Thesis on

Pathological changes in diseases of the liver Especially in relation to the changes in the Bile ducts & the production of Cirrhosis

By

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This Thesis is an investigation of the Morbid Anatomy of bile ducts, in relation to various pathological states

1. Angiocholitis
2. Secondary states produced in the liver
   a. Biliary pigmentation
   b. Hepatitis
   c. Cirrhosis &c.

This Thesis is the result of a research carried out under the kind supervision of Prof. Delepine of Owens College, from specimens of liver supplied by the Pathological Museum of the University

I have endeavoured to contrast my actual observations with those of the best authorities both British & Continental, a list of which I have appended. In the preparation of my slides of which I have made about 170. I have hardened some by Alcohol, others by Mullers Fluid. Some of the preparations I have cut direct by the freezing method, some by embedding in paraffin, others have been first embedded in Celloidin & then cut by the freezing method.

The stains which I employed are.

1. Picro Carmine. 2. Haematin. 3. Haematin & Rubin Orange. 4. Iodine. 5. Methylaniline, violet 6. Grams Method (for bacteria).

The sections were mounted some in Farrants Solution & some in Canada Balsam.

I append herewith some micro-photographs which I have taken of the slides prepared by me & which show the most important features & points of special interest to an investigation of this kind

There are numerous causes from which an increase of the interstitial tissue of the liver may arise & may be the source of one of the abnormal states which ultimately assume the phase known under the name of Cirrhosis

It has long been held & there appears to be substantial grounds for the belief that certain types of cirrhosis are undoubtedly produced from some source of irritation either having its origin in some substance circulating with the blood or reaching the liver substance through the medium of the bile ducts or lymphatics

It is not my intention in this thesis to deal with the subject of Chronic Interstitial Hepatitis but rather to confine myself to an inquiry into the effects produced in the livers by mechanical interference with the flow of bile & of the more complex changes due to inflammatory lesions of the bile ducts & changes in the composition of the bile itself

In order therefore that I might possibly obtain some useful information from a comparative study of the changes produced in the liver, I have selected a number of cases in which the bile ducts were affected in various ways.

The following are the cases selected; the numbers given are the numbers of the specimens in the Pathological Museum at Owens College

3741 Gall stones, obstruction of Cystic duct.
3976. Cancer of Pancreas. obliterating Common bile duct
4431. Liver of Sheep (Distomatosis)
3701. Liver of Cow. (Distomatosis)
4482 Liver of Rabbit (Psorospermosis)
1319. Carcinoma affecting Gall bladder & Duct)?
574 Suppurative Angiocholitis
568. Biliary Cirrhosis
1227 Liver with multiple abscesses.
1817. Malignant Icterus with subacute parenchymatous & embolic hepatitis
813 Liver with Granular Surface, soft & bile Stained / Biliary Cirrhosis
1321 Anterior Edge of Left Lobe congested, bile Stained & pigmented
2783 Biliary cirrhosis pigmentation of liver cells.
4270 Liver of child 9 months old which had been affected with jaundice since it was 15 days old

4449. Liver of child aged 2 yrs, jaundice during life

3534. Advanced Cirrhosis in a child of 8 yrs possible passing thro Hair dye ?

1573 So called Hypertrophic Cirrhosis

784. Syphilitic Gumma in Liver with Cirrhosis

The first two cases which I shall describe are examples of simple mechanical obstruction of bile ducts. the one a case of obstruction by Gall stones, the other a case of Cancer of the Pancreas obstructing Common bile duct. These produce purely mechanical lesions without infection, & I shall describe the effects on the bile ducts & their epithelium, the surrounding connective tissue, the distribution of the newformed connective tissue throughout the section & the secondary changes in the liver cells themselves.

The first section which I shall describe shows a condition known as Steatosis, this condition is also described by Lancereaux who says it is a result of Chronic alcoholism. not having the notes of the case from which this specimen was obtained I can not say whether there was a history of Chronic alcoholism as well as obstruction of the Cystic duct by Gall stones. I will now give the extract about this condition

(See over

Lancereaux & Hackesbauer "Anatomie Pathologique Tom 1 p 88.

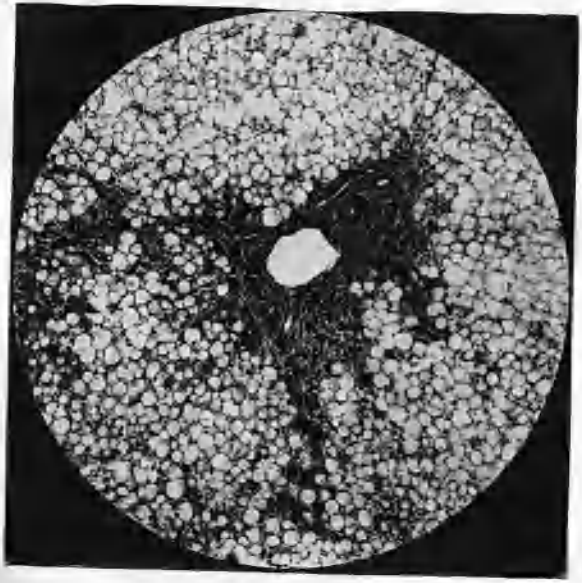
There has been described a form of diseased liver in which the parenchyma is greatly altered as the result of alcohol, but where cirrhosis is either absent or insignificent. This is the Steatosis of the liver described by Lancereaux who says it is one of the commonest forms of liver disease caused by "Chronic Alcoholism" On section he states that the liver has undergone extensive fatty changes, almost all the liver cells have lost their normal shape, have become spherical & filled with granules or globules of fat.

In the case which I am about to describe I found very marked Cirrhosis. this may be due to the biliary obstruction. whilst the fatty changes might have been brought about by alcohol. but of the latter I have no information. The micro photograph which I have made of this section shows the fatty changes. very distinctly & also the cirrhosis

Case I. No. 3741. A case of Gall Stones obstructing Cystic duct Capsule

There is marked thickening of the capsule, the newformed connective tissue is rich in round cells, this infiltration of round cells & also the

No. 3741.



Case 3741 Cld

thickening of the capsule is greater in some parts than in others.

Connective Tissue.

Connective Tissue in Portal Zones.

There is a great increase in the connective tissue in the portal zones; this tissue is greatly infiltrated with round cells. it is also very vascular, the blood capillaries are plainly seen & are filled with blood. This increase of the connective tissue is practically confined to the portal zones & is arranged as circular bands around the portal vessels, that surrounding the bile ducts being thicker than that around the hepatic artery.

Blood vessels.

Hepatic Artery

The walls of the artery are thickened especially in the fibrous coat. It is surrounded by a thick band on newformed fibrous tissue

Br. of Portal Vein.

The Interlobular vessel is dilated & filled with blood

Intralobular vein

Where it is possible to distinguish it, it is found to be dilated

Bile duct

Larger duct

They show marked signs of angio & periangiocholitis & in one or two places in the section they are seen to be completely filled with a granular material The epithelial cells of the duct are swollen & show signs of granular degeneration

Smaller duct

They are very numerous & distinct & show proliferation of their epithelium. Some are filled with biliary material

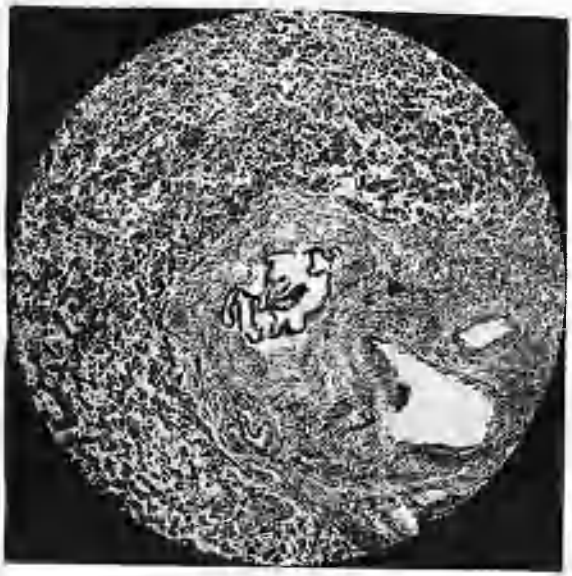
P.

Parenchyma

Practically the whole of the liver tissue is replaced by fat globules, Here & there bordering on the connective tissue at the periphery of the lobule are seen hepatic cells. which however show fatty changes.

There are also present in this specimen great numbers of double rows of cells. in the newformed fibrous tissue These are the so called newformed bile ducts

No 3976.



3976. A case of Cancer of the Pancreas obstructing Common bile duct

This section shows dilatation of the bile duct cerrhosis & also biliary pigmentation

Capsule

There is no marked thickening of the capsule but its deeper layers is very rich in round cells.

Connective Tissue

Connective Tissue in Portal Zones is greatly increased & this connective tissue in some parts of the section is seen to extend between the lobules forming a perilobular cerrhosis. Again from these interlobular bands one sees young connective tissue passing up between the columns of the hepatic cells. The nuclei of this young connective tissue are very distinct. There is also great round celled infiltration throughout the new formed fibrous tissue & here & there are seen masses of bile pigment in the fibrous tissue

Nowhere in this fibrous tissue can I make out any of the so called newformed bile ducts

Blood vessels.

Hepatic Artery is enlarged & its walls greatly thickened

especially is this thickening seen in the fibrous coat

Interlobular veins

They are dilated, their walls greatly thickened

Intralobular veins

They are also dilated but nowhere in the section do they show the same degree of enlargement as do the interlobular veins

Bile duct

Large ducts

These ducts are greatly dilated, their fibrous wall is greatly thickened. The epithelial coat is in the greater number of the ducts detached & thrown into folds.

The epithelium itself shows signs of granular degeneration

Smaller duct

They are very numerous & distinct, they are dilated in some cases. in others their lumen is obliterated by a mass of bile pigment. Others show proliferation of their epithelium which in turn shows granular degeneration & many of the small duct are filled

with a granular material

Parenchyma

There is great loss of hepatic tissue.
In some parts of the section the hepatic cells appears normal, in other parts one sees pale areas of hepatic tissue, here the cells are under high power in a state of fatty degeneration
The cells on the border of the portal zones show granular changes they are flattened & some are greatly atrophied & The cells throughout the section are infiltrated with bile pigment.

In this specimen the changes have commenced in the large bile ducts then extended to the small duct causing obstruction & occlusion in some. As a result of the stagnation of the bile we have had angio & peri angiocholitis set up, this has extended to the small duct with a result that a condition of Cirrhosis has been caused which in my opinion is Biliary in origin. There has also been some resistance to the blood flow which is shown by the branches of the portal vein being dilated. Their thickened walls together with those of the Hepatic artery are due in my opinion to the blood being charged with reabsorbed bile.

No. 4431

The next 3 cases are examples of obstruction of bile duct by parasites

No. 4431 Liver of Sheep (Distomatosis

Capsule.

