by a reticulin of connective tissue. It is now of especial significance that the reticular fibers according to Mollier and Huecк, the processes of the cells of the reticulum (filaments which are not round) from numerous membranes which span the space from different directions, often appearing as thread-like thin partitions which anastomose with each other. "They form a system of interstitial spaces which are inter-connected by varyingly large, differently arranged openings (windows)". Cell boundaries can not be seen; the system must be regarded as a syncytium. Since a border of protoplasm often can not be observed, the adoption, according to Huecк, is obvious that the form of the chamber wall can change, that swelling and shrinkage processes in the protoplasm can close off the chambers from each other or by liquifcation of the boundary walls to form fistualr structure, they can run together. The interstitial spaces will be designated as blood chambers.

According to modern view, the interpretation of the change of the "unarranged" reticulium into the arranged one with the formation of tube-like structures should now dispose of the idea that some authors have found an open bloo' path and others a closed one, depending on special conditions of investigation. The connection between arterial capillary and sinus is formed just by the arranged reticulum as through a direct connection between the arterial and venous legs inwhich case the tube-like structure of the reticulium represents the connecting section. One can talk of an arranged (that is, closed) and of an unarranged (that is, open) blood path.

We come now to the question of whether th.. connection of this blood path which lies in the reticulum takes place at the arterial capillary or at the sinus.

When Schilling Hueck thus understands that through the process of channel formation, that is the functional connecting inseries of several of these chambers change the tube-like structures which lead sinus or "become the sinus" while the reticulum cells are collected in the endothelial covering. Thus we would like to discuss this observation in as much as we do not think that the Sinus could be transformed by mechanical and chemico-physiological means into a small reticular flood tubes or ultimately into an unarranged reticulum. Because even in the filled spleen in which a stretching especially occurs, the sinuses are seen in especially clear formation. Also the number of the sinuses present is obviously dependent only on the animal species so that we would like to oppose a direct change of Sinus into reticulum. Otherwise it agrees with the venons capillaries which are generally very difficult to demonstrate, the very beginning of the sinus, as they were described by Weidenreich as pulp ducts which empty in a tubular manner into the venons sinus and whose existence was clearly recognised by Hueck. Here

the analogous changeover of the capillaries in the arranged and unarranged reticula ought to occur just as in the arterial leg. According to this writer the open or closed pathway in the foregoing sense probably is found in regions of the lymph nodes as well as in the red pulp where the capsular arteries lay which represent the direct offshoots of the central artery. It is probable that last mentioned frequently exhibits a picture of closed discharge into the sinus just like the modular capillaries or the nodular capillaries which lie in the area of the lymph nodes and originate from the follicular arterie and bend back to the follicle.

The pulp of the spleen is differentiated into the white and red pulp; the former corresponds to the assemblage of the lymphoid cells, chiefly the malphighis corpuscles, the latter corresponds to the tissue placed in betwen which consists of the reticulum and the cells enclosed in it.

As already considered earlier, lymphatic elements appear in the media and adventitia of the splenic arteries, as soon as the artery has become free from the trabeculae. This lymphatic layer forms the lymphatic sheath of the arteries; they increase in thickness in places and thus form the follicles. As is evident from the shheme of the construction of the spleen, the nodules are subdivided by the definite connection to the reticulum. The aretery which runs in the trabeculae is surrounded by heavy strands of unarranged reticulum. The girth of the artery increases by deposition of a larger lymphatic center thus solidly bound coarse reticulum is displaced from outside and now forms a relatively clear boundary of lymphatic centers against the surrounding tissue since this is especially clearly expressed in sections which are stained with connective tissue methods. The next layer to the outside is known as the areola of the nodules. The sinus is generally lacking in this structure and the ends of the follicular arteries, described earlier,

are found here as well as those of the recurrent penicillar vessels. In the nodules themselves too zones can again be differentiated for which, according to Hueck, the designation of nuclear zone and mantle zone is to be preferred. In the nuclear zone are found larger, mostly clear lymph cells with loose vesicle shaped nuclei with clear nucleoli; it represents the so-called germ center. In the mantle zone are found small lymphatic elements with relatively small, darkly stained nuclei. In the germ center, one can observe relatively numerous mitosis. Also the nodules, nuclear and mantle zones are infiltrated by a more or less fine reticulum.

The red pulp, aside from the reticulum and the sinus is represented by cellular elements; reticular fibers produce first of all threads of protoplasm of the reticular cells of the "star cells", whose nuclei are found at the node points of the reticular ramifications. Star cells could be found in greater and lesser number; they form the well known macrophages, the results of which will not be treated more precisely here. Depending on the filling of the flood chambers one finds numerous or less numerous erythrocytes and "free swimming" leucocytes. Also myeloid cells could appear, sometimes grouped in centers, corresponding to a myeloid metaplasia. We will come back to the peculiarities in cell character in the different animal species later. Also the presence of megakaryocytes will be discussed there.

Finally it should be noted that we have the impression that certainty still does not exist on the lymph vessels in the spleen (see Hartmann). They will not be considered in this work.

D. The Stomach Salivary Gland

by Walter Lenkeit, Berlin

1. Normal Anatomy

a. Morphology

The stomach salivary gland of laboratory rodents differs from that of other mammals in extent and position.

In the rabbit the pancreas produces flat, tree-shaped fively branched gland system between the stomach skin layers in the corner of the dirodemus (Fig 62). A separation of head-, body, and tail-section is impossible. The small glandular lobes lie greatly isolated from one another; in fat animals they may be exchanged with the fat web lobes located betwen them. It is approx. 15-20 cm long and approx. 2-3 cm wide (Schander). The outward duct has a cross section of about 1 mm and opens approx. 40 cm from the opening place of the Ductus Choledochus. The additional Dvetus santorium, which is sometimes found on other mammals, is lacking (W. Krause, Freise).

The guinea pig pancreas shows approx. the same conditions; it only appears a little more compact, the glandular lobes lie closer together than in the rabbit. According to Schander's description, the body lies in the second duodenal loud, the right lobe in the first duodenal loop, the left in the large stomach heud. Both body and right lobe are 2 cm long. The left lobe is approx. 8 cm. The width of the body is approx. 1½ cm. The ductus pan- ticus opens approx. 7 cm from the ductus choledochus.

The distribution of the glandular lobes is not as thick in the rat as in the guinea pig; the position is nearly the same. According to Schander the body and right lobe are approx. 3 cm long. The left lobe approx. 6 cm. The pancreas juice runs through a number of small, only microscopically visilice,

channels into the gall bladder (Oppel, Munt) surrounded by pancreas tissue and by this detour reaches the duodenum with the gkx gall.

The mouse pancreas consists more of single lobuli.

b. Histology

The laboratory animals liver pancreas structure hardly differs from that of other mammals.

