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HEPATIC CIRCULATION AND ASSOCIATED VEINS IN A SIX MILLIMETER PIG EMBRYO

Department of Anatomy

by

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TABLE OF CONTENTS

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INTRODUCTION

The purpose of this paper is to give a description of the hepatic circulation and associated blood vessels of a 6 mm. pig embryo. The early work of His and Hochstetter upon the development of the larger veins and ductus venosus opened the way for later investigation in this field. Minot and Lewis devoted their attention to the study of the minute structure of the hepatic and other sinusoids. Thyng has described a pig embryo of 7.8 mm; Piper, Ingalls, Mall and Jordan have each described human embryos of lengths varying from 4 mm. to 7 mm, while Schulte, and Huntington and McClure have outlined the development of the venous circulation of the cat.

METHODS AND MATERIALS

A pig embryo of approximately 6 mm. length, first used by Allen as a basis for a pedagogical paper, was sectioned serially in the sagittal plane. The sections are ten micra thick and stained with carmine. From these sections several models have been constructed of blotting paper, somewhat after the method of Gage and

Schaeffer. Some difficulty was experienced in accurately lining up the sections, especially in model B. Attention will be directed to these inaccuracies as occassion requires. "A" is a model of the hepatic tissue, a portion of the digestive tract and a part of the heart and surrounding tissue. It shows few inaccuracies and is made up of blocks of from twenty to forty sections. Model B represents the blood vessels cast solid. In this model the portal vein, with its vitelline and mesenteric branches, the remains of the left omphalomesenteric vein, the heart and theocardinal systems were removed before photographing figures 1 to 5. The portal vein and its main tributaries are shown in figure 6. Reference was made to serial sections of other pig embryos of from 3.5 mm. to 10 mm. to determine the constancy of structures found in the models.

THE HEPATIC SINUSOIDS

Grossly the liver presents a picture similar to that of the adult thyroid gland. It consists of two main lobes, connected by an isthmus which extends from side to side, ventral to the alimentary tract. The right lobe is much the larger and more distinctly divided into dorsal and ventral portions.

Minot, Lewis and others interpreted the blood spaces within the liver as being formed by the invasion of the hepatic epithelial cords into the omphalomesenteric veins, pushing before them the endothelium of the vessels in the formation of many anastamosing channels. Minot gave the term sinusoids to these channels. According to Ingalls, the left, then the right umbilical vein is tapped by the sinusoids. Following this most of the blood from the umbilical veins passes through the liver. By the fusion of several sinusoids, the ductus venosus is formed. This is a short circuit from the left umbilical vein to the right horn of the sinus venosus. To some extent the contentions of Minot and Lewis have been opposed by Mollier, Schulte and Bremer who have described capillary plexuses in the septum transversum as (ultimately) becoming incorporated in the hepatic circulation. This is interpreted to mean that at least a part of the intra-hepatic sinusoids come from preformed capillaries. There are a few such blood spaces in the septum transversum of this and of other embryos studied by the writer. These (fig.11) communicate with the blood spaces within the liver.

The sinusoids vary in size from mere capillary spaces of 10 micra diameter to large spaces such as the right superior posterior sinusoid which has a vertical diameter of 350 micra. The capillary sinusoids are fairly uniform in size, averageing about 15 micra. The sinusoids may be grouped as follows:

Left dorsal group.- Thegross contour of this group is not accurately portrayed in model B (fig.3) because of the model running to a point dorsally; whereas the dorsal surface should be more nearly flat. Most prominent in the left dorsal group is the large curved sinusoid (fig.10, LD) about 100 micra in diameter, leading from the left umbilical vein to the left horn of the sinus venosus. In its course it supplies smaller sinusoids to the left dorsal lobe and the left ventral lobe, especially the lateral portion.

Left ventral group.- The circulation of the left ventral lobe is composed of freely anastamosing capillary sinusoids (fig.5, LV). There is no large sinusoid corresponding to that of the dorsal lobe; hence the proportion of hepatic parenchyma to blood space in the lower lobe is greater than in the dorsal. Laterally, the plexus in the left ventral lobe sends twigs to the cephalic portion of the original left umbilical vein (fig.5,OLV). It also communicates freely with the left dorsal group of sinusoids. The chief supply to this plexus is from the dorsal division of the left umbilical vein(fig.8, DLU). The ventral division, through its dorsal branch (fig.8, DB), contributes sinusoids to the most ventral part of the left ventral group. Most of the efferent vessels empty into the sinus venosus direct.

Medio-ventral group.- Medially there is a small group of sinusoids (figs.4 and 9, MVS) ventral to the gall bladder, and extending cephalic to it. These sinusoids receive blood from the umbilical anastamotic branch (figs. 2 and 6, UAB) and from a small ventral twig of the right umbilical vein (fig.4, BMV). To the left, the medio-ventral group drains into the caudal part of the right posterior superior sinusoid (fig.9, RSP) and into the right ventral group. A direct channel (fig.3, Diag Ch)extends from the right umbilical vein through the medio-ventral plexus to the left of the umbilical vein. (This will be more fully described later.)

Right dorsal group.- Schulte describes the development of this group in the cat: "The ventrolateral sprouts of the liver invade the septum transversum which increases rapidly in size and continues to be actively angiogenetic. An invasion of the omphalomesenteric and umbilical veins is not present until the stage of 4.0 to 4.5 mm. At this period on the right side a mass of liver sprouts fills the angle of confluence of these vessels and a long falciform process of the liver grows out upon the dorsum of their fused segment. Hereupon follow rapidly the resolution of this segment into sinusoids and a reduction in the size of the distal segment of both veins." The structure of the 6 mm. pig embryo fully substantiates the above description.

The right dorsal lobe (figs. 1, 3, and 9) contains by far the largest group of vessels and encloses the largest individual sinusoids (fig.9, SR and RSP). Its blood supply is from the right umbilical and the portal veins (fig.1, RU and PV). This lobe is little more than a shell of hepatic cells, surrounding one large sinus, hereafter designated as the right dorsal sinus. A constriction (fig.9, 6) separates the right dorsal sinus into two parts, sinus reuniens (fig.9, SR) (vena hepatica revehens of Hochstetter; sinus S of Allen) and a large sinusoid (fig.9, RSP) already referred to as the right superior posterior sinusoid. The latter begins with the expansion of the portal vein, turns to the right, and receives the right umbilical vein ventrally, then curving cephalad and ventrad as the sinus reuniens. Most of the sinus reuniens is extra-hepatic, as can be seen by the absence of small communicating sinusoids medially and cephalically (fig.9). The right dorsal sinus might be looked upon as the part of the right omphalomesenteric vein which has not broken up into smaller sinusoids. The caudal two-thirds is surrounded by many capillary spaces which radiate from it and freely anastamose in the formation of a plexiform network.

In the model, the right ventral group of sinusoids (fig.4, RVS) rests upon the lateral surface of the right umbilical vein. Tt is composed entirely of capillary sinusoids. The body cavity separates it from the right dorsal group (fig.9).

RELATION OF LARGER VESSELS TO SINUSOIDS

1. Left umbilical vein.- Upon leaving the body wall to enter the septum transversum, this vein (fig.5, LU) has a diameter of 250 to 300 micra. It becomes reduced abruptly in caliber upon entering the septum and turns sharply to the right to anastamose with the right umbilical vein (fig.1, U Anast). In the 7.8 mm. pig embryo described by Thyng, the anastamosis between the right and left umbilical veins is in the cord. A small vessel (figs. 2 and 4, UAB) arising from the channel between the two umbilical veins communicates with a group of sinusoids ventro-cephalad of the gall bladder and ends (fig.7, a) in the ductus venosus.