There is no thickening of the capsule

Connective Tissue

Connective Tissue in portal zone is markedly increased & extends along the interlobular fissures joining with similiar growths from neighbouring portal spaces. but the process has not advanced so far as to form a complete perilobular distribution. This fibrous tissue is very rich in round cells. It is around the bile ducts which contain the Distomata that the increase in connective tissue is best seen, which is illustrated well in the microphotograph of this section

Blood vessels

Hepatic Artery

In those parts of the liver which are least affected the artery appears to be fairly normal, but in one part of the section where the accompanying bile duct is enormously dilated & inflammed & filled with distomata, the artery shows marked signs of Arteritis

4431. Old

The Interlobular veins

In the greater part of the section the veins except for their walls being slightly thickened show no other change but in the part of the section just described the vein shows marked signs of phlebitis, its inner coat being greatly thickened & its lumen is filled with a hyaline substance

Intralobular veins

These veins appear normal

Bile ducts Large

In the greater number the vessels appear in a state of chronic cholangitis. Their walls show considerable fibrous thickening. & are dilated

The epithelium of these ducts show granular degeneration & the lumen is filled with a substance which I consider to be composed of inflammatory material together with the broken down & granular epithelium

A large number of the ducts contain distomata

Small ducts

They also show dilatation & inflammation The lining epithelium showing signs of granular degeneration & in some cases the lumen is

entirely obliterated

Parenchyma

The liver cells appear normal on the whole; the cells at the periphery of the lobules bordering on the new formed connective tissue are flattened due to pressure, otherwise healthy.

There are also present in this specimen, numbers of the so called bile ducts.

The changes produced in this specimen are entirely due to the inflammatory condition of the large & small bile ducts, The inflammed & thickened condition of the blood vessels in the portal zones, are due to inflammation having spread from the ducts. The connective tissue in this case, in the greater part of the section is confined to the portal zones but we also see it extending along the inflammed ducts which run between the lobules & only in a few cases are the lobules entirely surrounded

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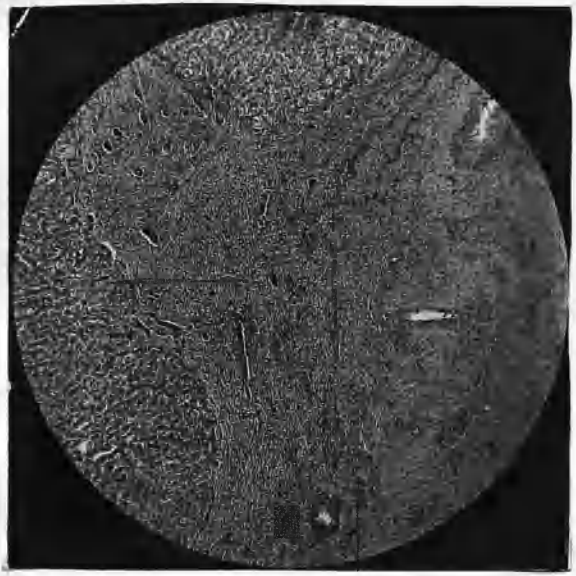


3701. Liver of Cow. Distomatosis

This case is a similar case to the preceding one but in addition we have had infection ~~of~~ by some micro organism which has produced a suppurative condition of the bile ducts, also hepatic abscesses & in this case the cirrhosis is very much advanced.

sule

There is marked thickening of the capsule, the nuclei of the new formed fibrous tissue being very distinct

nective Tissue

The connective tissue in the portal spaces is very greatly increased, the greater part of the section appears to be composed of a mass of fibrous tissue in which one sees islands of hepatic tissue, some of which consists of single lobules but the greater number are composed of several lobules which are very irregular in shape.
The connective tissue is very rich in round cells. In some parts we have areas of dense masses of fibrous tissue the nuclei of which are not so distinct.

No. 3701.

3701. Cld

Blood vessels

Hepatic Artery

Throughout the section the artery so inflammatory changes, the walls being greatly thickened, the thickening being specially marked in the external & middle coats

Interlobular vein

Its walls are greatly thickened & in some case the vein appears to be in a state of thrombosis

Intralobular vein

The vein does not show anything abnormal

ile ducts

Large bile ducts

It is here where the lesion is most marked the ducts are in a state of suppurative c cholangitis with marked peri cholangitis. The largest duct shown in the section, a micro photograph of which altho not a success, shows the enormous thickening of its walls, the inner wall of which is thrown into folds & is covered

with layers of a fibrinous material, others are filled with a granular material in which one sees numbers of round cells. & some of the smaller of the large ducts appear to be directly connected with a hepatic abscess which I shall speak of under the parenchyma

Smaller ducts

There are very numerous & show very marked signs of inflammation, their epithelium where it can be made out is swollen up & shows granular changes, here & there we have areas composed chiefly of these dilated ducts, especially is this marked in the parts surrounding the large duct of which I have just spoken.

Parenchyma.

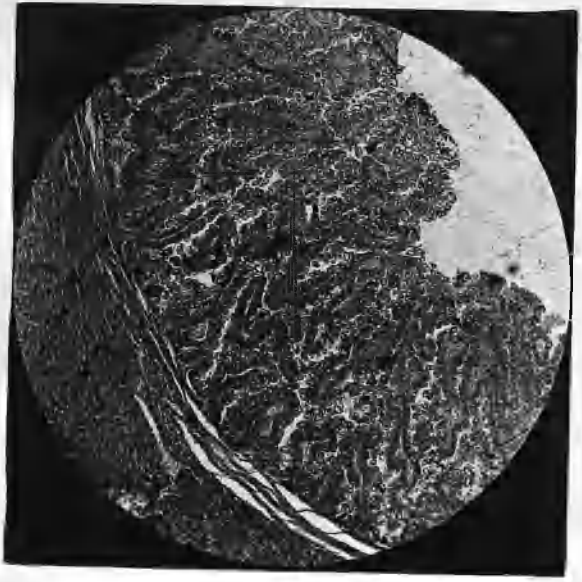
There is great loss of the hepatic tissue through out the section. The liver is in a state of hepatitis it is bile stained & here & there in the tissues one sees masses of round cells. the centres of which appear to be in a state of coagulation necrosis, these being in my opinion true abscess. these are several in number but are all in the same part of the section

There are present in this section enormous numbers of the so called bile ducts (new formed) which can plainly be seen to be formed from the atrophied hepatic cells

Summary

This specimen shows a very advanced cirrhosis secondary to the acute inflammation of the bile ducts. The large bile ducts show a state of suppurative cholangitis & this has extended to the smaller ducts, In addition to the inflammation of the ducts caused by the distomata there has been a septic infection the nature of which I have not been able to make out.

No. 4482.



4482 Liver of Rabbit (Psorospermosis).

Capsule.

There is no thickening of the capsule but the hepatic tissue immediately below the capsule is greatly infiltrated with round cells.

nective Tissue

In the greater part of the section there does not appear to be any great increase in the connective although in the portal zones near to the Psorosper-mahc nodules. the connective tissue is increased & this is greatly infiltrated with round cells.

od Vessels

1 Hepatic Artery

The artery is not very distinct but where I have been able to distinguish it I have found its walls slightly thickened

3 Intralobular veins

Some are dilated but ~~doc~~ others do not show this enlargement but in all cases they are filled with blood.

2 Interlobular veins

Throughout the section they are dilated & filled

with blood but their walls are not thickened.

Bile vessels.

Large duct

They are dilated, their walls thickened & surrounding with fibrous tissue & show marked signs of inflammation, some are filled with a fibrinous material in which one sees epithelial cells in various stages of degeneration, some are filled with bile

Small ducts

They appear to be increased in size & number, there is proliferation of the epithelial cells, the lumen of the duct appears to be narrowed from the swollen condition of the epithelial cells. but in the greater number there is no complete obstruction although in one or two places the duct appears to be plugged with inspissated bile. There is a great infiltration around these ducts of round cells & in some of the duct, the epithelial cells show signs of degeneration & are filled with bile pigment.

Sections

Parenchyma

The hepatic tissue as we have already state immediately beneath the capsule is greatly infiltrated with round + bile pigment +. The hepatic cells retain their columnar arrangement + appear normal. altho the tissue is infiltrated with bile this is well marked around the portal zones. + here the tissue is also congested with blood

Here + there throughout the section one sees large nodules which are surrounded by concentric bands of fibrous tissue, in the other layers of this fibrous tissue one sees groups of bile + blood vessels; some of these bile ducts are dilated + filled with bile + a fibrinous material +. The inner walls of these nodules ~~are~~ is known in an enormous numbers of folds which practically fills up the nodule + it is on these folds that the coccidia are found in great numbers.

This specimen shows a simple inflammatory condition of the bile ducts due to the presence of the Psorosperms. without an septic infection The cirrhosis is not well marked.

1319

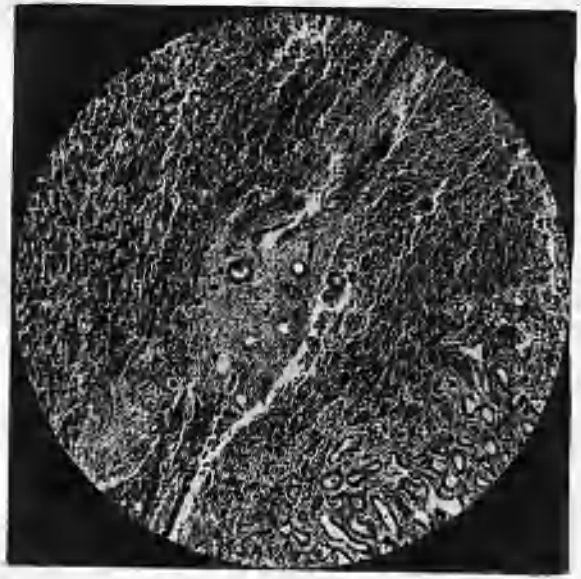
A Case of obstruction of the bile ducts apparently beginning in the Gall bladder

This section shows a portion of the liver & part of the wall of the Gall bladder, the wall of which is greatly thickened with newformed fibrous tissue & is adherent to the liver. The type of cancer in this specimen shows under the microscope to be a case of Cylendrically epithelioma. The cancerous tissue has invaded the greater part of this specimen of the liver resulting in atrophy & degeneration of the hepatic tissue & a great increase in the connective tissue produced the condition know as Cirrhosis

Capsule

The capsule cannot be distinguished from the fibrous tissue of the gall bladder, in the lower layers of this fibrous tissue one sees enclosed portions of hepatic tissue & bile ducts, This connective tissue is very vascular & infiltrated greatly with round cells, these cells forming here & there large clusters. The nuclei of the fibrous tissue are very prominent

No. 1319



Connective Tissue

In those parts of the section where the cancerous infiltration is not so great, one sees a great increase of the connective tissue in the portal zones. this tissue is greatly infiltrated with rounds cells & the nuclei of the fibrous tissue are well seen.

Blood vessels.