The regular appearance of centroacinic cells in the rabbit should be mentioned. In the rabbit, islets of Langerhans, and sometimes even the gland cells, contain granulations which, according to research by Koh and Takahashi help disolve ammonia potash silver solutions. The granulations are located in the protoplasma either perimiclearily, or more difuse. They are most numerous in the cells on the periplexy of the islets, while usually absent in the center of the islets. The reaction is not as strong in the rabbit as, for example, in man or in the pig. An important granulation increase develops after hunger, and a drop results after resumption of food. Takahashi could establish an increase after feeding of raw meat or casein, and after injecting small doses of insulin. The silver reaction may be strengthened by the acidosis resulting from an addition of diluted hydrochloric acid. The reduction capacity may easily be halted by fixing formalin and Muller's solution. According to Takahashi the silver granulations are not identical to the so called secration grains, however, they produce the resulting silver grains by penetration of the cell reducing substance. No silver granulations may be found in the centroacine cells and in the excretery duct epithelia. The ductus pancreaticus covered with simple cylindrical epithelium contains numerous mucous cells (R. Krause).

Kons and Takahashi found silver granulations both in the glands and the islets of the guinea pig pancreas. According to Kull, the chromaffin cells, described in connection with the guinea pig stomach (p 86), are also evident in large numbers in the parenchyma and in the pancreatic excretory duct. Mucous cells (Oppel), glands and Tunica propria (Oppel, Kull) are normally found in the excretory ducts of rabbits.

The silver reaction is extremely low and sometimes even negative in the islets of Langerhans of the rat.

The islets in the mouse are always devoid of granulation.

E. Liver and Gallbladder

By Fh. Rosek and E. Lauda, Vienna

1. Normal

The macroscopic structure of the liver and gallbladder of the research animals under consideration differs greatly from the human liver because of the division of the organ by deep rinckles. Lesser, but characteristic differences also exist among the laboratory animals.

a) Rabbit: A right and a left section may be distinguished in the rabbit liver (see Figure 63) (weight according to Wall 3 - 4% of body weight); both differ individually in the actual dorsaly laid main lobe, and the accessory lobe lying ventraly, towards the diaphragm. The right half of the liver is near this main lobe, from which a lobus gradratus, may be divided (see below) by means of a liver section, which is only attached to the main lobe through a narrow bridge, which divides itself into the large lobues candatus and the small lobus papilliformis.

The liver division into separate lobes takes place in varying measurements and also in various ways for different individuals.

The gallbladder is usually located in a deep furrow which does not reach the front edge of the liver on the caudal ventral surface facing the stomach, near the medial edge of the right mainlobe. The section of the right liver lobe lying medialy to the gallbladder, which produces the tie with the left accessory liver lobes by means of a bridge disposed differently in its section close to the diaphragm, is known as lobus guadratus. The structure of the hepatic porta run along the right rim of the lobus papilliformis and ventraly to the attachment of the lobus candatus. The ductus choledochus, approx. 1½ mm wide, lies next to the latter and the arteria hepatica ventraly in front of

the vena porta, and usually on the ductus choledochus. The vena portae sends a large branch to the lobus candatus while passing the latter's medial rim, and finally divides into a number of branches at the hepatic porta. The arteria hepatica is a branch of the arteria gastrodnodenalis, which turns around the caudal pile of the back wing of the lobus papilliformis, which comes to rest on the front surface of the vena portae and of the ductus hepaticus and here splits into smaller branches of various individual types, which lead to the duodenum, the Pyloris and to the liver orifice (arteria hepatica). The ductus choledocus is composed of the joining of a number of ductus hepatici and of the ductus cysticus and further in its trajectory picks up the gall duct leading from the lobus candatus. It terminates into the duodenal section near the pylorus.

The gallbladder is a flat, relatively small structure, which, as noted above, is hurried in a deep liver fold. It should be noticed that nearly 3/4 are covered by the right principle lobe, therefore is nearly totaly under peritoneal cover, with the exception of a thin strip which binds it to the lower section of the liver surface at the bottom of the fold. The ductus cistycus is nearly bent at right angles at its place of origin at the gallbladder neck. It also runs in a deep liver fold which constitutes the beginning of the Forsa vesicae fellae and similarly to the gallbladder has a grosi circular peritanial covering, which occassionally even builds a mesentery of the gall duct attached to the liver. The Vena cava inferior lies close to the medial and dorsal sections of the lobus candatus, but here is never completely sunk into the liver tissue. It is visible for a short space on the upper poe of the ventral surface of the lobus candatus and then passes behind the right main lobes to the hiatus venae covae of the diaphragm. In the area of this section it is closely

united to the front and lateral parts of the main growths of the lobus candatus and lobus papilliformis and only attached to the liver in a very limited way. The lobus candatus has an independent, strong vena hepatica, which immediately opens into the rising vena cava inferior. The lobus candatus therefore produces a gnasi independent liver section in the rabbit; it consists of special portal circulation and of a special vena hepatica. The lobus candatus is therefore only attached to the remaining liver tissue in a limited manner.

b) Guinea pigs: The guinea pig liver as far as lobe construction (Fig 64) is built in a manner similar to the rat liver discussed below, bearing in mind, that the latter has no gas gall bladder and therefore no lobus gnadratus. Here too the liver is divided into two main sections by the incisura hepatis, each of which falls into a dorsal main lobe and into an accessory ventral lobe. The guinea pig liver also has a lobus candatus and papilliformis equal to the rat liver in size and structure. The gall bladder represents an organ the size of a small cherry, which is placed in a deep fold of the caudal surface of the right accessory lobe. This liver bed reaches up to the front liver edge and seen from above forms a semicircular shelf , in which the gallbladder protudes slightly over the upper surface of the liver. The guinea pigs gall bladder, as that of the rabbit is nearly completely covered by the peritonium, while the gallbladder bed is covered by the peritonial liver cover except for a narrow area at its base where the gall bladder is attached to the liver tissue. The gallbladder therefore is only attached at its most ventral sections, in a fold of the liver tissue. The first sections of the ductus cysticus are also sharply bent in the case of the guinea pig, and here too ~~link~~ have a double, peritonenen which forms a

type of mesantery, only slightly connected to the lower surface of the liver, however a striking duplicate peritonial surface spreads between the gallbladder and the ductus cysticus on the one hand and the duodenum on the other hand, which originates near the center of the dorsal surface of the gallbladder and from the edge of the ductus cysticus facing the duodenum and is dorsaly attached to the hepat-duodenal ligament. The ductus hepaticus passes in the left and ventral section of the latter, the vena portae to the right and slightly dorsaly. The ductus choledocus, which originates it the confluence of the ductus cysticus and the ductus hepatici and is slightly expanded at this point, is approx. 1 cm long and right away opens into the duodenal section close to the stomach. On the way to the porta hepatis the vena portae sends a strong branch to the liver, which drops into the fold between the lobus candatus and the right main lobe, and soon subdivides into branchs directed to the two lobes just mentioned. The arteria hepatica, a branch of the arteria gastropancreatica splits into a number of branches in the ligamentum hepateduodenale.