A slender band of mesenchyme, covered with endothelium, extends dorso-mediad and slightly cephalad across the vein near its entrance into the septum transversum. This band does not appear in the figures. There is no corresponding band in the right vein, nor in either umbilical vein of other embryos studied.

Assuming a course dorso-cephalad, the dorsal division of the umbilical vein (fig.8, DLU) is joined by the diagonal channel (fig.7, Diag Ch) from the medio-ventral group of sinusoids under the gall bladder (fig.3, Diag Ch). The main branch of the dorsal division then curves dorsally and to the left. It is at first a large sinusoid, but soon breaks up into smaller ones which communicate with a small group of capillary sinusoids near the median plane immediately caudad of the sinus venosus. It is also the chief supply of a large group of sinusoids in the upper left lobe of the liver. A few of the more dorsally and caudally situated sinusoids of the left ventral group (fig.8, LV) flow into this main sinusoid. It is apparent from models A and B (figs. 5, 8 and 10, LDS), that the smaller sinusoids of the dorsal lobe, continuing farther to the left, join a large sinusoid which empties into the left horn of the sinus venosus. A ventral branch of the dorsal division (fig.10, VBD), closely associated with a group of sinusoids described above as lying immediately caudal to the sinus venosus, follow a similar course, but empties into the sinus venosus in conjunction with the median communicating branch of the ductus venosus.

The ventral division of the left umbilical vein, like the dorsal, breaks up rapidly into smaller sinusoids. This takes place through two main branches. A dorsal branch (fig.8, DB) is the chief supply to the left ventral lobe, but retains its identity and joins the sinus venosus immediately to the left of the dorsal sinusoids described. Its communication with the sinus venosus near the median plane will be described later. Three converging large sinusoids (fig.10, VBD; fig.8, DB; fig. 8, MC) terminate in the sinus venosus near the median plane, all taking origin from the left umbilical vein. The major portion of the ventral division turns to the right at an angle of 20 degrees, and dorsally at an angle of 45 degrees, making a sinusoid of 90 micra diameter. This is the ductus venosus of Aranzius (figs. 2 and 7, DV). It communicates with the sinus venosus to the right of the median plane (figs. 7 and 8, Mc) as mentioned above, then terminates in the sinus reuniens (figs. 2, 6 and 7, DV and SR). In its course, the ductus venosus receives blood from the medio-ventral group of sinusoids and from sinusoidal branches (figs. 6 and 7, 3) of the portal vein. Ingalls mentions a channel from the cephalic end of the left omphalomesenteric vein to the ductus venosus, but none was found in this embryo.

Vestiges of the original left umbilical vein (fig.5, OLU) appear as disconnected spaces of minute size in the body wall lateral to the left ventral lobe and as blind diverticulae from the umbilical vein and left horn of the sinus venosus. The left ventral lobe and the body wall send a few twigs (fig.5, 1) into its cephalic end.

2. The right umbilical vein (figs. 1 and 2, RU) is smaller than the left, and withingthe septum transversum diminishes in size more abruptly. The model indicates that much of the blood from the right umbilical flows into the left umbilical vein through the anastamosis (figs. 1 and 2, U Anast) between the two. After anastamosing with the left umbilical vein, the right

umbilical gives off a slender branch (figs. 2 and 4, BMV) to the lower right corner of the medio-ventral sinusoids. This branch is also the beginning of a small, irregular diagonal channel (fig.3, Diag Ch) or group of anastamosing sinusoids, which pass medio-cephalad to join the dorsal division of the left umbilical vein. Upon reaching the liver, the right umbilical vein increases in size, supplies a branch of considerable size (fig.4, BRV) to the right ventral lobe and finally bends sharply dorsad to join the portal vein. Several small sinusoids take origin from the right umbilical vein near its junction with the portal (fig.9, RU and PV) and form a capillary sinusoidal plexus. These reunite in a sinusoid (fig.9, CS) which empties into the sinus reuniens. One of these (fig.9, 7), however, is larger than the others, and retains its identity as it progresses cephalad giving off capillary sinusoids to the adjacent hepatic tissue.

The original right umbilical vein (fig.2, ORU) persists as a small vessel in the body wall, lateral and dorsal to the right lower lobe of the liver. Near its cephalic end it turns sharply medio-ventrad to join the sinus venosus at the base of the right common cardinal vein.

3. Portal system.-In general the portal system of this embryo presents a stage of development which is between that found in Thyng's 7.8 mm. pig embryo and

Piper's 6.8 mm human embryo. There are, however, certain marked differences, as will be noted below. The paired vitelline veins unite in the umbilical stalk ventral and to the right of the intestine. At the caudal extremity of the dorsal pancreas, the common vitelline vein expands into a large blood channel (fig.6, OMV) which corresponds in this stage to the early dorsal plexus between the caudal and cephalic omphalomesenteric rings. This channel collects blood from the superior mesenteric vein (fig.6, SM) and anastamotic branches from the right and left subcardinal veins (fig.6, ARS and ALS). The paper by Allen mentions the anastamosis between the subcardinals and the portal system. This anastamosis is not an anomaly, for it is present in pig embryos of 6 mm, 7 mm, and 8 mm. It is clear that the right limb of the caudal omphalomesenteric ring has disappeared, while the left limb of the cephalic ring persists as a mere plexus of veins (fig.6, Plex P) to the left of the dorsal pancreas.

Beginning at the anastamosis of the right subcardinal vein with the omphalomesenteric vein (fig.6), the portal vein continues cephalad as a vessel of 90 to 100 micra diameter. At the median dorso-caudal corner of the right lobe of the liver, the portal vein turns sharply to the right to join the right umbilical in forming the right superior posterior sinusoid (fig.9, RSP). No mention of this sinusoid is found in the literature, although the writer found it in embryos of 6 mm, 6.5 mm, and 7 mm. In the 6.8 mm. human embryo described by Piper, the portal vein joins the ductus venosus at its junction with the left umbilical vein. Small sinusoids (figs. 6 and 7, 3) cephalic to the gall bladder afford a direct communication between the portal vein and the ductus venosus. From these sinusoids, others (figs. 3 and 4, 4) extend across to the left lobe ventral to the stomach. The latter sinusoids, together with the cranial portion of the ductus venosus, are probably to be regarded as the remnants of the cranial ring of the omphalomesenteric vein described by Hochstetter, Ingalls and others. Figures 1 and 5, VB? show the veins of Broman to be intimately associated with these sinusoids.

Mall, reporting a twenty six day old embryo, writes: "It is the left omphalomesenteric vein which remains in the specimen. The vein passes around the dorsal side of the alimentary canal, and about the middle of the liver unites with the umbilical vein."

The later development of the portal system is discussed by Johnson as follows: "The growth of the portal veins takes place by an increase in the length and by the formation of new branches which spread themselves between the lobules."

4. Sinus venosus.- This structure (fig.2, SV) traverses the embryo between the heart and the liver. Its large right horn (figs. 1, 2 and 4, RH) receives

(a) dorsally, the right common cardinal vein (RCC), (b) caudally, the common hepatic vein formed by the confluence of the sinus reuniens with the ductus venosus, (c) to the right the remnant of the original right umbilical vein (figs. 2 and 4, ORU) and (d) to the left (fig.2) the transverse trunk of the sinus venosus. The left common cardinal (fig.5, LCC) and the anterior remnant of the original left umbilical vein (OLU) join as they enter the smaller left horn of the sinus venosus. The large sinusoid (fig. 10, LDS) in the left upper lobe of the liver empties into the sinus venosus mediad of the junction of the left common cardinal with the left umbilical vein. Near the median plane, the sinus venosus acquires a communication from the ductus venosus. The termination of the ventral branch of the dorsal division (fig. 10, VBD) of the left umbilical vein immediately to the left of the communication of the ductus venosus with the sinus venosus has been described.