Hepatic Artery

The walls of the artery are greatly thickened

Interlobular vein

The walls are greatly thickened & the veins are dilated & some are filled with blood

Intralobular vein

Where one can make the vein out it does not show anything abnormal

Bile duct

Large

Her walls are thickened & the duct are dilated show proliferation of epithelial cells & are surrounded by bands of fibrous tissue

Small ducts

In the portal zones the small ducts are very prominent, they show proliferation of their epithelial cells & in some cases their lumen is obliterated by masses of bile matter. In the cancerous portions the bile ducts are difficult to make out owing to the cancerous being of a glandular type similar to the bile ducts, but in some cases under the high power one would say that these cancerous tubes were in connection with the duct themselves. In several small ducts the lumen appears to be entirely obliterated by inspissated bile

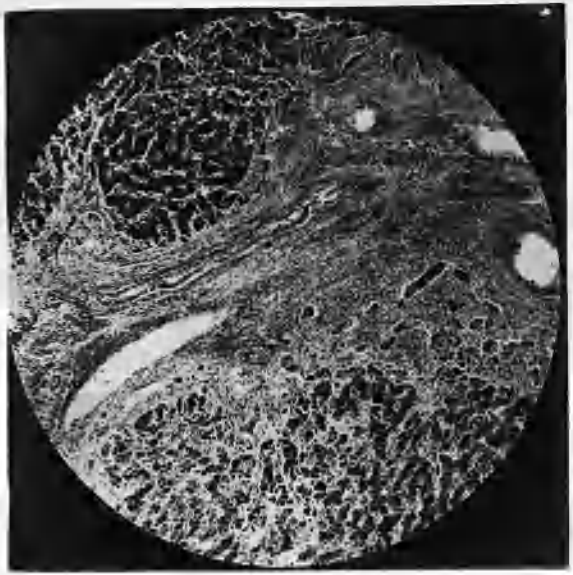
Parenchyma

There is throughout the section a great atrophy of the liver cells, the hepatic tissue is greatly infiltrated with round cells, these bordering on the connective are flattened & show signs of granular degeneration. In other parts of the hepatic tissue, there is congested with blood In those parts of the section where the cancerous infiltration is not so great., the hepatic cells retain their columnar arrangement & appear fairly normal. No where in the section can I

find any fatty degeneration, in some parts the hepatic tissue is infiltrated with bile pigment

In some parts of the section one sees some of these so called new formed bile ducts but they are not numerous

No. 574.



374.

A Case of Biliary Cirrhosis, Suppurative Angiocholitis

Capsule

There is no marked thickening of the capsule but the blood vessels in the capsule & in the connective tissue between the capsule & the liver tissue are dilated & filled with blood

Connective Tissue

There is very marked increase in the connective tissue in the portal zones. This new formed tissue is also seen to extend along the inflammed ducts which run between the lobules forming an incomplete form of Perilobular cirrhosis, In some parts of the section as is shown in the accompanying microphotograph we see this C. tissue extending into the lobule between the hepatic cells. This new formed tissue is very rich in round cells & here & there we find masses of bile pigment enclosed in the meshes of this tissue. In one part of the specimen this increase of Connective tissue is very great & in the tissue is seen a large bile duct showing marked inflammatory changes

Blood vessels.

Hepatic Artery.

The artery shows great thickening of its coats & its walls on staining a section with Methylalene violet

also show lardaceous degeneration

Interlobular vein

The walls of the vein are also thickened & the vein is also dilated

Intralobular vein

The vein is well seen, there appears to be a slight increase in size & its walls are also slightly thickened

Bile ducts

Large ducts

These show very marked signs of inflammation Their walls are greatly thickened & the ducts together with the hepatic artery & interlobular vein are surrounded by a dense mass of connective tissue The epithelium of the ducts appear to be lost & they are filled with an inflammatory exudation composed of muco-pus & bile pigment. Around these ducts are clusters of round cells, some of which show necrotic centres, These clusters also appear to be connected with the small bile ducts. In others of these large ducts where the inflammation is not so advanced the ducts have the appearance of being in a state of catarrhal inflammation the lumen being filled with degenerated epithelial cells.

Small bile duct

The small bile ducts show great proliferation of their epithelium & are filled with bile. Some of these ducts appear to be connected with large masses of round cells some of which have necrotic centres. Along the whole of the bile ducts there is an infiltration of the tissues with round cells.

Parenchyma

The whole of the hepatic tissue is infiltrated with round cells & bile pigment. The unstained specimen show the biliary staining of the tissue very markedly. The hepatic tissue is also in some parts infiltrated with blood cells. Here & there throughout the section there are large masses of round cells, some of which appear to be connected with the bile ducts, these masses are in my opinion the commencement of true abscesses & appear to predominate on one side of the biliary duct this has also be noticed & described by Gamboult. In the hepatic lobules which are furthest away from these inflammed ducts the hepatic cells appear to be normal except for the infiltrated of the cells by bile pigment which appears to be general. Throughout the section

In those lobules in the areas of the large inflammed bile ducts the hepatic cells show signs of granular degeneration but nowhere can I see any signs of fatty changes x
Although I have stained specimens by Laeffer & Gramms method I was not able to find any bacteria. Staining with methylaneline violet shows amyloid degeration this was conformed by pouring a watery solution of Iodine over the fresh cut surface of a piece of this liver x

I also observed in this specimen numbers of the so called new formed bile ducts

In this section one sees a large number of large & medium sized bile ducts affected; this has spread to some of the small ducts resulting in obstruction to the duct & hence the infiltration of the tissues with bile. There has also been here present some infective organism the nature of which I was not able to discover, the changes in the hepatic cells appear to be confined to those which were bordering on the inflammed duct.

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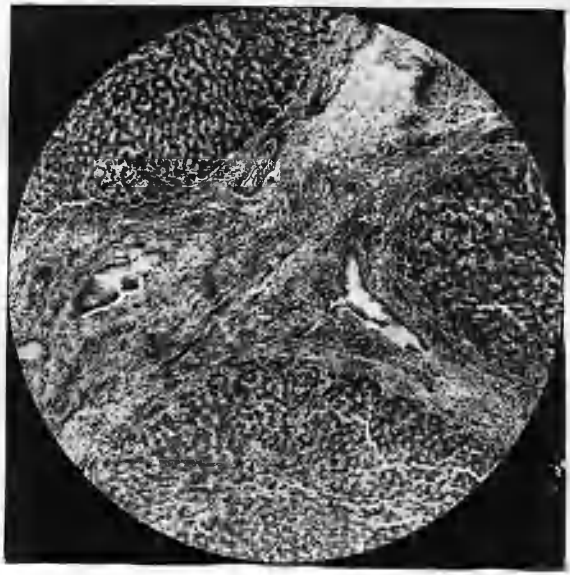


1227. Liver with multiple abscesses.

This is a similar case to the preceding one but is more advanced. In this case there were secondary abscesses in the lung & kidney. Some of the abscesses are branching & are apparently connected with the bile ducts

Capsule

There is marked thickening of the capsule, this thickening is especially well seen in that part of the capsule under which is seen a large abscess. which is surrounded by a thick wall of fibrous tissue, the fibres of which appear to be arranged concentrically.

Connective Tissue in Section

There is a great increase in the connective tissue in the portal zones throughout the section this connective tissue is prolonged along the inflammed bile ducts which run between the lobules, but there is not the appearance of a pericellular cirrhosis. One also sees young connective between the columns of the hepatic cells. The connective tissue in some of the portal zones is largely infiltrated with round cells but this is not general.

1227 Cld

Blood vessels

Hepatic artery.

The walls of the artery are greatly thickened & in some cases is filled with a granular & fibrinous material in the portal zones. in which there is seen the accompanying vein is in a state of thrombosis

Interlobular vein

They are dilated, their walls greatly thickened & filled with blood & a number of cases the vein is in a state of thrombosis

Intralobular vein

In some of the intralobular vein there is no abnormal changes, in others they are slightly dilated their walls slightly thickened & in a few cases are seen to be filled with a fibrinous material, in one case the vessel is in a state of thrombosis, the thrombus is seen to arise from the greater part of the inner wall, the vessel is in the vicinity of a very large abscess.

Bile ducts

Large Duct

They show very marked signs of inflammation the fibrous coat is greatly thickened, the epithelium where present is seen to be swollen & very granular Some of the large ducts are filled with muco purulent

material. In one case a large duct communicates with a large abscess, the contents of which is composed of caseous material which is full of pus cells & on staining by Grams method. Staphylococcus Pyogenes were found in abundance.

I may say that in the subject from which this specimen was got secondary abscesses were found in the lung & kidney.

Small duct

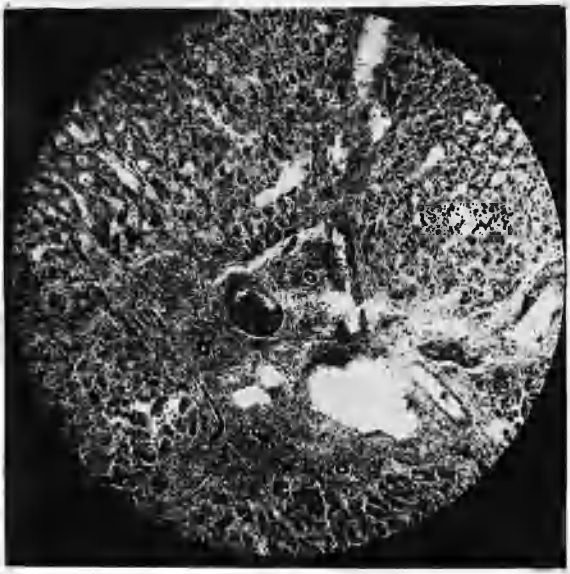
They are very numerous & are in a state of inflammation, their epithelium is swollen up & granular & obliterates the lumen. In some of the smaller duct one can still make out the cylindrical shape of the epithelium but in the majority of the small duct, the epithelium appears as one mass of granular material

Parenchyma

There is great infiltration of the hepatic tissue with round cells. Bile pigment but feble staining is not so well marked as in the preceding section In the centre of this specimen there is a large abscess which is surrounded by a dense layer of fibrous tissue; the contents of the abscess is chiefly composed of a caseous material, & pus cells. Surrounding the abscess the hepatic cells appear to be elongated & flattened & show atrophy. These changes in the liver

cells are probably due to pressure. I was not able to make out any fatty changes in this specimen

No. 1817.



1817 Malignant Icterus, with subacute parenchymatous & interstitial hepatitis

This specimen was from a child which was affected with what is clinically know as Malignant Icterus. The child became suddenly ill several weeks after apparent recovery from Scarlet Fever. In this specimen one sees that nearly all the terminal bile ducts are obstructed by casts of inspissated bile with a result that the tissues are greatly infiltrated with bile ×

Capsule

There is no thickening of the capsule

Connective Tissue in Section

The connective tissue in the portal zones & from this we have prolongations of connective tissue extending along between the lobules & from this we have young connective tissue passing into the lobule between the hepatic cells × In some of the portal zones there is great round celled infiltration

Blood vessels.