The vena cana inferior in the lower medial sections enters the lobus candatus, runs through it deeply buried in the liver tissue, and after its exit runs along the back surface of the latter's main lobe, and only attached to it by tissue in one part of the circumference.

c) Rat: A large part of the right accessory lobe appears under the right costal arch in the opened ventral cavity, while the main lobe can only be seen in a limited area and is otherwise completely covered by the accessory lobes. The medial edge of the right lobus accessories runs along or slightly to the right of the mediauline. The largest section of the liver visible when the ventral cavity is opened is formed by the left main lobe; the latter's underside nearly completely covers the entire front surface of the stomach up

to the pylorus. The underside reaches up to the right mamillary line, where it encounters the lower edge of the still visible right main lobe (Abl. 65).

By turning the ventraly disposed, wingshaped lobe to the left we uncover the elements of the porta hepatis: Ductus choledochus, vena portae, arteria hepatica and the hepatoduodenal ligament. They evidence the following contrasting topography. The ductus choledoctus which is formed by the combination of several hepatic ducts corresponding to the various lobes, usually is situated ventraly and on the outer right hand side of the portal vein. It is sometimes 3 to 4 cm long and opens deep in the duodenum, after reaching the duodenum and passing through a section of the pancreas. It is easily identified as a strongly thickened thread fiber, smooth silley shing structure. The hepaticus which opens into the choledochus, lying next to the duodenum is part of the lobus papilliformis. This branch mux crosses the arteria haepatica and the vena portae ventraly. The arteria hepatica lies closely in front and slightly to the left of the vena portae. The convex upor liver surface, which mainly consists of the right lobus accessorius, becomes evident if one lifts the costal arch and pulls the liver down. The ligamentum falciforme is squeezed between the right and left lobus accessorius. A ligamentum carovarium dextrum is not evolved. A ligamentum coranarium sinistrum attaches a small piece of the lobus accesorius and the left main lobe to the cranial edge of the left side of the diaphragm. The opening of the vena cava inferior from the liver is located at the point where the convexity of the right and left lobus accessoricus meet and are organically attached. The cava is located in the dorsal sections of the lobus candatus and of the right main lobe and is here completely covered by liver tissue. A gallbladder is lacking.

d) Mouse: As the mouse liver is mainly constructed like that of the rat, you may consider the description of the later. The mouse liver also consists mainly of two main lobes, from which two accessory lobes are separated by a deeply cut fold, and by the lobus candatus and lobes papilliformis which are built like the corresponding rat lobes. These too, the main portion of the liver consists of the left main lobe and the neighboring lobes. However the following differences from the rat liver exist. The ligament which streches from the under surface of the lower main lobe to the ventrally lying wing of the front surface of the small stomach curvature is exceptionally thin and at spots shows dehiscences. The liver is only attached to the lower surface of the diaphragm in the small area next to the vena cava inferior by a ligamentum falciforme. A ligamentum coronarium sinistrum as well as a ligamentum coronarium dextrum may be absent. The mouse, in constrat with the rat has an egg shaped gallbladder the size of a ricegrain, lying between the two liver lobes, and which is attached to the incisura hepatis by the most outwardly sections of the ligamentum falciforme.

The structure of the liver opening are as easy to reach in the mouse as in the rat. Its topography is identical in both animals. The cutus cisticus opens into the ductus choledochus on the liver side of the opening of a ductus hepaticus leading to the right liver. The vena cava inferior is attached to the back surface of the liver and ~~ix~~ in general is never completely covered by liver tissue as in habitual with the rat.

h. Histology

1. General Section

Certain basic comments concerning the general histology are given here, although we must assume that the general histological structure of rodent livers. The building-up into lobes, the dual blood supply etc, are well known facts.

The liver building-up into lobes does not mean that the organ is composed of a great number of independent, self contained units. The liver, fetaly a large, centroacinous gland, not segmented into lobes, is later cut into sections by inward proliferation of the Glisson capule binding tissue, which, however, in general does not cause the single parts to loose the relationship with one another. The small lobe therefore produces either an anatomical or a functional unity. Theile, Weber, Beale and Krukenberg have shown in thorough works, that complete separation of the liver lobe is not only permicious in man but also in rabbits, rats and mice. The interdependance of the separate lobes varies in clarity with the different types of animals, the isolation of certain liver sections in a lobe is for example most extensive in the pig.

The lobe construction is usually quite easily recognised among the animals under consideration, but a separation of the single lobes by strands for binding tissues may not always be found. The lobes often overlap without limitation and narrow, perifportals zones are only to be found in the region of the large gall duct, which are brought into evidence by binding tissue collaring. Therefore when none of the species under study show structures of isolated lobes, a comparison of the rabbit, guinea pig, rat and mouse livers will still show certain differences with respect to the structure of periportal fields and the separation of lobes from one another.

Only very small perifortals vessel from larger gall ducts, may be found in

the mouse and rat and very sparse areas of binding tissue, which appear as small, parenchymatous islets exist between several lobes bordering on one another. No periportal binding tissue sections completely enclosing the lobe and no indication of the latter may be seen between the lobes; the lobes border on one another with no definite deliniation. The recognition of a central vein, limit of the parenchyma section which is part of a lobe, presents great difficulties for the inexperiences, and even the experienced runs into insurpassable obstacles during attempts at a more definite deliniation. The circumstances are a little different in the case of the rabbit and the guinea pig, where a definite segmentation of the liver parenchyma into lobes is clearly visible with a magnifying glass. This is even more definite with the guinea pig than with the rabbit. Even when this area is only limited by a definite binding tissue in certain sections of the lobes and is profuse in others the relative quantity of binding tissue in the animals mentioned still remains an identifying mark as compared to the rat and mouse. One must not take this to mean that the rabbit and guinea pig lobes are separated into isolated parenchyma sections by periportal strands of binding tissue; here too, as shown above, there are numerous links among the various lobes of the liver cellular trabeculum; it is also impossible to speak here of the units of parenchymal glands. However, binding tissue strains in rabbits definitely show, that single binding tissue threads pass from one periportal field to the next, and encircle the lobes; these binding tissue threads are often interrupted; the lobe delimitation is therefore not complete. The fiber often vanishes completely at a certain distance from the periportal area, while the binding tissue is only quite apparent at other places as stated above. The strands encircling the guinea pig lobes are more evident. However, the intertwining of the liver cellular trubiculum in neighboring lobes is also evident here under strong magnification. The delimation is therefore not com-

plete, despite the fact that very definite differences exist between rat and mouse.