Figure 2 reveals the sino-auricular opening (SAO) as a small channel in the ventral portion of the right horn.

5. Since certain other veins, not so imtimately associated with the liver appear in the models, a brief description of them may be of interest. The <u>inferior vena cava</u> has not been completely formed at this stage. It is a minute vessel which can be traced cephalad in the mesentery from the right subcardinal

vein almost to the region of the veins of Broman. Subnephric veins (fig.9, SN) arise from the ventral wall of each posterior cardinal vein, immediately cephalic to the mesonephros. Each subnephric vein extends caudally, ventral to the Wolffian body, from which arise its tributaries. The relations of the veins are best shown in figures 12 and 13, since they do not appear in the photographs of model B.

SUMMARY

As a result of a study of models of the liver region of a 6 mm. pig embryo, the following points were noted:

1. The sinusoids within the liver are divisible into five groups: left dorsal, left ventral, right dorsal, right ventral and medio-ventral.

2. The left umbilical vein anastamoses with the right upon entering the septum transversum.

3. Within the liver the left umbilical vein breaks up into a dorsal and a ventral division; the dorsal supplies the left upper lobe, retaining its identity as a large sinusoid. The ventral division supplies the left ventral lobe and form the ductus venosus.

4. The extra-hepatic course of the original left umbilical vein has almost disappeared; there is how-

ever a complete channel to the right of the liver marking the path of the original right umbilical vein.

5. The right umbilical vein enters the liver and joins the portal vein to form a large sinusoid occupying most of the right dorsal lobe of the liver. This large sinusoid joins the ductus venosus to form the right horn of the sinus venosus.

6. In this embryo the portal system is well developed. It receives communicating branches from both the subcardinal veins.

7. It is the right horn of the sinus venosus which receives most of the blood from the vitelline, mesenteric and umbilical veins.

8. The vena cava has not yet tapped the hepatic sinusoids.

9. Certain veins, designated as the subnephric veins, have been described.

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EXPLANATION OF FIGURES

Abbreviations

ALS Portal branch anastamosing with left subcardinal,

ARS Portal branch anastamosing with right subcardinal.

At Atrium

ACC Anterior wall of left common cardinal vein.

BC Body cavity

BMV Right umbilical branch to medio-ventral sinusoids.

BRV Umbilical branch to right ventral sinusoids.

CS Capillary sinusoids from right umbilical.

DA Dorsal aorta.

DB Dorsal branch of ventral division of left umbilical vein.

Diag Ch Diagonal channel from small ventral branch of right umbilical to dorsal division of left umbilical.)

DLU — Dorsal division of left umbilical vein.

DV — Ductus venosus.

EEC — Extra-embryonic cavity

EIC — communication between extra- and intra-embryonic cavity.

GB — Gall bladder.

HD — Hepatic duct.

LB — Lung bud.

LCC — Left common cardiral vein.

LCCO — Left common cardinal opens to left of and above point of arrow (fig. 10).

LD — Left dorsal group of sinusoids.

LDS — Large sinusoid in left dorsal lobe.

LH — Left horn of sinus venosus.

LS — Left subcardinal vein.

LU — Left umbilical vein.

LV — Left ventral group of sinusoids.

LVV — Left vitelline vein.

MC — Median communication between ductus venosus and sinus venosus.

mes — Mesentery

MN — mesonephros

MPV — Mesentery supporting portal vein.

MVS — Medio-ventral group of sinusoids.

OGB	Opening of gall bladder.
OLU	Original left umbilical vein.
OMV	Omphalomesenteric vein.
ORU	Original right umbilical vein.
PC	Pericardial cavity.
Per C	Peritoneal cavity.
Plex. P	Plexus to right of dorsal pancreas.
PPC	Pleuro-peritoneal cavity.
PR	Parietal recess.
PSL	Line marking posterior surface of liver.
PV	Portal vein.
RCC	Right common cardinal vein.
RDS	Right dorsal group of sinusoids.
RH	Right horn of sinus venosus.
RPC	Right postcardinal vein.
RSP	Right superior posterior sinusoid.
RU	Right umbilical vein.
RVS	Right ventral group of sinusoids.
RVV	Right vitelline vein.
SAO	Sino-auricular opening.
SM	Superior mesenteric vein.
SN	Subnephric vein (communicates here with posterior cardinal vein.)
SR	Sinus reuniens.
ST	Septum transversum.
Stom	Stomach

SV Sinus venosus.

U Anast Umbilical anastemosis.

UAB Umbilical anastamotic branch to medio-ventral group of sinusoids.

US Umbilical stalk.

VBD Ventral branch of dorsal division of left umbilical vein.

Vent Ventricle.

VLU Ventral division of left umbilical vein.

1 Communication between left ventral sinusoids and original left umbilical vein.

2 Junction of ductus venosus and sinus reuniens.

3. Communication between portal system and ductus venosus.

4. Part of cranial ring of plexuses.

5 Opening of branch from umbilical anastamosis.

6 Hepatic tissue causing constriction between sinus reuniens and right superior posterior sinusoid.

7 Small sinusoid

EXPLANATION OF FIGURES

Figure 1. Model B. Dorsal view.

Figure 2. Model B. Ventral view.

Figure 3. Model B. Caudal view. Umbilical veins and portal vein our of focus.

Figure 4. Model B. Right lateral view. Left half removed.

Figure 5. Model B. Left lateral view. Right half removed.

Figure 6. Model B. Medial view of right half. Portal system in place.

Figure 7. Model A. Looking from the right. Cut through the plane of the ductus venosus.

Figure 8. Model A. Cut through the same plane as Figure 7. Looking from the right.

Figure 9. Model A. Cut through the plane immediately to the right of the portal vein. Looking from the left.

Figure 10. Model A. Cut through the plane to the right of the opening of the left common cardinal vein into the sinus venosus. Looking from the right.

Figure 11. Camera lucida drawing of a capillary space in the septum transversum.

Figure 12. Reconstruction. Showing relations of the right subnephric vein.

Figure 13. Reconstruction. Showing relations of the left subnephric vein.