Hepatic Artery

Its walls are thickened otherwise the artery shows nothing abnormal

Interlobular vein

They are dilated, their walls are thickened

Intralobular vein

In the greater part of the specimen these vessels do not show any abnormal characters except that a few appear to be slightly dilated

Bile ducts

The larger ducts are found to be dilated their walls thickening. Many show an absence of their epithelial coat but where one is able to examine it. the cells are found to be in a state of granular degeneration

Smaller ducts

They appear to be numerous, some of them show proliferation of their epithelium with which some are filled together with inspissated bile. The terminal ducts appear to be filled with bile. Around some of these ducts there is marked infiltration with round cells

Parenchyma

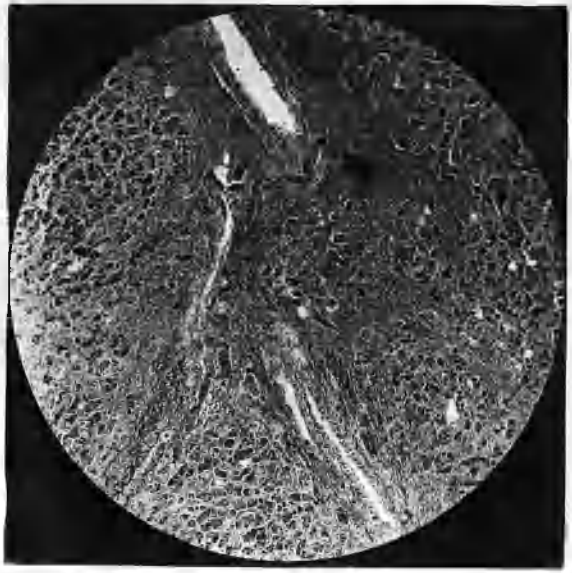
In the greater part of the section the hepatic cells lie in a matrix of connective tissue, here & there one sees a lobule in which one sees the cells are arranged in columns as is seen in normal condition. Respaces between the columns are filled with bile

In other parts the cells are altered in form & are absorbed. There does not appear to be any signs of fatty changes in the cells.

Sr

In this specimen the terminal bile ducts appear to be seat of the disorder, the majority of the terminal bile ducts being plugged with bile. Some of the ducts show marked inflammatory changes. The irritant or poison appears to have been conveyed to the liver by the branches of the portal vein which also show inflammatory changes. but the nature of the poison or irritant I have not been able to make out.

No. 813.



813. Liver with granular surface, soft, bile stained
This specimen is a good example of biliary cirrhosis & shows markedly fatty degeneration

capsule

The capsule is thrown into small elevations but there is not marked thickening

Connective Tissue

There is an increase in the connective tissue in the portal zones & from these zones it diffuses throughout the specimen, cutting off & surrounding the hepatic cells.

Blood vessels

Hepatic Artery

The artery do not show anything abnormal

Interlobular vein

The veins in this specimen do not show any dilation or thickening

Intralobular vein

It is very difficult to make it out but where it can be examined, shows no enlargement.

Bile duct

Larger duct

They are surrounded by thick layers of connective tissue. Show marked thickening in their

walls. In many cases the epithelium appears to have been shed, in others it has a granular appearance In none of the large ducts can the shape of the epithelial cells be made out.

Small ducts

They are numerous, the epithelium is swollen up with a result that the lumen of the duct is narrowed In many the epithelial coat is detached. Others are plugged with granules of bile pigment.

Parenchyma

The cells lie in a stroma of connective tissue In some parts of the specimen the cells appear normal in others they are swollen up Others show the cells in a state of degeneration, others show fatty changes, some of the cells being nearly replaced by a fat globule in others the cells is seen to have in it a few number of small fat globules. Between the cells there is infiltration of granule of bile pigment throughout the specimen

There are also present in this section numbers of the so called new formed bile ducts, some of these show very distinctly that they are formed from atrophied liver cells.

No. 1321.

1334 Anterior Edge of the left lobule of the Liver
Congested + bile stained

Although the whole of the specimen which I am about to describe shows marked changes, it is the extreme portion of the edge of the specimen in which the changes are most marked + I intend describing this part separately from the rest of the specimen

Extreme portion of the Edge of left lobule of the liver

The capsule is thickened + appears to be continuous with the Connective tissue of this part of the section. Immediately below the capsule there is a zone of the connective tissue which is greatly infiltrated with round cells. x This portion of the section consists chiefly of masses of fibrous tissue, which masses are arranged round the small bile ducts which are very numerous. x As one gets further from the edge one finds small groups of cells (Hepatic) enclosed in this fibrous tissue, coming still further one comes to the remains of lobules which are flattened out + as + we proceed further into the lobe, the lobules assume more their normal form. All these lobules are surrounded by connective tissue which extends into the lobule as far as the central vein + from these smaller bands pass between the columns of the hepatic cells.

This part of the section is greatly congested with bile, the walls of the larger ducts are greatly thickened & they are dilated, in some cases the epithelial coat has become detached & is seen lying in the duct being thrown into folds. The smaller ducts are very numerous, their epithelium is swollen up & in many cases detached obstructing the lumen, in others the lumen is still present but greatly reduced in size & the majority of the small ducts are plugged with inspissated bile & around all the ducts is a thick band of fibrous tissue

The walls of the branches of the hepatic are thickened the interlobular veins are also thickened & some are dilated The hepatic cells can not be distinguished in the extreme part of the edge but as one goes further into the lobe groups of hepatic cells enclosed in the connective tissue & stained with bile can be made out. These cells also show atrophy & are altered in shape.

We also see in this portion great numbers of these so called new formed bile ducts

Rest of Section

Capsule

The capsule is very slightly thickened & immediately below there is an infiltration of round cells.

Connective Tissue

There is an enormous increase in the connective tissue in some of the portal zones. but in all the

connective tissue is greatly increased in amount. This tissue is also greatly infiltrated with round cells. Here & there we find this connective tissue extending between the lobules along the inflammed interlobular ducts

Blood vessels

Hepatic Artery

The walls of the artery are thickened & is surrounded by Connective Tissue

Interlobular vein

It is greatly dilated in some parts, in all cases its walls are thickened

Intralobular vein

In some the walls are thickened but this is not general but it is specially marked in some places.

Bile Ducts

Large duct

There is evidence of a very acute inflammation in these ducts, they are greatly dilated & thickened. In many the epithelium has been shed & in its place one see layers of a fibrinous material outer inner wall & in some cases the duct is completely filled with this material, in others which are not so large, they show great thickening of their walls, their epithelium is

detached & thrown into folds

Small duct

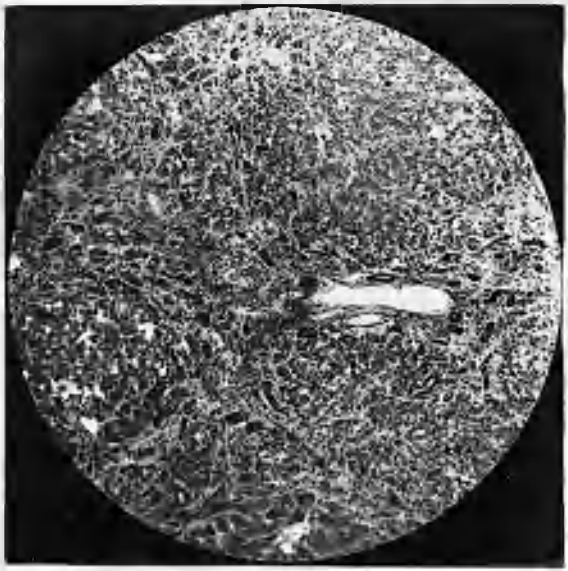
They also show marked inflammatory changes their walls being thickened, their epithelium shows proliferation & degeneration & many are filled completely with inspissated bile. All the terminal ducts appear to be filled with bilary matter.

Parenchyma

There is great atrophy of the liver parenchyma which is greatly infiltrated with bile & round cells. The hepatic cells show atrophy especially those cells bordering on the connective tissue (interlobular). The spaces in the lobules between the hepatic cells are filled with bile, Some of the hepatic cells show fatty changes. but this is not general.

This specimen shows marked Angio & Periangiocholitis of the bile duct, the larger duct being the ones most affected. the vessels in the portal space, the hepatic artery, & portal vein show also signs of inflammatory changes which is secondary to the periangiocholitis. I think that some obstruction to the post Common bile duct. might possibly be the cause

No. 2783.



2783. A case of Biliary cirrhosis

Capsule

There is great thickening of the capsule

Connective Tissue

The connective tissue in the portal zones is increased is infiltrated with round cells & contains great numbers of the so called new formed bile ducts From the connective tissue in the portal zones bands of connective are seen to pass along the inter-lobular fissures. in some case completely surrounding a lobule but in the greater part of the section the connective tissue forms a diffuse stroma in the meshes of which one sees groups of hepatic cells, in others single cells, The connective tissue is also infiltrated with bile

Blood vessels

Hepatic artery

There is a slight thickening of the coats but. in the greater part of the section the artery is not easily made owing to the connective tissue being so largely infiltrated with round cells.

Interlobular vein

In some parts of the specimen the veins are dilated & their walls slightly thickened

one vein in particular shows great dilatation & great thickening of its walls

Intra lobular vein

In those parts of the specimen where the lobules still retain somewhat of their normal shape, they are seen to be dilated. but in the rest of the specimen it is difficult to make out. but where it can be distinguished one always sees it dilated

Bile ducts

Large

This specimen only contains one large duct which shows great thickening of its walls & loss of its epithelium, the vessel contains a fibrinous material

Small ducts

They are very numerous & their epithelium is swollen & shows proliferation which fills up the lumen & in some cases the duct is seen to be completely filled with these cells & Many of these ducts are completed plugged with a mass of inspissated bile, around these small ducts there is great round celled infiltration & in some cases they are collected in masses.

Parenchyma

This specimen shows the hepatic cells in all conditions, Some of the cells appear normal some are swollen, some show fatty changes many of the cells being practically replaced by a fat globules, in others the cells is filled with minute fat granules. The greater number of the hepatic cells show atrophy, The Hepatic tissue is greatly infiltrated with bile, small masses of bile pigment being distinctly seen in the tissues

This specimen also shows numbers of the so called new formed bile ducts

This cirrhosis is certainly of Biliary origin. The great dilatation of the veins (interlobular) being caused in my opinion by the pressure of the connective tissue on the vessels in the lobules. obstructing the blood flow.

No 4270.

4270. Liver of Child, 9 months old which had been affected with jaundice since it was 15 days old possible obstructive lesion ?

Capsule

There is no thickening of the capsule. In the tissue immediately below the capsule there is very marked round celled infiltration

Connective Tissue

There is a great increase in the connective tissue in the portal zone especially, is this well marked in those zones situated nearest to the capsule In the greater part of the section this increase in connective tissue is limited to the portal zones, but here & there, one sees bands of fibrous tissue enclosing in some places one in others one or more lobules of hepatic tissue. This fibrous tissue does not appear to invade the lobule itself, but in the meshes of these bands one sees groups of hepatic cells, which appear flattened & This newformed connective tissue is very rich in round cells.

Blood vessels

Hepatic Artery.

Its walls are greatly thickened

Interlobular vein

Shows nothing abnormal

Intra lobular vein

In some parts it is seen to be markedly dilated in other parts the vein shows nothing abnormal

Bile ducts

Large ducts

The large bile ducts show marked inflammatory changes, their walls are thickened & some of the ducts have lost their epithelial lining. But one sees along the inner wall of the duct, flat elongated cells. One of the large duct is seen to be filled with a granular substance

Small ducts

These are very numerous. They show proliferation of their epithelium, the lumen of the duct is narrowed & in some cases is entirely obstructed by bile & epithelial cells. Around these small ducts there is great round celled infiltration

Parenchyma

The hepatic tissue is greatly infiltrated with bile & round cells. The hepatic cells appear normal, there being no signs of fatty or other changes.