The demarcation line among lobes as shown above, is not only created by interposition of strands of connective tissue but also by a number of other circumstances; this is more true in the case of the guinea pig and rabbit than in that of rat and mouse. As the venae centrales runs in different directions to the area the liver capillaries draw in a quasi perpendicular direction to the corresponding liver lobe axis, the cellular trubeculi of the liver and the capillaries of the various lobes meet at their borders from different directions, so that the border area may be recognized despite overlaping of the liver cellular trubeculi. A further circumstance becomes apparent under weak magnification: the liver cells are often smaller near the edge of the lobes, the grains are therefore thicker, so that more intensive grain coloring seen under weak magnification in certain areas of the field of vision indicates lobe borders.

Mainly in the case of the guinea pig for example, theliver section immersed in a hemalium-eosinpreparation does not only appear because of clearer strands of connective tissue, but also through this more intensive blue stain corresponding to the grain coloring of certain sections severed into lobes. The number of copper cells also seems to have increased in this area. However a complete separation of lobes is also impossible in the guinea pig; this is especially true in the case of lobes in which the central vain runs more or less parallel to the line of incision.

In this respect there are no great differences between rat, mouse, guinea pig and rabbit. A schematic vien of a liver cellular trubeculum shows in the first place two rows of liver cells placed side by side, which in their center encircle the gll capillaries. However, according to this view a liver cellular

Trubeculum may be produced by a chance joining of single cells, which following a given direction of incision are enclosed by capillaries on both sides. These liver cells are in contact with other liver cells in a direction perpendicular to that of incision under production of gall capillaries. The so-called liver cellular Trubeculi are not in themselves periplerically restricted to the periportal area, but on the contrary often pass into liver cellular Trubeculi of other lobes, a fact, which arises from the description of the slightly evidenced, often nearly absent demarkation between lobes. Such overlaping is so common among rat and mouse that a lobe demarkation can usually not be given at all; small zones of nonregular cell arrangements, which continue the connection with neighboring Trubeculi and clarify the lobe demarkation, are only caused, as described above, when liver cellular Trubeculi pull in different directions to one another. But a sharp demarkation can not even be found in the rabbit and guinea pig, with the exception of the definite reach of a large periportal fidi. Overlaping liver cellular trubeculi may be seen as soon as the interlobular connective tissue splits into threads. There is no basic difference in the construction of a liver cellular Trubeculium in the guinea pig, rabbit, rat and mouse. As indicated above, the width of the liver cellular Trubeculium is often composed of only one cell and this appears to be the rule in the horizontal section of the lobe near the central vein, while the Trubeculum forks towards the periphery. An inspection of a greater number of preparations might impress one with the fact that the monocellular liver cellular Trubeculium is rarely found in mouse and rat, a discovery which may only be cleared up by reasons of a wider mesh capillary net among these animals. We may conclude from the preceding, that single zone Trubeculi never cross the entire lobe to the lobe periphery, since the Trubeculium is only an optical cross section in the alveolar structure of the parenchyma.

2. Special Section

a) The Liver Capsule

The liver capsule of a number of studied animals consists of a thin, evenly wide layer of strands of connective tissue, in which the presence of elastic strands was not noticed. The fact that the liver capsule or that its capillary endothelia encloses the apparently blind ends of the liver capillaries in the area between two liver cellular trubeculi, appears of interest. The liver circulatory system in certain areas, does not only reach the liver capsule with these capillaries but larger veins, central or interlobular veins are also to be found under the capsule (especially in the rabbit. All these circumstances are most evident by use of Mallory's preparation.

b) Protoplasm of liver cells

As the plasma structures, which we observed in sectional preperations, are artifacts produced with regularity, the untreated cell study may best be compared to the actual relationships about to follow. Cell structure by the usual histological technique - we choose the Hematoxylin-Eosine stain after Formaline fixing - will be discussed below. Constant differences appear among the various types of animals, a fact which may be of importance to the animal researcher under certain circumstances.

Rabbit: The liver cell protoplasm is in general strongly granulated. However, finer protoplasma areas also exist next to the rough, an irregularly shaped porous area may be seen between these. A lumpy cytoplasma also exists where the latter recedes and where the protoplasm seems homogenous under weak magnification.

Guinea pig: The circumstances are similar to these of the rabbit, with

the difference that changes in the plasma structures between lobe center and periphery are not uncommon. The centrally located cells have a rough plasmatic web structure, correspondingly rough protoplasma strata. The cells nearing the periportal area evidence a thick, rough or uniformly fine granulated protoplasm. However, there are exceptions to this rule.

Rat: The protoplasm is almost uniformly finely granulated in single cells, but the rough strata with webb structure predominates as with the rabbit.

Mouse: The circumstances here are so very different from those in other types of animals, that even an isolated cell may be recognized as a mouse liver cell. The protoplasm is usualy strongly segmented, apparently precipitated into variously intensively colored strata; these are generaly connected by a fine network. This nucleus often appears to be freely lying in an empty space. The question of the nature of the strata constituting the plasma will not be taken up here. In connection with the protoplasm glykogene contents, please refer to the corresponding chapter. It should be stated that albumin granula have been evidenced in the liver cell by methylgreen - Ryrsuine stain, on which subject exists a voluminous literature (Berg, Paschleis).

The liver Cell Nucleus: The nuclei are never marginal. In the case of double nuclei both nuclei are slightly below normal size. The most striking difference possibly consists in the fact that the mouse nuclei vary greatly in size within the same area, and that nuclei may be found next to those of normal size, which reach a size 3 times greater than the rest. The following data, of importance in connection with the number of liver cell nuclei has been assembled from literature. Bridge found numerous cells with two nuclei- our personal observations corraborate his findings. Bohm and Davidoff discovered a predominance of binuclear cells in the liver of certain rabbits. Finaly Tubias Cohn discovered from two to four nuclei in liver cells

3 to 9 times over normal taken from rabbits fed on grass and oats. He also observed clear mitosis in these cases. This discovery appears of importance since, as shown by Biscezerro and Vassale, mitoses are extremely rare in the liver cells of grown, healthy animals. Figures which correspond to a direct division are found more generally. Lukjanow believed that he could prove a dependence of the nucleus number on nourishment, as binuclear cells in mice increased in numbers under more intensive fat nourishment. We were able to establish the occurrence of 3-nuclear cells in a rabbit once, and even though not regularly, found binuclear cells in other animal types. The occurrence of plural nuclei during cell reproduction has been described by various authors.

From two to four nuclear bodies may be found among the animals under discussion. They are most easily studied with use of Heidenbain's stain, or by application of Kolmer's modification. They are not necessarily always round, may also evidence a single shaped appearance and are of varying size. The nucleus chromative structure generally appears extremely porous and very finely granulated, this is especially true in the case of Heidenhain S stain. Occasionally it may also consist of rough threads. No differences were found in the chromative structure of various animals. The chromative is equally distributed in the nucleus and does not appear to be greatly accumulated at the edges. Under normal conditions, we were unable to establish any evidence of degeneration in the various animals from the point of view of pyknosis and chexis. According to Schlater the nucleus treated with sublinate or pikrinsublinate - glacial acetic acid shows a mainly homogeneous, alveolar structure.