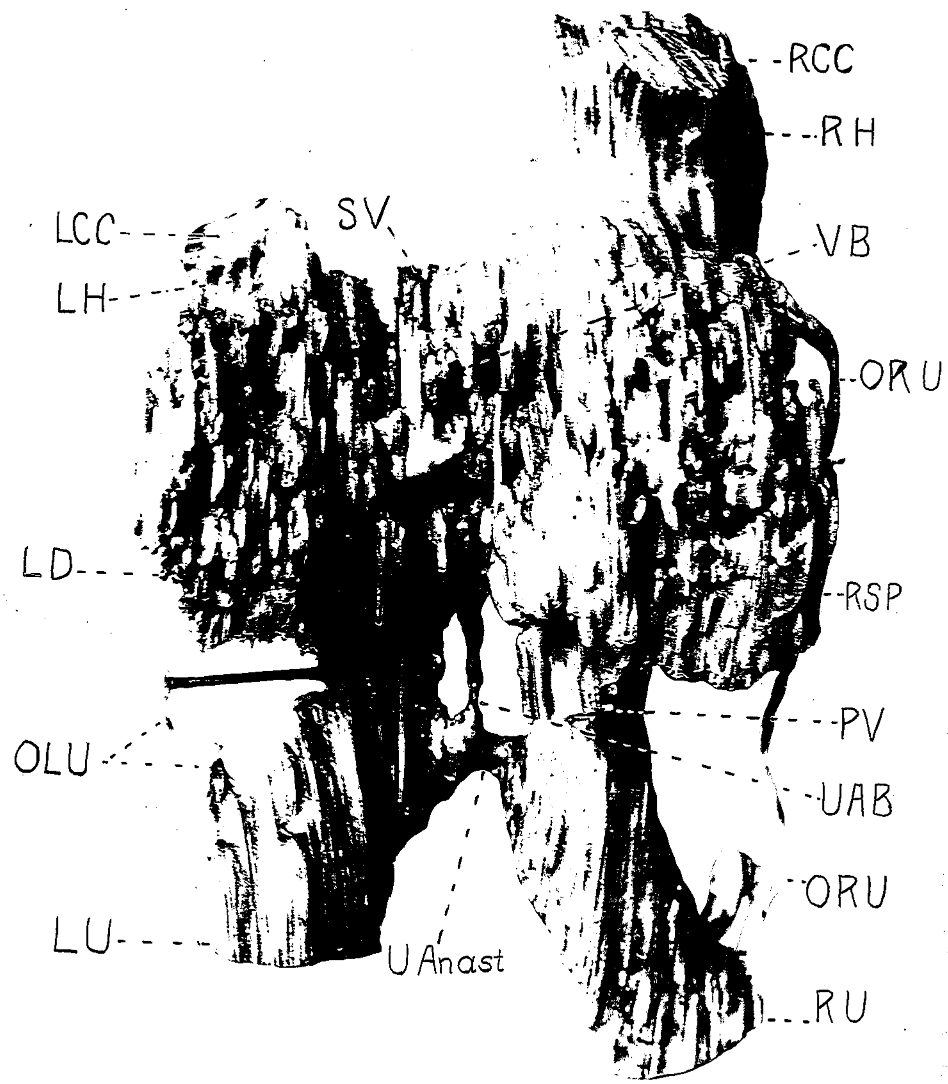

Fig. 1

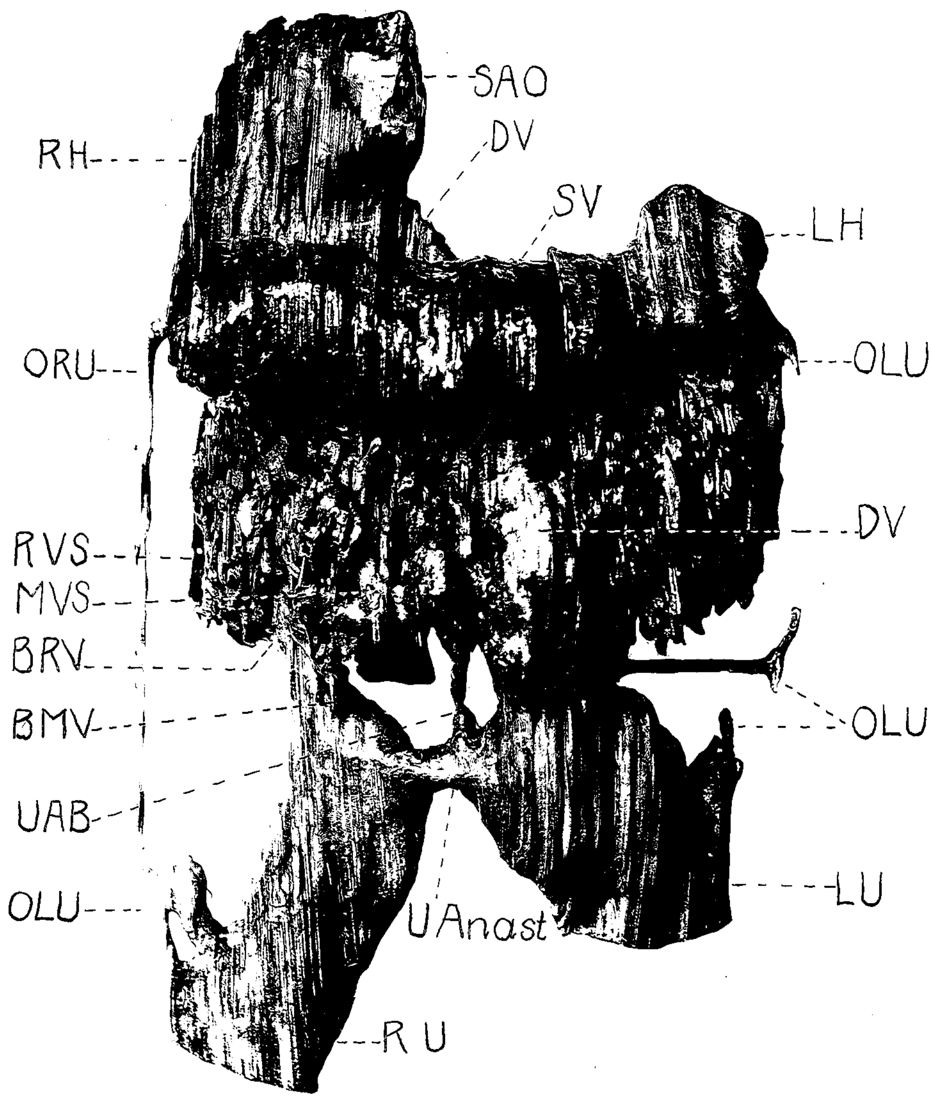
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Fig. 2