There is also present in this specimen numbers of the so called newformed bile ducts

No. 4449.

4449. Liver of child aged 2 Jaundice during life

Capsule

There is slight thickening of the capsule & its surface is thrown into small furrows.

Connective Tissue

There is a great increase in the connective tissue in this specimen. The portal vessels in the portal zones are surrounded by a dense band of connective tissue, from these zones the connective tissue diffuses itself throughout the section as a dense fibrous stroma in which one sees hepatic cells. Nowhere in the specimen can be find a complete lobule. The connective tissue is greatly infiltrated with round cells.

Blood vessels.

Hepatic Artery

Its walls are thickened

Interlobular vein

They are thickened & dilated throughout the section, in some parts the thickening of the walls of the vein is very well marked some of these veins contain blood. The blood capillaries are plainly seen & are seen to be engorged with blood.

Intra lobular veins

They are found to be dilated throughout the section

Bile ducts

Large ducts

They show thickening of their walls. The epithelium of the duct is detached in some cases is lost, in others the ducts are filled with a fibrinous material or a substance composed of fibrinous matter with bile, some cases show the contents of the duct undergoing fatty degeneration. In those ducts where the epithelium can be examined it is found still to have its cubical shape

Small ducts

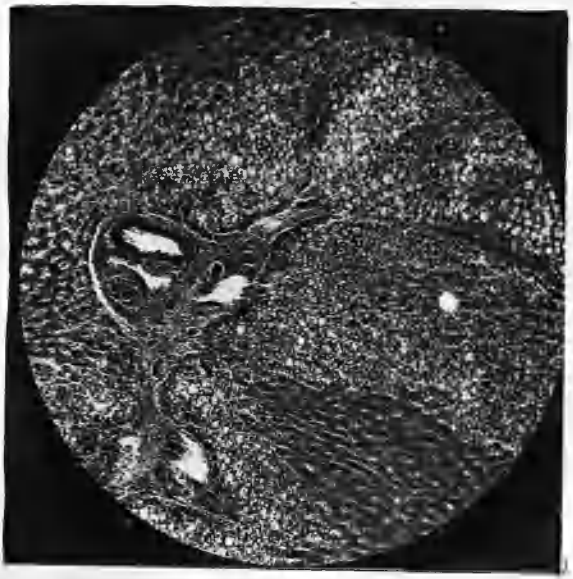
There is great obstruction in the smaller ducts. The ducts show proliferation of their epithelial cells, the latter being swollen up obliterating or nearly so the lumen of the duct. In many cases the epithelial coat has become detached. Many of the ducts are filled with the same fibrinous material which was observed in the large ducts & this in many cases show signs of fatty degeneration. In other parts of the specimen the ducts are replaced by a mass of fibrous tissue in which the nuclei are well seen

Parenchyma

There is great loss of the hepatic tissue throughout the section, nowhere do we see the hepatic cells arranged in columns as in the normal specimen. The shape of the hepatic cells is altered from pressure of the surrounding connective tissue. The cells also show fatty changes & are stained with bile pigment. The whole of the hepatic tissue is stained with bile The fatty changes in the cells is very general throughout the specimen

There are also present in this specimen numbers of the so called newformed bile ducts

No. 568.



568. A case of Biliary Cirrhosis with Perihepatitis

Capsule

There very great thickening of the capsule which is also thrown into folds. The deeper layers of the capsule being denser than the superficial layers. the latter ~~also~~ being more infiltrated with round cells than is the deeper layers. From the capsule one sees prolongations of the connective tissue passing down into the liver.

Connective tissue

The connective tissue in the portal spaces is greatly increased, & it is to these zones that the connective tissue is chiefly confined; this tissue is infiltrated with round cells

Blood vessels

Hepatic Artery

The walls of these vessels are greatly thickened in some parts of the specimen but in other parts this thickening is not so pronounced. The vessel is enclosed in a thick fibrous sheath of connective tissue

Interlobular vein

These vessels are dilated & some of them are filled

es with a fibrinous material in which one sees blood corpuscles

Intralobular vein

In some parts they are greatly dilated but throughout the section they are enlarged.

Bile Ducts

Large Duct

This section shows no large bile ducts

Small ducts

They are very numerous. Their walls being thickened, the epithelium shows proliferation & degeneration, The lumen in many of the ducts are obliterated, some of the duct contain bile Some of these small duct are filled with ~~one~~ mass of inspissated bile & in one case the obstruction is caused by a biliary concretion which does not show any of the characters common to calculi which are formed in the gall bladder.

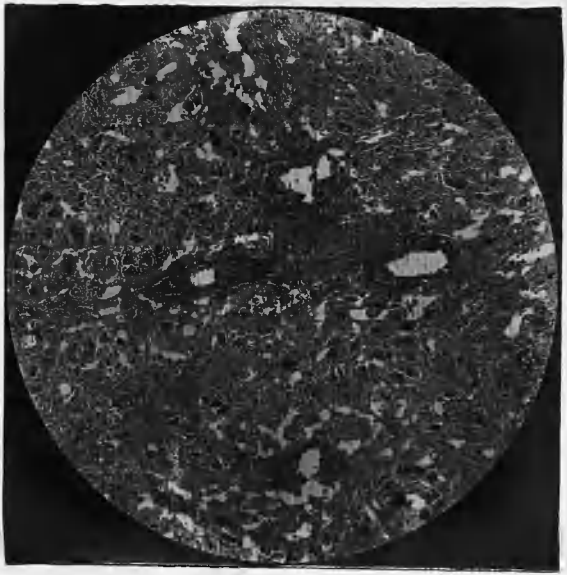
Parenchyma

There is great atrophy of the hepatic tissue, The outer zones of the lobules are pale, due to the fact that the portion of the lobule is greatly infiltrated with fat many of the hepatic cells being replaced by fat globules

The central parts of the lobules are dark in comparison
. due to the normal condition of the hepatic cells
in this part of the lobule. This fatty infiltration
is seen best at the periphery of those lobules which
abutt on the connective tissue of the portal zones
In some parts of the section this fatty infiltration
can be traced throughout the lobule. In some
parts of the specimen one sees masses of bile
pigment in the tissues

In these specimen also contains numbers of the
so called newformed bile ducts

No. 1513.



1513. A Case of so called Hypertrophic Cirrhosis of the Liver

Capsule

There is no thickening of the capsule

Connective Tissue

There is a great increase in the connective tissue throughout the section. The Connective tissue forming a dense stroma in the meshes of which one sees hepatic cells. There appears to be an greater increase in the connective tissue in the portal zones surround the bile ducts & proceeding with them in the interlobular fissures Around these ducts the tissue is infiltrated with round cells

Blood Vessels

Hepatic artery

The artery shows thickening of its walls

Interlobular Vein

They are slightly dilated in the greater portion of the specimen but here & there one sees them more dilated than in the greater part of the section

Intralobular Vein

This vein is very difficult to make out

Bile ducts

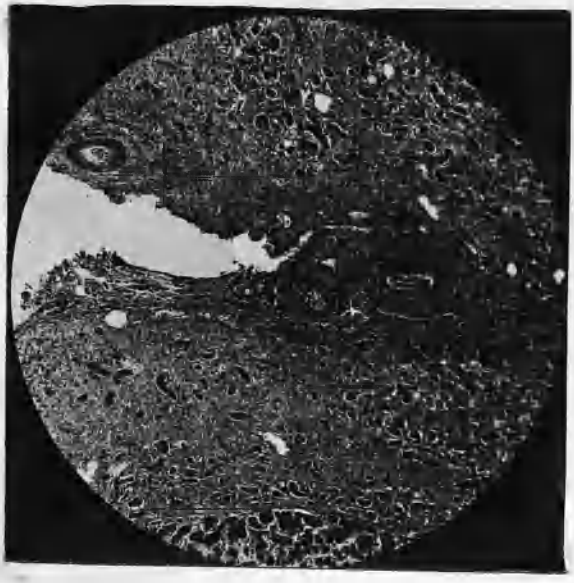
The bile ducts which appear to be affected most in this specimen are the interlobular ducts these are found to be dilated, their walls thickened & can show inflammatory changes. There is also obstruction in these ducts the beyond the obstruction the duct is greatly dilated forming a pouch seen in from my own specimen. The small ducts are very numerous, are lined by epithelium & have a distinct lumen. Many of the intercellular spaces appear to be lined by epithelial cells.

Parenchyma

The lobules appear to be composed of cells & groups of cells distributed in an insular arrangement in the meshes of the interstitial tissue. The lobules are so broken up by the connective tissue that it is very difficult to distinguish the separate lobules, many of the cells contained in this tissue appear to be atrophied probably from pressure. A great number of the cells appear normal. No where can I see any infiltration of the tissues with bile, but here & there I have found some of the cells containing fat granules. This latter condition of the cells Hand. Cornil Hayem & others say never exists in a true case of Hypertrophic Cirrhosis

This condition of the liver appears to be caused by an inflammation affecting chiefly the interlobular bile duct & I have no hesitation in saying that in this specimen just described the connective tissue is greatest around these ducts & appears to have spread along the minute bile ducts. The causation of this condition just described is attributed by several authors to microbic infection but the character of the micro-organism has not been made out., Adami an american author they state that he has found in Bovine disease of Cattle a diplococci & also a Diplo-bacillus & he argues that as he has been able to discover this in cattle it is not unlikely that they would be found in man. I may say that in this disease, case there is very marked cirrhosis of the liver & it was from the juice of the liver that he made his cultivations.

No. 3534.



3534. A case of Biliary Cirrhosis in a child stated to be 8 years of age, the condition being probably due to poisoning through hair dye. This specimen shows retention of bile.

Capsule

There is slight thickening of the capsule

Connective Tissue

Immediately beneath the capsule there is a great increase of connective tissue, in which one finds a few atrophied & normal liver cells. These being probably the remains of atrophic lobules. This connective tissue is greatly infiltrated with round cells & is very vascular, the tissues being engorged with blood, some of which has extravasated into the cellular tissue. In this connective tissue one sees great numbers of small bile duct which are seen to be filled with bile. The cellular tissue being also infiltrated with bile. This connective tissue extends into liver as large bands, cutting off & surrounding the hepatic lobules, in some places one, in others a number of lobules. Fine bands of this connective tissue are seen extending into the lobule itself, cutting off portions

of the lobule in some cases cutting off & surrounding the hepatic cells & as a result some of the portions of the specimen appear to be a diffuse stroma of connective tissue in the meshes of which one seen atrophied & degenerated liver cells. The connective tissue surrounding the vessels in the portal zones is greatly increased in amount. Throughout the specimen the connective tissue appears to be engorged with blood & bile. There are present also in the specimen great numbers of the so called newformed bile ducts, which are distinctly seen to be formed from atrophied liver cells.

Blood vessels.