The Gall Capillaries: The age old dispute on the existance of ~~gisk~~ gall capillaries may be considered finally ~~settled~~ settled, in so far as such nets are the rule among rodents. It is impossible to consider the pertinent literature in this work, but one is referred to Oppel's final compilation on the

subject, mainly dwelling on the dispute between Retzius on the one hand, and Hering and V. Eberth on the other.

(Figure 66, Rabbit Gall Capillaries, Golgi method).

The accuracy of the view-point on the existence of ~~ghxt~~ gall capillaries in the animals we studied is easily proven by preparation, subjected to the Golgi method (see Figure 66). A great number of independent nets may be found in certain areas of both rat and mouse as well as in the guinea pig and rabbit. At times one even gets the impression that there exists a small number of blind end and side branches. This is particularly the case in thicker sections which are microscopically studied at an average section height, or in which the gall capillaries are followed through the section. Even though Von Mollendorff-Stohr, while describing the human liver, feel authorized to state, that the number of nets is in no way as great as would be assumed during study of certain fine sections under weak magnification - the authors in question base this on the fact that the nets are only simulated, by the zig-zagging, small canals with side branches criss-crossing at various levels - this was in no way true for the types of animals we studied. The number of actual nets is certainly extremely high. We would also like to remark, that thick sections give more accurate pictures than thin areas, since the quantity of intact, uncut nets may only be found in a relatively low number in thin sections.

However, there is no doubt that blindending side branches of the gall capillaries exist among all the animals under consideration. The diameter of these side branches is equal to that of the main vessels, a fact which indicates that this is not a question of intracellular secretion capillaries described by various authors. The side branches are of varying lengt and at times reach the size of the liver cell cross section. Their extremeties may terminate in small, button-like broadenings. The side branches of two main capillaries

running parallel to one another in the liver cellular Trubeculum intertwine in that area. Aside from these evident, blind ending capillary side branches which reach into the liver cells, small protrusions may be found in the Golgi-preparation, often appearing as dots along the main and side branches, and only visible under strong magnification, which correspond to the growths described as intracellular secretion capillaries. The nature of these protrusions may not be ascertained with the Golgi preparation as cellular borders can not be perceived, but the fact that these protrusions are thickly grouped around the capillaries allows one to assume with certainty that these protrusions actually represent the so-called cellular structures. The large capillary side branches described above at times evidence a dichrotonucal forking, possibly resulting in a button-like swelling of both ends. It must finally be said that both side and main gall capillary branches may be stretched out or sinuous. The last case might be conditioned by artifacts which will be considered at later date.

Homogenous results were not obtainable in specific preparations, by the Golgi method and conclusive results on the existance of such an intracellular system of vessels could not be reached by the Otani method, of which we will speak below.

In connection with the question of an independent gall capillary wall; and with direct reference to Oppel's theory, we would like to state the fact, that while using the usual research method we saw no membrana propria in any of the animals we studied. We must therefore, most probably deny the existance of the latter. When the liver, as is generally accepted, is reduced to a tubular structure in the last extreme, the gall capillaries constitute the glandular lumia, the liver cells of their walls, and the hypothesis of a membrane propria separating lumen and cell would be illogical *a priori*.

No basic difference exists in the gall capillary morphology of the rabbit, guinea pig, rat and mouse for, as shown above, the system consists of nets ending in large and small blind side branches, in all animals, nevertheless a comparative study of the morphology results in certain differences, which according to our tests, may be given as follows: the main difference between the rabbits and other animals is the fact that the gall capillary nets are comparatively few, a fact which is evident even when considering a thicker section of medium height (see above). The blind ending, large branches cross beyond the nets in all cases. Also interesting is the fact that the larger gall ducts are strongly intertwined in many areas of the preparation - because of which rabbit liver is easily identified in Golgi preparations - and that the small, so-called intracellular gall duct protrusions are much more numerous than in other animals. From a technical stand point we should finally point to the fact that rabbit gall capillaries in contrast with those of the guinea pig are difficult to identify when subjected to the Golgi method and that only small areas of the same section generally react to stain. The stronger intertwining of the gall capillaries may, as shown above, be considered an artifact; however the relatively constant result only in the case of the rabbit in a way points against this opinion. Differentiating morphological data may not be established with certainty for the guinea pig, rat and mouse. The rat liver may possibly have slightly rougher nets and relatively less side branches.

As stated previously, one may also bring gall capillaries into evidence by use of certain Hematoxyline stains. Even though the use of this process helps clearly understand the relation of the gall capillaries to the liver cells - a great advantage over the Golgi method - according to our experiments it has the disadvantage, that it is not uniform, and that it often

fails with certain types of animals. While one usually obtains clear rabbit gall duct pictures by this method, guinea pig, rat and mouse preparations can't be used in the study of the smaller gall ducts; this is partly because the liver cellular protoplasma, or the plastosome of the last named animals stain strongly, keeping the gall duct structures from appearing. Rabbit preparations, as stated, produce clear pictures. The gall capillaries run either cross ways or in length between the liver cells. One clearly sees that dichotomicaly separated gall duct capillaries eventually will terminate on a liver cell, images, which may be caused by the impression of dichotomicaly forked, intracellular capillaries. An exact study of the preparations indicates that this is not the case. This leads to the conviction, that these images correspond to surface sections including the topmost cellular surfaces, that the vessels in question are buried deep in the liver cells and that they represent intervellular gall capillaries. In the first place, this is based on the fact that one cannot perceive any blood capillaries entering the liver cell at a same level, and that the nuclei of the corresponding cells are invariably located higher or lower. The intercullular structures critically discussed above, can not even be found with certainty by the Hematoxyline methods.

The passage of gall capillaries into gall ducts is clearly seen in Golgi preparations (see Figure 67). The passage is generally quite sudden. This passage is rarely seen with staining methods which bring out the liver cells, as also stated by Von Mollendorff among other things. According to this author the cylindrical cells of the gall ducts, alternated into a thin strata of the epithelial cells unite directly onto the liver cellular trubiculi.

Large Gall ducts, Gallbladder and Periportal Area

The situation in the rabbit is the following: as described in the chapter on gall duct capillaries, a number of capillaries join to form small gall ducts. The area of junction is either in the peripheral sections of the lobes or more often in the periportal field. The small gall ducts are coated in a flat, endothelial, one row epithelium, which soon changes into a cubic, and with the gall duct growth in size, into a uniform, which; one row cylindrical epithelium. Beside the normal epithelial cells in the ductus hepaticus of the rabbit, Tobioas Kohn distinguishes large, swollen, light cells, which are not to be found in intraportal sections, and finally Transition forms between these light and the dark cells. The total lack of fat in the epithelium of the rabbits' extraportal gall duct section is striking in comparison to the abundance of fat in carnivorous animals.