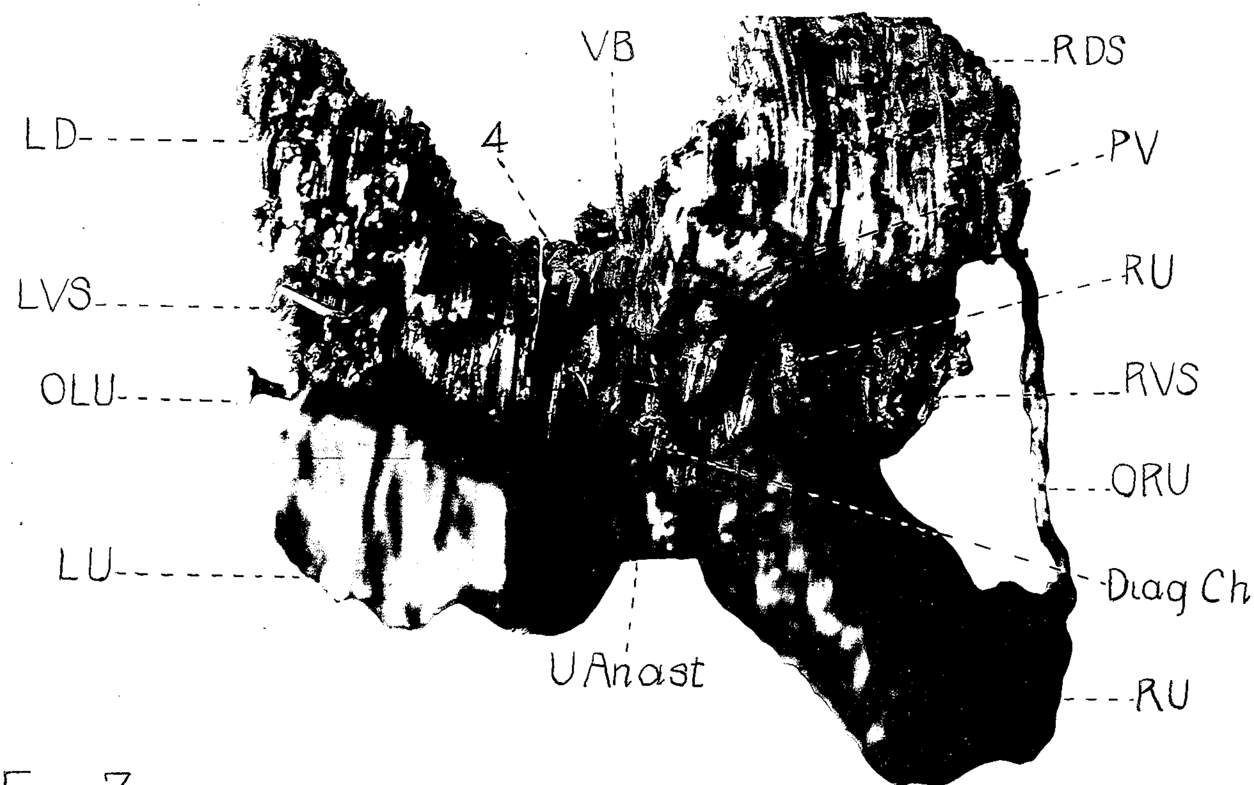

Fig. 3

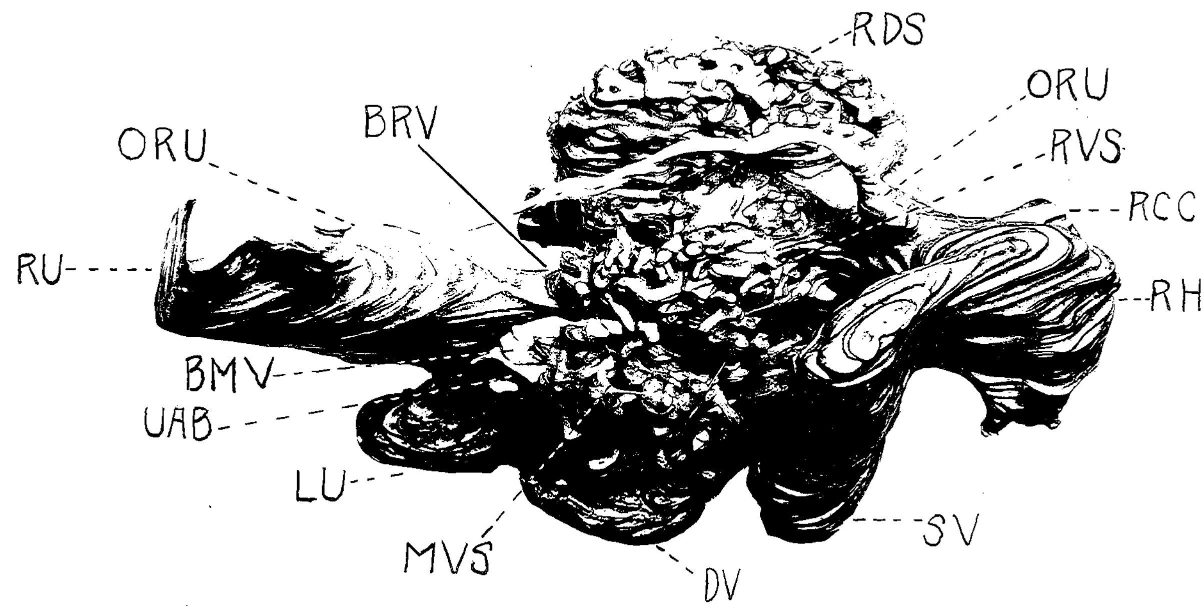

Fig. 4

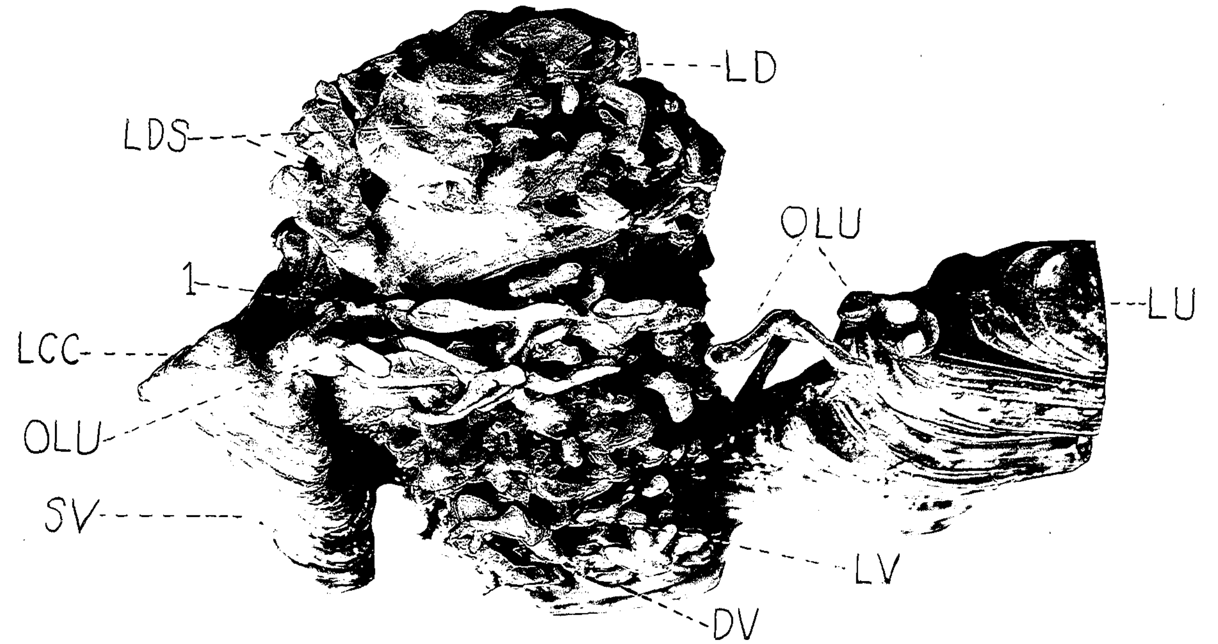