Hepatic Artery

The walls of the artery show great thickening & the lumen is narrowed & surrounded by a Barbera circular band of connective tissue

Interlobular vein

The interlobular vein is dilated its walls in some parts of the section are greatly thickened & show signs of inflammation

Intralobular vein

Shows nothing abnormal where one is able to distinguish it.

Bile ducts

This specimen does not show any large ducts but the largest ducts which I examined show marked inflammatory changes. Their walls are very greatly thickened, their epithelium is proliferated has become detached & shows very marked granular change. The small ducts show proliferation & a swollen condition of the epithelium, the lumen of the ducts are in a great number of cases obliterated. The small bile capillaries are seen to be dilated & filled with bile pigment &c. The meshes in the cellular tissue are filled throughout with bile

Parenchyma

On looking at the stained specimen with the naked eye; one sees pale areas. scheated in a darker substance, these pale areas. represent. hepatic lobules, some of these areas. vary from the size of a small pea to that of a pen head. One can also make out the dilated interlobular vein

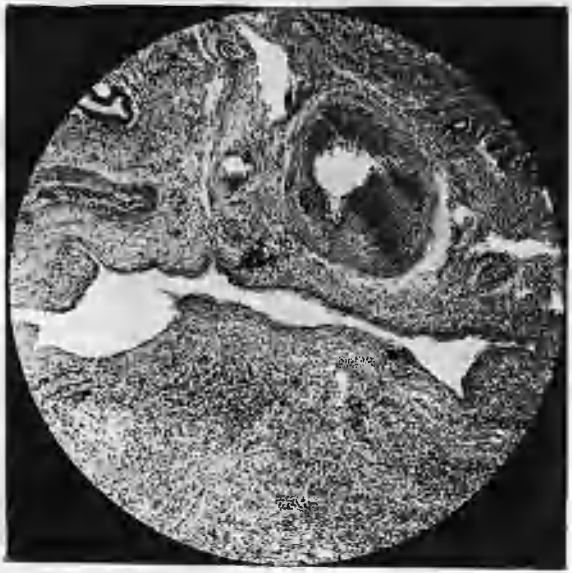
Microscopically.

One sees a great loss in the hepatic tissues In some parts of the specimen one sees a group of lobules in other parts single lobule

& still in other parts small portions of lobules even single hepatic cells; surrounded by connective tissue & In some of the portions of the specimen where the lobules are most normal, the hepatic cells do not show any abnormal characters. retaining their columnar arrangement. Other lobules show degenerative changes, the both fatty & granular. the cells found in the meshes of the connective tissue are greatly atrophied & one can easily see their transformation into the so called new formed bile duct

This specimen has many of the characters similar to cases of phosphorus & arsenic poisoning The presence of some powerful poison or constant (probably arsenic lead?) circulating in the blood causing inflammation of the vessel walls & a great emigration into the tissue of leucocytes. The presence in the tissue of a large amount of yellow pigment granules together with the inflammatory changes of the bile ducts & obstruction in some of the duct. The Cerrhosis in this case is of Biliary origin but the great loss of the hepatic tissue is probably due more to the presence of the poison in the blood than to compression by the connective tissue

No. 784. Syphilitic Gumma in Liver



No 784. Syphilitic Gumma in Liver + Cirrhosis

Capsule

There is no increase in the thickness of the capsule but its surface is nodulated

Connective Tissue

Proceeding from the capsule one see bands of fibrous tissue which enter the liver intersecting the lobules + from these bands we see prolongations of new connective tissue passing into the lobule surrounding the hepatic cells This fibrous tissue is very vascular + its nuclei are well defined
The connective tissue in the portal zones is greatly increased the nuclei of the connective tissue cells are very distinctly seen + the surrounding tissue is greatly infiltrated with round cells

Blood vessels

Hepatic Artery

The artery show very marked changes, there is thickening of its coats especially is this well seen in the inner + outer coats. The lumen of the artery is nearly obliterated, the arteries being in a state of end arteritis obliterans, the artery + vessels in the portal zones are surrounded by dense masses of fibrous tissue

Interlobular vein

In some cases the vein appears like normal others it is dilated

Intralobular vein.

In this specimen I had great difficulty in making out the vessel at all but where I was able to distinguish it, I could find nothing abnormal

Bile duct

Large duct

Its walls are thickened this is especially well seen in some parts of the section. The epithelial cells are swollen, show marked proliferation & also show granular & fatty degeneration. One of these ducts is entirely filled with detached epithelial cells in various stages of degeneration

Smaller ducts

They are very numerous. Their epithelium is swollen & shows proliferation, The lumen of the duct is still visible but greatly narrowed

Parenchyma

There is great loss of hepatic tissue, the lobules are surrounded with connective tissue

forming a condition of pericelular cirrhosis but from these circling bands one sees growing connective tissue growing into the lobule & breaking up to surround the hepatic cells. The hepatic cells show atrophy from pressure, they also show in some parts fatty changes. Here & there throughout the section one sees masses of caseous matter surrounded by dense masses of connective tissue these are the gummata, the centre of these masses show fatty changes

In this specimen we see great numbers of the so called newformed bile duct

This specimen shows very markedly that this cirrhosis is not due primary to the bile duct but rather to some poison circulating in the blood this is shown in the fact that the arteries have been most effected. There is no doubt however that the poison has also effected the bile duct which are in an inflammed condition, some of these showing degenerative changes in their epithelial cells & these may have had an additive influence in the causation of the cirrhosis. In over two of the sections I found one or two of the small bile duct completely plugged with a bilious concretion

Literature on Angio-cholitis & the secondary states produced in the liver, as the results of the angio & peri angiocholitis

Charcot. maladies du foie 1877.

This book I translated & make the following extracts

From page 163. As a result of obliteration of the Common bile duct you get distention of the duct beyond the seat of obstruction, soon this distention effects the intra hepatic ducts & there it produces an alteration of the liver which is sometimes designated as "Icterus of the liver" & Biliary congestion of the liver. The surface of the liver is smooth, never granular, it is yellow in colour, dark green or olive. The lobules are ill distinct & the green colour is most marked in the central parts of the lobule. The bile ducts of a certain calibre are dilated & there may occur biliary apoplexy especially on the surface of the liver (This I have seen in my own specimens) or it may be forced in the parenchyma of the liver. There is an increase of the connective tissue throughout the whole organ, this is best seen in the portal zones extending around the bile ducts & then extends more or less into the fissures in such a manner as to sometimes surround the lobules in its whole extent & as a result we get the progressive narrowing of the hepatic parenchyma but never breaking out like Common Cirrhosis in the

formation of hepatic granulations.
There is also pigmentary infarctions which fill the bile capillaries. Sometimes the hepatic cells are destroyed & replaced by fatty granules.

These facts have been recognised by est

1. T. Williams. On the pathology of Cells. Guys Hospital Report. Oct 1874
2. Budd. 2nd Edit p 243-244 (Glage LIV XII Taf ii aran Gaz des Hopit 1860

Frerichs also admits in certain cases that there is a total destruction of the hepatic cells.

In a case of which I show a microphotograph, this is well shown it is from one of the specimens which I took for this thesis (no 3741).

The dilatation of the bile ducts appear to effect specially the large ones, those which lodge in the portal spaces being comparatively loose, in their connective tissue sheath, extend as they do not at the onset encounter the resistence offered by the parenchyma of the liver. The interlobular ducts only undergo on the contrary a comparitively slight distention.

This dilatation of the bile ducts never fails sooner or later lobe followed by an alteration more or less well marked in the walls of these ducts & also in the character of their contents (Angio cholites)

When the common bile duct is ligatured

in animals & when killed 12 to 15 days afterwards the walls of the dilated passages were uniformly covered by a regular cylindrical epithelium, the bile enclosed in the ducts at this stage does not offer any well marked features except for a certain amount of viscidity. In men the conditions are not quite the same, in the principle ducts, the cylindrical epithelium has more frequently disappeared & one meets here & there shreds of epithelium in a semi liquid material which fills the ducts. This condition is seen in (4431)

Frerichs.

He states that the cylindrical epithelium is replaced by a flat epithelium. but in my observations I did not find this so.

On the contrary the cylindrical epithelium is preserved in the interlobular ducts, only in place of being lined regularly, one sees the cells sometimes massed together in such a manner as to obliterate the lumen of the duct. whilst at other times the obliteration is caused by a substance which appears to be composed of muco pus bile pigment, the fibrous walls of the bile ducts both large & small is notably thickened (These latter conditions of the epithelium, duct walls, & contents I have confirmed in my own (specimens) (observations.

M. O Wyss.

He states that there is no doubt. that this obstruction

of the small bile passages has often the result of separating in some manner the secreting portion of the liver from the excreting portion. In

In these circumstances Frerichs states that whilst the bile capillaries in the lobule are distended with bile the large ducts are filled with a mucous liquid uncoloured, & this does not disclose the least trace of bile pigment or acids by reagents. This is however rare most commonly the dilated passages contain a viscid bile in which float mucous masses, some flat masses of cylindrical epithelium & often also biliary concretions. At other times again, although rarely, the ducts contain muco-pus but you may say that in such a condition one has a true case of Suppurative Angiocholitis Cancer of the head of the head of the Pancreas sometimes produces this condition. (No 5714 shows this condition)

Ziegler's Pathology (Special)

Chronic retention & stagnation of the bile may lead to degeneration & inflammation of the liver, in other words to Biliary Hepatitis. This condition is equally liable to supervene whether the obstruction is in the Common bile duct outside the liver or in the interlobular ducts. It is thus possible for an original haematogenous hepatitis giving rise to retention of bile & become at length complicated by a secondary Biliary Hepatitis. The causes which determine whether retention of bile shall be long tolerated without appreciable

consequences or shall after a time give rise to Hepatitis cannot in all cases be determined, But it is no longer doubtful that for the induction of Suppurative Hepatitis some form of infection must be superadded & that the usual infective agent is the Bacillus Coli Communis. This microbe entering the bile channels from the bowels sets up in them cholangitis (Angiocholitis) or inflammation of the duct, then hepatitis as a consequence In certain cases other organisms such as the Pyogenic Micrococci, The Typhoid bacillus or the parasites such as Distomata gain access to the bile ducts & acts as excitants of inflammation

Gallstones in the Common bile duct favour the entrance of organisms from the intestines through the duodenal orifice into the bile duct

Mayo Robson says in his book on Diseases of the Gall bladder & bile ducts that Block has demonstrated that the bile in cases of disease of the Gall bladder or Bile duct always contains micro-organisms When the flow of bile along the duct is arrested micro-organisms often invade the gall bladder & duct either from the blood or intestines

Charcot & Gombault (Arch. de Physiologie et Pathologie 1876 (p 153) demonstrated the organisms in the gall bladder after ligature of the Common bile duct in the dog.