According to Renaut, a cross section of a rabbits' ductus choledochus (near the opening) evidences acinous glands in the mucosa under the epithelium, followed by layers of flat threads of muscle in various directions, and finally connective tissue. The glands are serous. Mucous glands mouth at the base of the longitudinal fold. The surface epithelium is cylindrical with a striped articular border. Numerous mucous glands are located at the level of Vater's ampullae, they are differentiated from the Brunner glands by the fact that the latter's glandular basis is coated with granular cells.

The gall bladder mucous cover evidences a clear matted structure, with a limited number of serous glands in the submucosa.

The topographical structure of the guinea pigs' small gall ducts is similar to that of the rat (see below); here too, small ducts may be found in the periportal sections of the lobes, most of the remaining gall ducts are seen in the periportal chambers. Similar circumstances exist in connection

with the gall duct epithelium; the larger the gall duct, the higher will be the epithelium. However, since the epithelium of the small gall ducts is cubic and changes into a high, very uniformly constructed cylindrical epithelium in the larger ones, a margined difference exist from the rat. The nuclei lie at the base of these cells, the fraction set in a lumen direction is filled with a homogenous protoplasma. The cytoplasm appears to have swelled in a cellular cup manner in single cells of the large gall ducts; the protoplasm is roughly vacualated, unregularly granulated secretions (mucous?) may be seen in single Vacuoles stained with hematoxyline. The last cells described are rare. The coating of the large gall ducts may be cut up. According to all appearances, the small interacinous gall ducts in the rat result from the union of gall capillaries and also from very small, epithelium covered gall ducts originating in the lobe. The epithelium of the smaller interlobular gall ducts is not constructed from cubic epithelia as in the rabbit, but mostly from stretched out, endothelial cells. Even the latter's nuclei are drawn out and remind one up to a point, of the Kupffer starcells. This epitheluim only changes to a cubic form, after the union of a large number of such cts into larger ones. The nuclei round off, the cells become higher. The epithelium of the final gall duct, according to Ranvier, evidences cylindrical cells and between these cells broadened near the base with intermediate forms between the two. The membrana propria of the small gall ducts is constructed from a layer of connective tissue, with nuclei lying parallel to the flat, endothelial-type gall duct epithelial-cell nuclei and only differ from the latter because of their more compact structure.

The hepatici are rather large, canals, covered by a single layer cylindrical epithelium, located within the liver capsule in the liver paranchyma. The

periportal connective tissue is exceptionally rich in the immediate vicinity of the canal, the nuclei are exceptionally compact within the connective tissue and, in their morphology, are hardly different from the nuclei of smaller gall duct epithelia. Incisions of the ductus choledochus immediately after its exit from the liver and at a distance from the liver opening, in the area near the main gall duct, show a great number of, perpendicularly cut, smaller ducts the formation of which can not be explained without further research. The perpendicularly cut smaller ducts first appear as protrusions from the choledochus, which may correspond to the Luschka ducts in other animals' gall bladder wall. These cross sections may however, contain small gall ducts which run into the choledochus. In this respect one may put forth the fact that a great number of small gall ducts exist in the section of the ligamentum hepatoduodenale nearest the liver, which are obviously connected to the main duct. More precise study of this question appears necessary.

The mouse gall ducts are so very different as far as the epithelium, from the ones of the other animals studied, that the mouse livermay be identified by this characteristic only. The epithelium not only of the smallest but even of the largest gall ducts in the periportal area is low, endothelar, in the larger gall ducts it reminds one of the endothelial coating of the spleen sinus and only changes into a cubic epithelium in the large intraheptal gall ducts, and only assume a cylindrical character in the extrahepatal gall ducts and in the gall bladder. The nuclei remain quite large in relation to the protoplasm, the wide protoplasm band, which may be found in a lumen direction in the other animals, does not exist. Serous and mucous appendicular glands are not to be found intrahepatically in the mouse. Thorough research is necessary in connection with the appendicular glands of the extrahepatic duct.

We may make the following remarks in connection with gall duct muscle structure. We were able to determine, with certainty, flat muscle structure in the mouse choledochus and in the smaller gall ducts, The rat excretory gall duct, according to Ranver, has no flat muscle threads, the wall is built of longitudinal bundles of connective tissue, mixed with elastic threads, which are arranged along the duct axis in longitudinal net-like meshes. The guinea pig ductus choledochus and cysticus have a considerable layer of muscle (Variot), more thorough research is still necessary with respect to the muscle structure of smaller ducts. Hendrickson did thorough research in the various muscle layers of rabbit excretory ducts as compared with those of dog and man, and arrived at the following conclusion with respect to the rabbit (quoted according to Oppel):

"The ductus cysticus and hepaticus have a cross-, a length- and a diagonal-muscle layer; The ductus choledocus only a cross- and a length-muscle layer. Each ductus preserves its typical structure at the joining point of the ductus cysticus hepaticus and choledochus; the walls of each pass into that of the next. We were able to establish the existance of flat muscular threads in the interhepatic gall ducts of the rabbit both in Gieson- and in Mallory-preparations."

Extensive research by Doyon exists in connection with the muscle structure of the gall bladder wall. It is a question of oral and elliptical meshes, unlike those of other animals, for ex. dog, cat, pigeon which are muscle bundels. grouped together from a limited number of main directions, which strongly cut into one another. According to Hendrickson the rabbit gall bladder has 3 layers of muscular bundels: a cross-, a length, and a diagonal layer. A muscular

sphincter in the duodenal section of the ductus choledochus of the same animal type has been described by the same author, it corresponds to Oddi's sphincter in other animal types; as far as we know, there is no previous literary evidence on the latter's existence in the guinea pig, rat and mouse.

F. Adrenals

by Karl Lowenthal, Berlin

with 2 illustrations

1. Normal Anatomy

a. Morphology

With the adrenals of the laboratory animals, experimental research has been employed and consequently there exist a considerable number of observations on the nature of the healthy organ. However, they are not assembled in a satisfactory amount and were not performed systematically enough so that many contradictions still exist. Only in the last year has one undertaken larger series of studies on the normal anatomy of the adrenals. I will thus review slightly the older literature and for the following description use for the most part, only those works of value for our purpose. Since under certain conditions, which fall in the field of non-abnormal (variation), the organs pass through visible variations, mention should be made also of them. The pathological anatomy of the adrenals is chiefly not worked out. That is actually remarkable since these organs regularly show clear and definite conditions in many injuries to the entire organism just as they do in man. As yet little information exists despite of this.

The position of the adrenals corresponds in general to that in most animals. According to Schauder, in rabbits the right adrenal empties into the space between the cranial part of the kidney and the posterior vena cava; the left one also lays next to the posterior vena cava in the cavity of the cranial pole of the left kidney but a fingers width removed from it. In the mouse the organs lay mediocranial from the upper poles of the kidneys; the left with the abundant subcutaneous fatty tissue is about 1¼ mm, the right is 3/4 mm distant from it. With removal of the fat tissue, they are in contrast only

about 3/4 and 1/2 mm.