Fig. 5

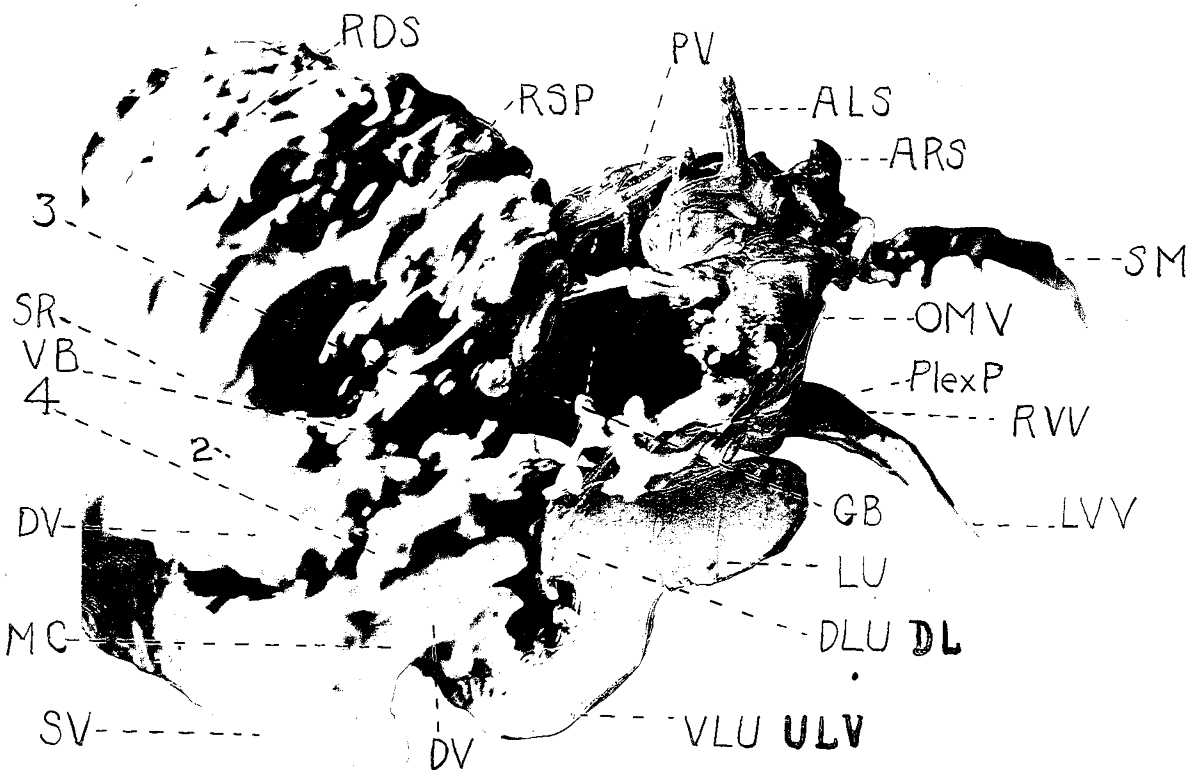
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Fig. 6