Netter in 1886 (Progres Medic 1886 p 992) confirmed this. He found in 24 hours after a septic ligature of the Common bile duct in dogs, organisms both Staphylococcus

+Bacillus Coli Communis could be cultivated from the bile + Of course The Bacillus Coli Communis exists normally in the human body

The inflammatory lesions resulting from the distention of the bile duct is not limited to the walls of the ducts themselves, they extend to the neighbouring parts causing the condition know as Perihepatitis & further also causing suppuration which presents itself under 2 principle forms

I. Sometimes one sees it occur in the neighbourhood of an ulcerated bile duct, as a large single abscess, the point of origin being probably an embedded calculus in an infected duct. Mr. Niemeyer states that the majority of large abscesses of the liver in our country have this origin

II. Sometimes it arises as small multiple abscesses scattered throughout the liver substance + also on its surface. On account of their size they are spoken of as Miliary abscesses. These are pesiform & lenticular in shape; they rarely exceed in size that of a haricot bean + They have been also called Biliary abscesses because of their contents which appears to be made up of pus + bile + These abscesses are visible to the naked eye, but there are others

which can only be seen under a microscope

It is easy to state in a superficial examination that these small abscesses arise close to the walls of the bile duct to which they appear connected Cruveilhier believes that these abscesses really occur in a dilatation of a duct filled with muco pus mixed with bile

One can easily follow all the phases of the formation of these abscesses, In the preparations which have been furnished by M. Malassey & in the sections of M. Gombault. the latter got from a subject who had died from Obliteration of the Common bile duct. by Calculus. In these specimens of Gombault the following phases were seen

1. The Cylindrical epithelium is most frequently preserved in the bile ducts
2. Embryonic cells & leucocytes accumulate in the neighbourhood of the duct. This mass of cells predominate on one side of the bile ducts
3. In a more advanced stage true globules of pus are formed frequently loaded with bile pigment in the centre of this mass of cells
4. The leucocytes agglomerate themselves forming finally a true abscess which penetrates into the substance of the lobule, crowding upon the hepatic cells which they flatten & dissociate
5. It is easy to recognise that the hepatic cells do not

take any part in the formation of these small abscesses

These small abscesses must not be confounded with the abscesses of purulent infection. These when they are superficial may be the point of origin of an adhesive peritonitis & their contents may open into the peritoneal cavity & form encysted abscesses of the peritoneum

Leyden. Charcot & Gombault. have produced experimentally biliary abscesses by ligaturing the Common bile duct in animals

As a further result of the Angio & Periangiocholitis one may find phlebitis in the branches of the portal vein, this is due to the close apposition of the branches of the portal vein with the bile ducts in the portal spaces. This I have noticed myself in the specimens which I have examined

As a result of occlusion of the Common bile duct & dilatation of the bile duct & stagnation of the bile, one gets the formation of Biliary concretions in the interhepatic biliary ducts. These are formed in 2 ways.

1.

Sometimes the calculi which are formed in the Gall bladder do not pass thro the Common bile duct but rise up into the Hepatic duct even.

into the liver where they are embedded in the ramifications of this latter duct. These intra hepatic calculi which can describe as a whole in order possess the physical & chemical characters of the Gall bladder concretions

2. Sometimes the intra hepatic calculi are on the contrary "Autochton" that is formed on the spot in consequence of the dilatation & inflammation of the bile ducts. As a result of obliteration of the Common bile duct we get fine biliary concretions which are often seen when there has been a stasis of the bile in the hepatic duct. At other times there is produced in the same manner a biliary mud or maybe true concretions more or less consistent. & sometimes laminescent. representing in some degree the internal mould of the duct where they have been formed. These concretions have never however a radiated structure, concentric lamina, or facets which distinguish the calculus formed in the Gall bladder.

The existence of true concretions of small size in the intra hepatic duct is rare

Frerichs mentions them 3 times

Thudicum " " 5 times in a 100 cases

The fine gravel on the other hand is very common

The next result is the formation of a condition known as Cerrhosis but before going on with the special form of Cerrhosis which my specimens show I will give the chief histological characters of the different forms of Cerrhosis Charcot & Gombault - divide Cerrhosis into 3 kinds

1. Multilobular, Venous or Atrophic Cerrhosis (Alcoholic)

This form is characterised by depositions of the newly formed connective tissue round the smaller branches of the portal vein, The bands of the fibrous tissue surround here several lobules of in the form of a ring, though smaller & thinner bands penetrate between the several lobules

2. Monolobular or Biliary Cerrhosis

This form is characterised by the development of fibrous tissue round each lobule. The newly formed tissue is formed round the interlobular biliary ducts, which themselves are found in a state of proliferation forming a network of thin walled canals in the interlobular spaces & are found filled with cubical epithelium. This form of cerrhosis is found idopathically as the hypertrophic cerrhosis a rare disease, described by Cornil & Hayem especially by Hanot (These de Paris 1876)

is characterised by persistent jaundice, permenent enlargement of the liver & absence of ascites. The histological changes found in this disease are also found in cases from obstruction as observed by.

1. Mayer. (Wiener Med. Jahrb 1872 ii)
2. Wickham Legg (St Barth. Hosp. report Vol IX)

in the livers of animals whose Common bile duct has been ligatured during life

3. The Pericidular Cirrhosis

The fibrous tissue in this form is found round several cells of one lobule, This form of cirrhosis is chiefly found in cases of congenital syphilis

The form of Cirrhosis which is present in the greater number of my specimens is Biliary in origin but I have others for comparison. I shall now go on with causes & effects of Biliary Cirrhosis

As a further result of this Angio & Periangiocholites is the formation of a condition know as Cirrhosis

Charcot & Gombault (Arch de Phys. normal et. path. 1876.

They obtained by ligaturing the Common bile duct in animals a form of monobobular or biliary cirrhosis. which is characterised by the development of fibrous tissue round each lobule. The newly formed tissue is formed round the interlobular biliary ducts, which are themselves found in a state of proliferation forming a network of thin walled canals in the inter-lobular spaces & are found filled with cubical epithelium These histological changes were found in cases of jaundice due to obstruction. They were also observed. in the liver of animals whose Common bile duct had been ligatured during life by. Mayer & Wickham Legg.

Litten (loc cit).

Litten made cirrhosis from biliary obstruction the subject of an experimental & clinical study & found on repeating the ligature experiments that when operating antiseptically, he was not always able to produce biliary cirrhosis & that occlusion of the Common bile duct without ligature (by the application of croton oil to the duct) was in itself sufficient to produce biliary cirrhosis & proliferation of the biliary canals. From these & other observations on human livers where there was more or less interstitial

Mayer. (Wiener Med Jahrb 1872 ii)
Wickham Legg (St Barth. Hosp Report Vol IX).

hepatitis without stagnation of bile Litten is inclined to agree with W. Legg in considering that the proliferation of the bile ducts is secondary to irritation by an inflammatory process affecting the perilobular fibrous tissue

Litten further observed 3 cases of mechanical obstruction of the common bile duct, which were followed by distinct atrophic cirrhosis with all the clinical symptoms & where after death marked proliferation of the biliary ducts & the changes of atrophic cirrhosis were found & by the light of these observations disputes the distinction made by Charcot between biliary & portal cirrhosis, at least as far as the biliary cirrhosis due to mechanical obstruction is concerned

Dreschfeld (Journal of Anatomy & Physiology XV. 1881)

He examined many livers where there was mechanical obstruction to the flow of bile from the most varied causes. In some of these neither monolobular cirrhosis nor proliferation of biliary ducts were found (notably was this the case in some of the cases of obstruction due to Gall-stones, in a case of pressure caused by an intrahepatic cyst (hydatid), & a case of simple inflammatory occlusion of the common bile duct & In other cases both Cirrhosis (monolobular) & proliferation of the bile ducts were well seen

The cases were 1. 2 Cases of Cancer of the Gall bladder with secondary deposits in the liver

2. Cases of Gall Stones.

3. 3 Cases of Cancer of the head of the Pancreas obstructing Common bile duct

He further states that the absence of the monolobular cirrhosis in some cases is not easy to explain, it is certainly not due to the short time of obstruction, as some of these cases were jaundiced for months, nor is it likely to be due to a propagation of the inflammatory process from the larger to the smaller ducts, or to the irritation set up by such a process as Litten & Wickham Legg suppose, for he found it wanting in the very case where the common bile duct was occluded & adherent to the surrounding structures by a simple inflammatory process. As it is only found where there is also interstitial monolobular hepatitis it is not improbable that it is secondary to this inflammatory process & might be compared to the proliferation of the alveolar epithelium of the lung in chronic lung affections characterised by an increase of fibrous tissue round the alveoli & to the alteration in the renal epithelium in cases of Interstitial nephritis a point to which Prof Charcot has often drawn attention

There is a type of Monolobular or Biliary Cirrhosis which is found in the liver (& is known) idiopathically, as the Hypertrophic cirrhosis, a rare disease described by Cornil, Hayem, & especially Hanot. This form is characterised during life by persistent jaundice persistent enlargement of the liver & absence of ascites Microscopically,

There is a diffuse & very abundant increase of the connective tissue without any obstruction to the bile flow in

in the larger ducts & the perfect preservation of the hepatic cells which have no tendancy neither to undergo fatty degeneration nor to be infiltrated with pigment

According to Cornil, Hanot, Charcot & Gombault, although no obstruction to the secretion, nor inflammation can be demonstrated in the larger bile ducts, the interlobular canals become dilated & ramify into finer ducts, forming immediately in front of the margin of the lobule, a network from which finer branches proceed to disappear between the hepatic cells. All these canals are lined with cubical epithelium. In the ultimate division, the calibre often appears to be plugged by this epithelium. In the vicinity of these canals the indications of the newformation of connective tissue are the most distinct. According to the above authors the network of the finest bile ducts lie already in the peripheral zone of the lobules where hepatic cells have here been compressed by the proliferating connective tissue & reduced to atrophy. It is consequently none other than the network of bile capillaries which in some unexplained way have acquired an epithelial lining

Hanot as well as Charcot & Gambault base upon these appearances the theory that in the cases of hepatic cirrhosis hypertrophic cirrhosis, accompanied with early Icterus, the primary lesion consists of infla. Spontaneous inflammation of the inter lobular bile ducts, induced by some unknown cause & that the interstitial inflammation takes it start from the walls

of these ducts, They therefore distinguish Hypertrophic Cirrhosis with Icterus as a special form & include it in the same group with Interstitial Hepatitis due to closure of the Common bile duct, in which they have found similar changes of the inter & intra bile ducts. This group they separate as Cirrhosis of biliary origin or Biliary Cirrhosis. from the ordinary cirrhosis in which the proliferation begins in the vicinity of the interlobular veins, As regards the remaining Anatomical & Pathological changes in Hypertrophic Cirrhosis of the liver with Icterus. The enlargement of the liver is the most noticeable, the form of the liver is not perceptably alterated; the free margin is sharp the outer surface = often smooth & the cut surfaces present now & then somewhat prominent parenchyma islets, varying in size from a hemp seed to that of a poppy seed. & between these islets are found crossed pieces of fibrous tissue broader than the former by 4 or 5 times,

Microscopically

The lobules appear to be composed of separate groups of cells. distributed partly in insulas from in the interstitial tissue. dissolved & so changed in structure that the central vein was nowhere recognisable or only

partially so. In many lobules the capillary vessels were dilated, The connective tissue is very considerably increased, was composed of fibrous & spindle shaped cells & exhibited along principally the course of the vessels. a finely cellular infiltration The hepatic cells were here & there atrophied but on the main however well preserved, & were neither infiltrated with fat or bile pigment.