The size of the adrenals after distention and the weight and the quantitative relations of the individual components of the organ will best be undertaken according to the species of animal. Rabbits: Schauder: 7 x 4 x 3 mm; R. Krause: length 8-12, width 3-4 mm; Brauer: weight data only after fixation and indeed with different fixing media for both sides, therefore not useable in practice; Bager: size determinations on 101 rabbits from 0-42 months in age. Owing to the care with which these investigations were conducted I present the resul'ts in the following table which to be sure has been much simplified by me. I intentionally emphasize that here only the mean values of each individual age group are given whereas the amount of variation in as greatly correlated to equal aged as to equal weight animals.

See Table

I must later return to the table several times, thus in the case of the discussion of the quantitative relations of the individual organ parts. In any case it follows from the fingures of Bager including those not given here that first of all the weight of the adrenals is not directly proportioned either to the body weight or to the age of life, secondly it follows that the left adrenal is almost always larger than the right as is also the case in man and is easily explained from the spatial relations in the upper part of the abdomen. Thirdly it follows that the adrenals from puberty on are significantly larger in females than in males. These facts find their analogous in the other species of animals (Castaldi, Deanesly, Donaldson, Gweysse, Hatai, Hett, Kojima, Masue and others) and thus indicate that study and control animals should cover both sexes uniformly and that we must be aware of the establishment of a compensatory hypertrophy following the removal of one adrenal. Guinea pigs: Gwysse:

length 8-10½ mm in males, 10½-14 mm in females, in which connection gravid animals (see later) were also measured. Verdozzi: using females of 400-600 gr. they were about 1:1000 - 1:1350 of body weight. Sessesen and Carlson: 72 animals. Formula for calculating the expected weight y the adrenals of from the body weight X is namely: $y = ax - b - cx^2$, if, AL 400 g and $y = cx^2 - b - ax$ if x 400 g. The constants are in the first case (values for second in parentheses) a = 0.00083 (0.00069) b = 0.035 (0.214) c = 0.00000084 (0.0000014). Also here one finds a very large scattering of individual values, and mean weight of both adrenals together amount 40 mg with a body weight of 100 g, 90 mg with 200 g, 140 mg with 300 g, 165 mg with 400 g, 220 mg with 500 g, 305 mg with 600 g, 415 mg with 700 g, 555 mg with 800 g. Materna and Januschke: 13 animals, weight 380-800 g, mean 568 g, both adrenals 126 - 632 mg, mean 527 mg, predominantly males. Left adrenal 60-190, right 50-170, mean 107 and 89 mg respectively. Left distended 10.0 x 4.6 x 3.6 and right 9.6 x 5.6 x 2.7 mm with still greater range of variation. Castaldi: I cite the numbers for both sexes jointly: age 1 month- 40 to 80 cc in volume and 120 - 170 mg weight for both adrenals; Age 3 months - 100 - 20 cc and 230-360 mg; age 4-6 months 160 - 300 cc and 300 - 670 mg. Rat: Hatai: Body weight 5 g, weight of both adrenals in males (females) 1.6 (1.6) mg; 10 g and 4.4 (4.4) mg; 15 g and 6.4 (6.4) mg; 20 g and 8.1 (8.1) mg; 30 g and 10.7 (10.7) mg; 40 g and 12.9 (13.4) mg; 50 g and 14.7 (16.1) mg; 70 g and 18.0 (21.3) mg; 100 g and 22.2 (28.8) mg; 200 g and 34.2 (52.9) mg; 300 g and 44.6 (76.6) mg. Cameron and Carmichael: 4 young animals: weight 67 - 160 g. both adrenals 14-26 mg. Cameron and Sedzran: 4 older males - weight 255 - 289 g, 23 - 28 mg; 1 older female, 244 g and 53 mg. Donaldson in his great monograph on the rat utilizes the figures from Hatai; he emphasizes that the sexual differences in adrenal weight first appears at the age of 50 days. He also

mentions important racial differences; the adrenals of Mus norvegicus are about 2½ times as large as those of Mus norvegicus albinus. Mouse: weight determinations of the entire organ are not listed anywhere and this is understandable due to the minuteness of the adrenals. Only Leffkowitz and Rosenberg give the size as 1½ x 1¼ x 1 mm.

In an organ which is made up of two so basically different tissues, the mesodermal cortex and the ectodermal medulla and the former made up of very unequal sections, many researches have directed their aim to the relation of each individual part to each other. Naturally the findings of the various investigations are very difficult to compare with each other, since the methods are often incomplete and differ greatly from each other. We must again treat each species separately.

Rabbits: Only Bager presents precise figures (see table on p. 364). It shows that the cortex preponderates; whereas the medulla in the new born rabbit makes up about 1/5 of the weight of the organ, it drops until the time of puberty to about 1/30 of the organ weight. Guinea pigs: Castaldi; the cortex predominates; it decreases in a relation comparable to that shown by Bager for rabbits. I give therefore only the mean values for both sexes and all age stages jointly and also simplify these somewhat. Both adrenals 129.8 ± 8.83 cc; Cortex by itself 117.1 ± 7.09 cc, medulla by itself 13.1 ± 1.08 cm, $\frac{\text{cortex}}{\text{medulla}}$ = 8.9. Rat: Donaldson; up to 100 g body weight. the portion of medulla to the organ mass, remains in a generally constant relation. Corresponding to his standard figures put down in the monograph the amount of medulla averages 6.2% in males of Mus norvegicus and 8.3% in females; in Mus norvegicus albinus 4.7% in males and 5.9% of the total adrenal mass. Mouse: Miller; mean values are obtained only a few animals and with only slight age differences. Young female adrenals 1.8 cc, cortex 1.76 cc, 1.62 cc and 0.22 cc respectively.

Tamura: 10 normal females adrenals 1.42, cortex 1.20 , medulla 0.22 cc. Hett: Cortex in males 75-85, mean 82 in females 78-92, mean 8.7% of the total organ. Further data are found on the relations of the cortex sections to each other in the works of a number of authors; of these we will only mention here the following: Bater, Jajima, Kolmer, Tamura, and others.

C. The Periportal Infiltrates

In the liver and in the proximity of the periportal area of all research animals we studied, were found great conglomerations of cells which at times corresponded to lymph cells, and at times to large mononuclear elements, knowledge of which would be of great value to experimental pathologists. Until an extensive study of this question has been completed, we can hardly state with certainty for every case, whether the cell center may be expected as a normal occurrence. Thus in the case of the rabbit, for example, the question as to whether the infiltrate does not reflect a Pericholangitis described under Coccidiosis (see the latter) must remain open. We believe however, that we may describe the following discoveries as normal occurrences.