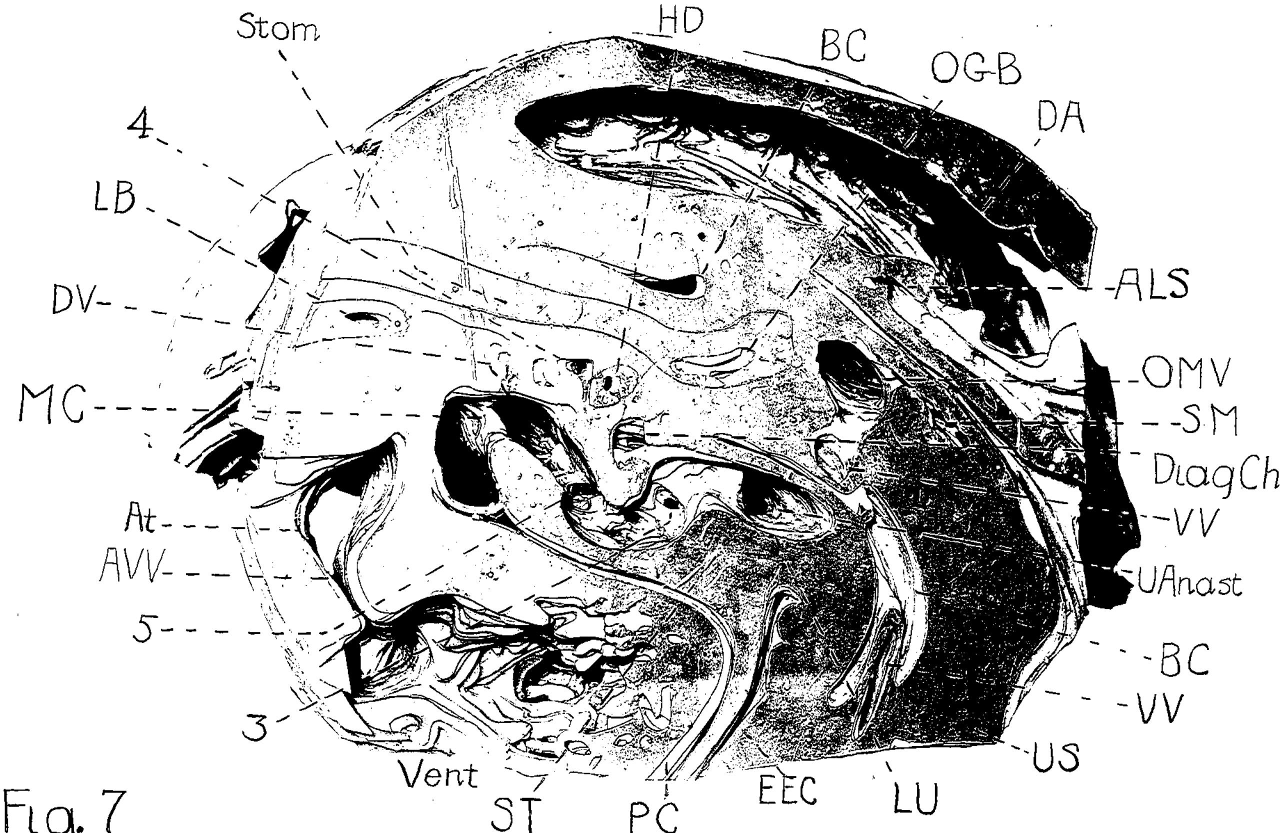

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Fig. 7

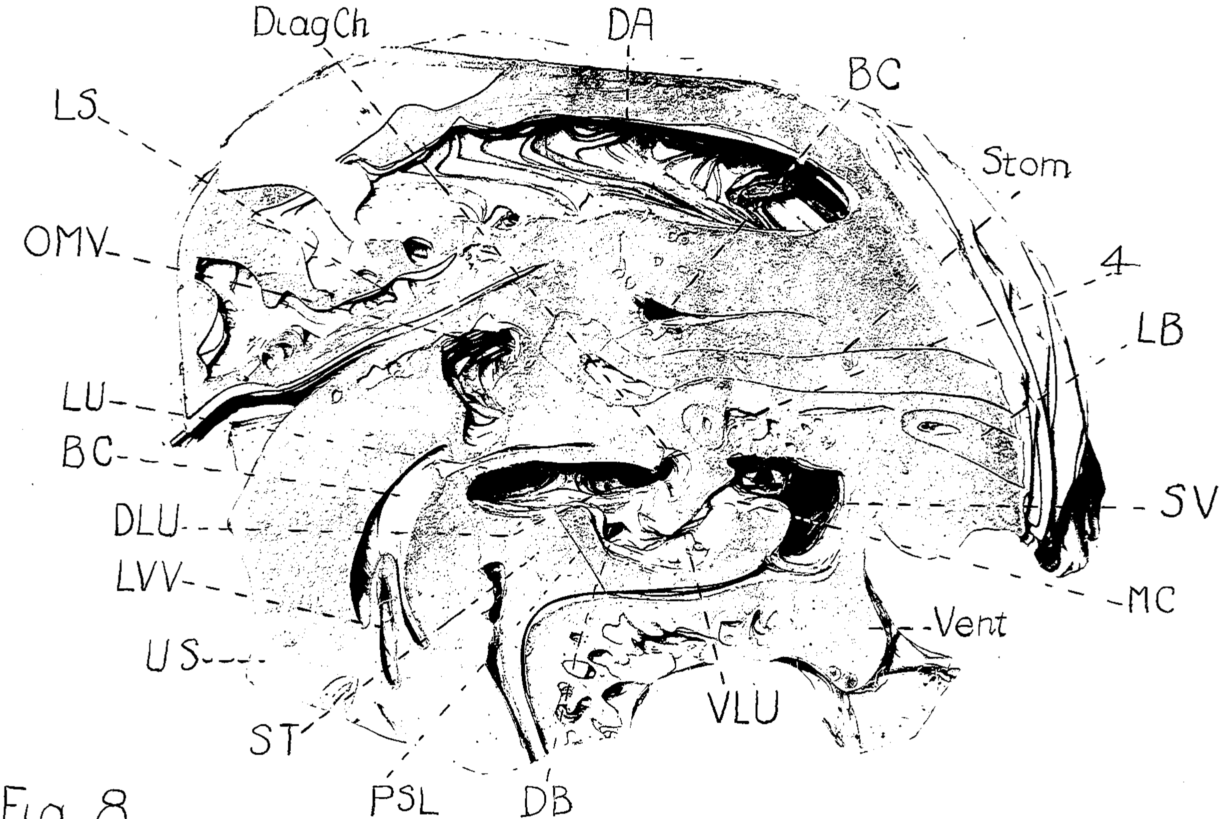

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Fig. 8

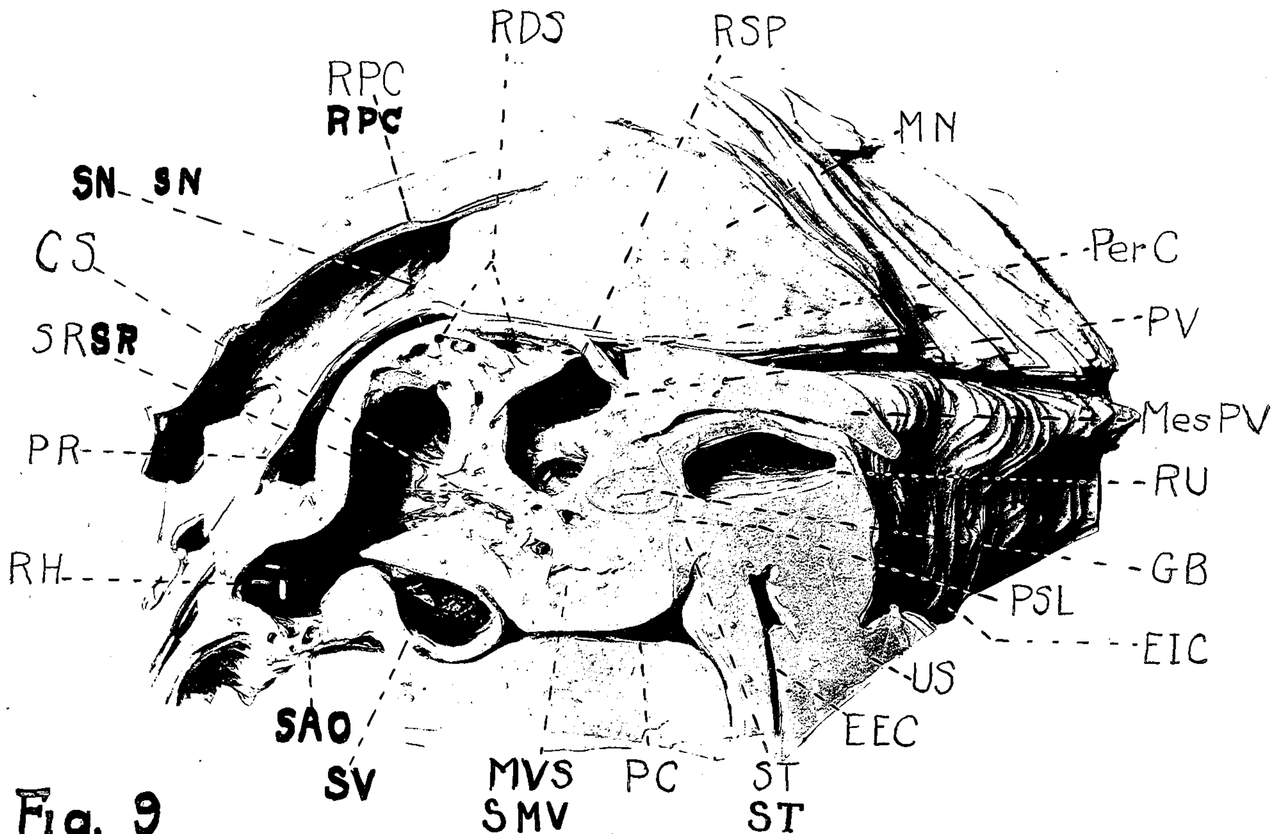
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Fig. 9