Cell centers are found in relatively great or small quantities in the rat liver, which under weak magnification give the impression of being conglomerations of circular cells. The greatest quantity of these cells are situated in the proximity of the large periportal areas or in that area which corresponds to the border of two overlaping liver lobes. These cellular groupings appear to be arranged mainly in a perivascular manner. In cases of scarce groups which lack an individual vessel it seems to be a question of cellular groups met on a diagonal. These structures resembling lymph-follicles, vary grately in size and extent; they may be nonexistent. These structures were described by Paschkis, Landa etc, and variously described. These cellular buildups, if objectively considered may be described as follows: it is mainly a question of relatively plasma poor cells, with large, dark colored nuclei. The nuclei are usually poligonous, and often longish and swollen, smaller structures may be detected in the protoplasm when subjected to a Hamatoxylin - Eosin preparation. Occassionally cells may be found in the peripheral areas of the group which have eosinophil nuclei (or rather pseudoeosinophile leukocytes in the rabbit)

or which are ungranulated and have one nucleus of the leukocyte type. Single elements with elongated nuclei, which according to all evidence are connected with the structure supporting the cellular complex and which have a lighter and more finely granulated chromatin structure may be seen near these cells. Cells of the neutrophile type which polymorphous nucle may be found in certain groups, and especially in their centers.

Analogous, very small groups may even be seen quite separately in the area of the lobe, near the vena centralis. The condition of cellular groups, as just described may be considered a usual occurrence in the guinea pig. The infiltrates are usually located in the periportal area, more rarely in very small dilations within the lobe. The group are either arranged arround a gall duct or along an interlobar vain or arround both. It appears of interest that the groups correspond to circumscribed structures and do not envelope long stretches of gall ducts and vessels, as indicated by viens along studies interlobular veins, which at least under weak magnification, clearly indicates the area of the cellular groups in questions. However one may notice, under stronger magnification, that the cellular groups is not sharply limited but that on the contrary the large interlobular veins have a very frequent adventitia, so that one even has the impression that foreign elements, not part of the adventitia are inserted into the vein walls. This cellular abundance of the tissue surrounding the veins and of actual vein walls appears to be the primary reason for the relatively evident appearance of the interlobular areas in the guinea pig (see above). With respect to the constitution of the cell groups, many varying circumstances exist within the same liver. Usually, as with the rat, it is a question of relatively large cells with large, unregularly shaped, but united nucleus. In other cases, single or numerous or even exclusive cells are to be found with puffed, or split or even karyohectic nuclei, so that as to give the impression of an

acute infectious leukocyte infiltration. Finally, single or more numerous cells with eosinophile nuclei, may be found mainly in the periphery of the groups. Abnormally large cells with basic protoplasma are rare; they may also indicate mytosis. The above described groups with strongly split, karichectic nuclei are very frequent when they are not located in the periportal field, but in the center of the lobe.

Similar infiltrate groups are also found in the mouse. There occurrance is however not as common. Many livers are found with no trace of cell infiltrates in the periportal area. The infiltrate arrangement is perivascular here too. However, they are also to be found in the neighborhood of the liver parenchyma. The fact that the rim of the infiltrates is usually not clearly defined is striking. As for as their constitution, they are at times composed of larger cells with bubble like nuclei, or sill of tightly squeezed small elements.

Infiltrates of the type described are rarely found in rabbit livers devised of coccidii. Epstein describes a small periadrentitial group in the liver of normal animals, which is partly composed of round cells and partly out of "interfilcilar histiocytes".

Despite our desire to describe as normal the data given above on rabbit, guinea pig, rat and mouse, one would like to caution that with respect to the liver, animal conducts, feeding etc. may be of influence on its structure, that the definite pathological character of one small group can never be determined with certainty, and that therefore, findings, as that of Epstein for instance, only permit one to draw a conclusion within the frame of certain experiments when a correspondingly large number of unspoiled normal animals have been simultaneously studied for control purposes.

H. Kupffer cells

The Kupffer cells produce the liver capillary endothelium. Whether or not this simple layer of endothelium rests on a base membrane is still a disputed question. It is certain that such a membrane can not be located by the present histological methods. The cell protoplasm can not be seen in the cellular surface, the study of Kupffer cells in normal animals, therefore rests nearly entirely on cellular nuclei. The cells may be considerably swollen under pathological conditions, usually citoplasma, swelling caused by phagocytoses. The nuclei of the Kupffer cells in normal animals are generally easily distinguished from the liver cell nuclei even under weak enlargment; they are primarily smaller, have a thicker chromatic structure, therefore are more intensively collored with nucleus stains and finally, usually have a different aspect. They are usually rod shaped. The rod axis usually lies along the liver capillary axis, or perpendicular to the central vein. Nuclei cut in lengths or accross are found depending on the line of cuts. Even though no great differences exist between the Kupffer cells of rabbit, guinea pigs, rat, and mouse the following small differences must be recorded. The greatest difference among the mentioned animals is the relatively high number of Kupffer cells in the guinea pig, a fact which allows the recognition of a preparation as guinea pig section. A previous article, has pointed out that the Kupffer star cells in the guinea pig are thicker in the periphery of the liver lobes whereby a less difficult division of the liver lobes is made possible in that area, while the absence of the periportal connective tissue would not permit such a separation. The guinea pig Kupffer cells possibly seem more obvious, because their cellular

structure is extremely thick. It should be possibly also be stated that one reaches the conclusion, after study of a large number of preparations, that the rabbit Kupffer cell nuclei are less ellongated-oval than those of the other animals. It should finally be stated that no type of phagocytosis was seen in the normal animal Kupffer cells. We never noticed erythrophagocytosis. See the respective sections in connection with Fatt, Glykogen and iron content of the Kupffer cells, or of their nuclei.

I. The liver and Gall bladder nerves.

Both the symaticus - and the Vagus strands reach from the sympathetic nerve into the organ, causing a change in the Ganglion coeliacum. Before we investigate this further, we must enphasize, that the pictures discovered only produce chance agreements, the same holds true for the spleen. Unfortunately the parenchymatous organs are the ones which for the most don't allow a certain vien into their nervous structure by a histological method. This is also indicated by a mass of histologico-technical data, none of which has been proven fully reliable.

We were able to establish nerve bundles in the periportal fields of the animals discussed, by use of the method of Agduhr and DeCastro. These nerve bundles divide and build finer nets (Retzius, Kolliker). Stohr was able to establish such a nerve net in the rabbit by use of the Golgi method. According to Stohr ganglion cells are rarely found in the periportal connective tissue (Schmincke).

Groupings of multi-, bisar unipolar ganglion cells may be found in the gallbladder wall. The ganglions are connected to one another by threads among which neurites and deudrites can not be differentiated. A thick mesh of impregnable threads results. The gall bladder nerves follow the vessels and then, having reached the adventitia, provides the various sections of the bladder wall (Stohr).