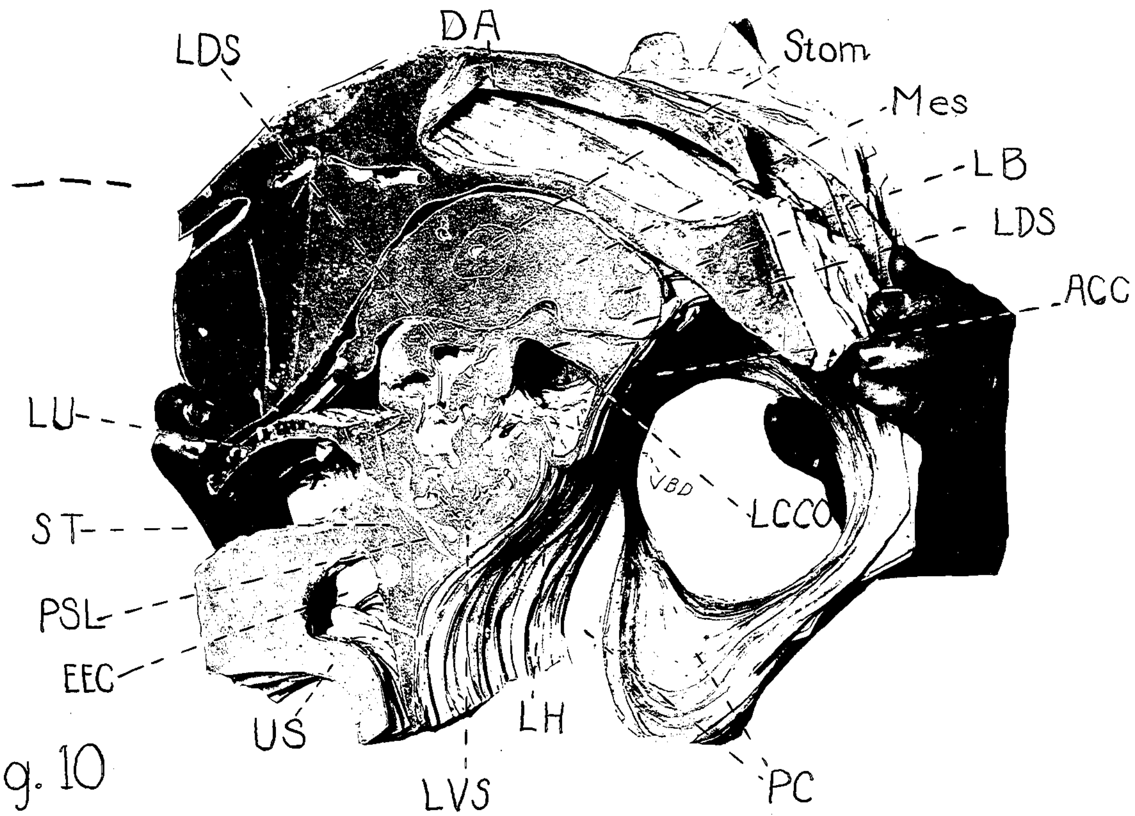


Fig. 10

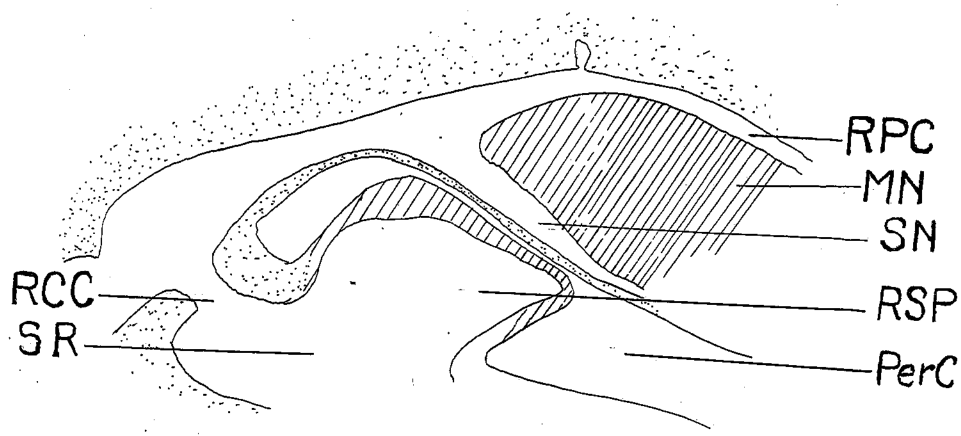


Fig. 12

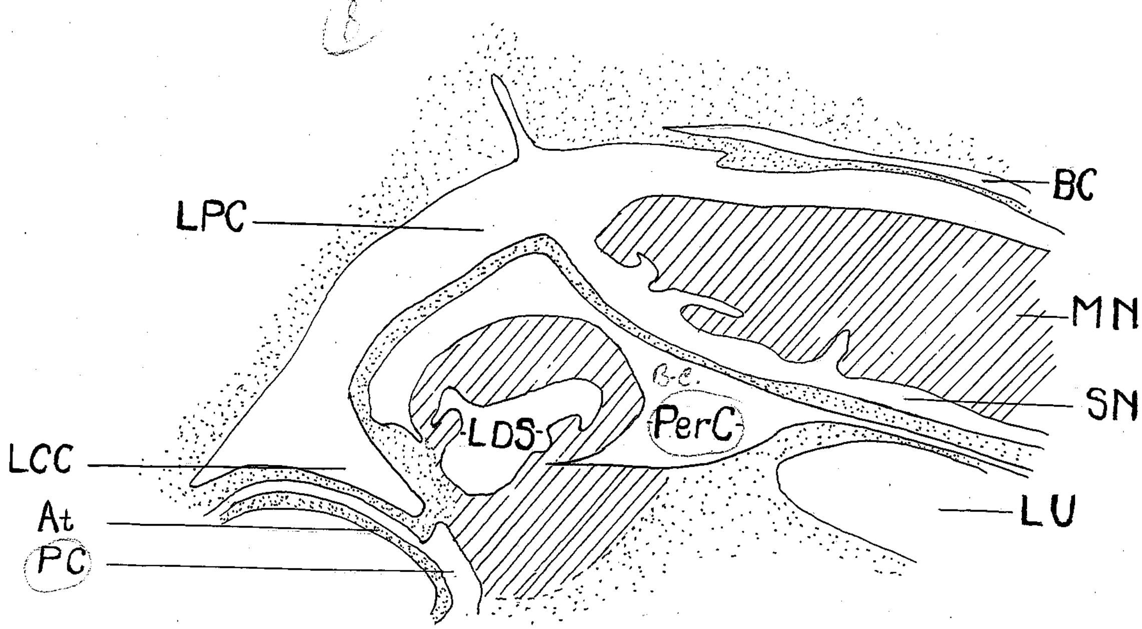
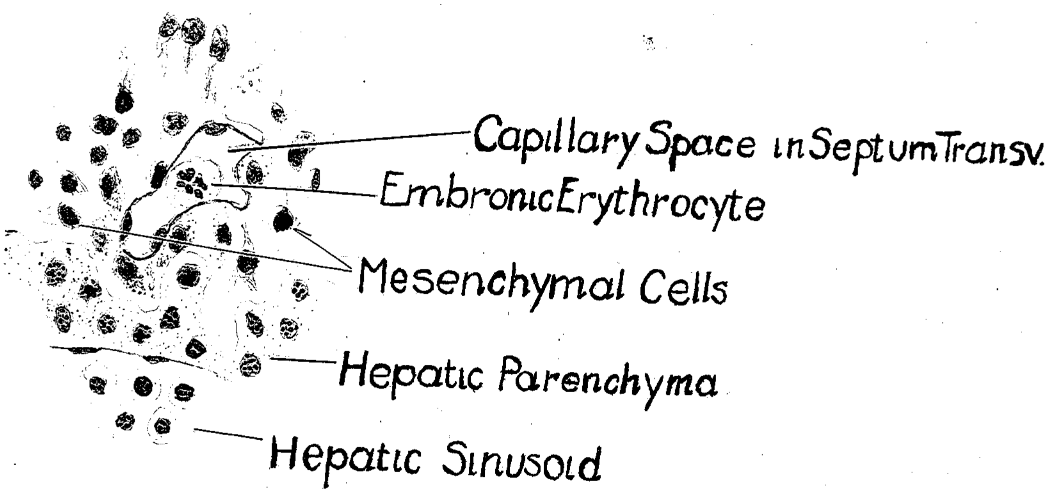


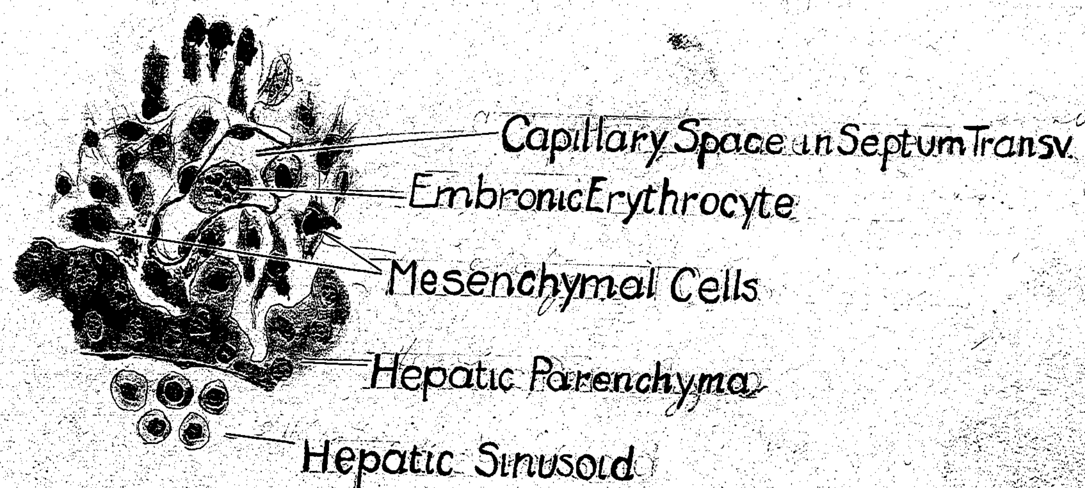
Fig. 13



Capillary Space in Septum Transv.
Embronic Erythrocyte
Mesenchymal Cells
Hepatic Parenchyma
Hepatic Sinusoid

Fig. 11

4



Capillary Space in Septum Transv.
Embronic Erythrocyte
Mesenchymal Cells
Hepatic Parenchyma
Hepatic Sinusoid

Fig. 11