The Interlobular Bile ducts appeared normal but in some cases were filled with bile pigment concretions.

Hanot says the bile capillaries are encircled with connective tissue which runs round the lobules. as bands & sometimes forming islands

The walls of the bile capillaries are thickened & the epithelium is swollen & the transverse & longitudenal sections show the canals to be distended.

In the connective tissue between the lobules the bile ducts show themselves in great numbers.

If the greater part of the lobule is not interlaced by the connective tissue, several may be completely enveloped without any bands of connective tissue projecting into their interior, They may have kept their original size or they may be from $\frac{1}{2}$ – $\frac{1}{3}$ of their original size

The Two principle & absolutely distinctive characteristics of this process are

1/ I.

Angiocholitis & Periangiocholitis of the small bile ducts in the portal spaces.

II.

The preservation & normal condition of the greater number of the hepatic cells, a certain number of them presenting a true hypertrophy

III.

The formation of newformed bile ducts is met with most forms of cirrhosis; acute & chronic lesions of the liver, but in none to such an extent as is found in Hypertrophic Cirrhosis with Icterus

Let us insist says Charcot. on the character of the limitation of the lesion to the bile duct of the portal spaces. The rest of the bile passages remain quite normal

2/

The proliferation of the Connective Tissue in the portal spaces is clearly best marked around the Bile ducts from which it extends in a diffused manner across the hepatic lobules.

The Subhepatic Region remains generally free from all proliferation

m. Hanot. Thése de 1875

Hayem has pointed out in the above Thesis & Ackermann has observed. contrarily to that which is seen in ordinary Cirrhosis., that the greater part of the hepatic cells preserve their normal characters, they are neither atrophied nor degenerated neither are they infiltrated with fat or various pigments These anatomical & pathological characters seem absolutely certain, they have been found over & over again by different authors when the cases have been genuine cases of hypertrophic Cirrhosis of the type we describe here

The Gall bladder does not present any lesion in this Cirrhosis The large blood vessels & bile ducts (large) are normal There is a total absence of amyloid degeneration

Hanot & Schmann

They state that there is a greater layer of Connective Tissue around the bile ducts with portal zone than there is around the portal vein

Luckermann

has not been able to discover this

Hanot. says that nowhere does the Connective Tissue show such development as it does in the portal spaces. & here we find the elementary

Structures

The Portal vein, branch of Hepatic artery & the bile ducts
He says that the eye is most struck on examining a stained section by the intense colour & thickness of the walls of the bile ducts, In each space he says one counts 1, 2, or more groups of bile ducts of considerable size each surrounded by a thick sheath of connective tissue. The lumen of the duct is lined by one or two layers of cubical epithelium highly coloured with well marked nuclei. The colour & thickness of the walls of the portal vein which are still thicker than in the normal state. The bile duct being about twice as thick as the branches of the portal vein

We have also a form of Cirrhosis caused by Syphilis. We recognise two forms of Syphilitic Hepatitis

1. Diffuse Syphilitic hepatitis
2. Circumscribed or Gummatous hepatites

1 Diffuse Syphilitic hepatitis.

This is observed as a concomitant of congenital lues in still-born children & in such as die a few days or weeks after birth & who come into the world with all the marks of syphilis upon them

Microscopical Characters.

There is a great increase in the connective tissue in the portal zones, apparently continuous with the perilobular tissue, a quantity of clear looking material with numerous nuclei, between the clear bands are seen masses which under high power are seen to be rows of liver cells which are undergoing more or less marked changes The interlobular connective tissue is seen to be almost everywhere broader & studded more or less abundantly with finely granular roundish & spindle formed cells. In the acini are found small groups of cells arranged in regular order around the capillaries, completely taking the place of the hepatic cells or crowding into them to a variable extent, so that they appear to become flattened & frequently afford evidence of different

stages of simple & fatty degeneration, The newformed cells in the intra acinous structure lie in the plainly perceptible connective tissue (Wagner Loc Cit S 240) which is developed either directly from the walls of the capillaries or from the interlobular connective tissue, Situated along its course we can often distinguish a structure such in cells growing into the interior of the acini from the periphery

As a consequence of the shrinking of the newly formed connective tissue, branches of the Ductus hepaticus may undergo a cicatrical constriction & as a result you would get pigmentation of the hepatic cells & also icterus

The close resemblence presented by diffuse syphilitic hepatitis to the early stage of ordinary interstitial hepatitis, seems to justify the assumption that when the affection is of long standing the livers must exhibit an appearance completely identical with the typical form of ordinary Cirrhosis

Circumscribed or Gummous Hepatitis

This condition has often been observed in childhood aswell as at a mature age & constitutes in connection with the lobulated livers, which represents its terminal stage, the most frequent form of Hepatic Syphilides

There are commonly found in the hepatic structure that in other respects is either normal, consecutively hypertrophied, or rarely many gummous nodules, varying in size from a pea to a hens egg

Microscopic Characters.

On examining a section of liver in which is one of these nodules, it is seen that the formation of a gumma is preceded by a syphilitic cirrhosis identical with that already described, but that at certain points the development of the fibrous tissue has taken place to such an extent that there are numbers of strongly marked fibrous bands intersecting the lobules & cutting up the liver tissue. These fibrous bands are very vascular. In the fibrous bands & around the vessels the first trace of the developing gumma is the appearance of a number of deeply stained embryonic cells, forming a ring which gradually increases in diameter & as this extends peripherally, the cells near the centre become angular, granular & atrophied. At this stage the gumma is an actively growing mass of connective tissue & Whilst the growth is going on in the gumma, certain changes are also to be observed in the vessels in the immediate neighbourhood

1 The walls are thickened & the increase is principally in the intima or with the internal elastic lamina, in

some cases the thickening of the intima is so great that the lumen of the vessel is almost obliterated & when it is not complete there is frequently a coagulum fixed in the lumen which would prevent the passage of the blood thro the vessel ; The outer walls of the vessel appear to be practically continuous with the gummatous growth & it is highly probable that the caseation which almost invariably ensues in gumma of the liver is brought about

1. By the contraction of the tissues at the periphery of the gumma itself & of the fibrous tissue surrounding it
2. By the Endarteritis obliterans causing the stoppage of the vessel
3. By the formation of a coagulum on the roughened or inflammed walls.

As soon as the blood supply to the gumma is cut off. Fatty degeneration, followed by caseation, later usually by absorption & cicatrisation

Psorosperms & Distomata in relation to Angiocholitis & Cirrhosis

Psorospermosis

Psorosperms are egg shaped bodies. 0.03. to 0.04 m m long & 0.012. to 0.02 m m broad with a uniform outlined shell, & granular contents, The latter either fill the entire cavity or is merely rolled up in a roundish little heap, while the rest of the space appears clear.

Eimer says that these Psorosperms are Sporozoa at rest

Leuckart. Parasite of man 1144. Psorosperms have only been found twice in ~~man~~ liver of man, The first is reported by Pulber. (Mém de la Soc. de biologie 1859. T V p 61.) Leuckart. (Parasiten ii p 741) reported the second, They are very common in rabbits (a case of which I shall show a microphotograph of. is from the liver of a rabbit) In such animals the biliary passages in the congested liver appear as sausage like distended yellow pouches. On being cut across a fluid resembling pus escapes from them, which, besides pus corpuscles & epithelial cells, contain enormous quantities of the structures in question

The wall of the Coccidium nodule consists of thick fibrous mass of Connective Tissue with frequent nuclei & fibres usually arranged concentrically

Besides numerous blood vessels, one can sometimes recognise, especially towards the periphery, smaller & larger groups of liver cells & of bile ducts which although enlarged in varying degrees maybe only slightly changed & often still continue a regular columnar epithelium. The proliferation of the Connective Tissue takes place not only outside the nodules, but extends also along the duct into the remote recesses. Where the acini are usually found crowded into close layers one finds in the diseased liver numerous bands of Connective Tissue of varying thickness which are embedded between the nodules. These enclose a number of bile capillaries which are often separated from one another only by their septa but here & there include little areas of liver substance between them. These are essentially the same changes as are observed in cases of severe hepatic cirrhosis except that in the latter the degeneration is restricted to this stage of development.

Neumann Parasites & Parasitic Diseases of Domesticated Animals

. States that the hepatic lobules undergo various changes. Sometimes they are replaced by Connective Tissue as in Biliary Cirrhosis, at other times they are atrophied by the peripheral compression of the parasitic cysts or by hypertrophy of the interlobular Connective Tissue.

Distomatosis

Zenker's Diseases of the Liver & Fatal Hem (Cyclopaedia of the practice of Medicine 1880.
Distomatosis

Vol. 6 p. 674. The changes produced by distomata in large numbers consists of a chronic cholangitis, with considerable fibrous thickening of the walls of the bile ducts & separation of a mucoid or purulent secretion at the surface of the mucous membrane which accumulates in the canals & dilates them. The distomata can probably not produce direct occulsion of the bile ducts but it is possible that they may indirectly, by means of the cholangitis, lead to closure of the excretory duct. as occured in a case of Bleimer's

Leuckart's Parasites & Parasitic Diseases of Domesticated Animals
States that the mucous membr of the bile ducts is everywhere tumefied, injected, ecchymosed & sometimes torn. The epithelium has been removed by catarrhal desquamation which often assumes a purulent character. The hyperplasia of the walls of the ducts may intrude on the surrounding tissues & act in the manner of a destructive adenoma (Bollinger)
There are small haemorrhagic centres in the parenchyma
Over the entire liver the cells are granular, infiltrated with fat & the Connective Tissue is in a process of proliferation
In the later stages the lobes are absorbed the tissue is firm & hard. The Connective tissue hyperplasia

the cirrhosis is considerable

The Capsule of Glisson is very granular

The Bile ducts

are the seat of a dilatation that augments from their origin towards the periphery

The smallest ducts are dilated to their ends & have acquired the calibre of ducts of the first order.

Thomas. states that in some of the small bile ducts where the ova have not been floated away by the bile, these may be present in such enormous multitudes as to form a stiff dark mass looking like fine wet sand & completely occluding the duct.

The presence of the Flukes have been regarded as the cause of the formation of biliary calculi but only 2 instances in support of this view one furnished by Simonds & Brouisson who in such calculi have found the one 12 Flukes & the other only 1

It has been attempted to assign to Cirrhosis the alterations that occur in the liver under the influence of its invasion by Flukes. But the localization of these lesions does not admit of their being allied with either Hypertrophic or Atrophic cirrhosis, in which they are always diffused, otherwise the existence of ascites is sufficient to eliminate Hypertrophic Cirrhosis

Upon the existence of a minute Micro-organism associated with cases of Progressive Portal cirrhosis

J.S. Adami. Montreal Medical Journal July 1898

He has found in Pecton calle disease where the chief character is a peculiarly extensive cirrhosis of the liver, a certain micro organism which is rather difficult to stain & he thinks that if thus an extreme cirrhosis of the liver is brought about by proliferation in the tissues of a micro-organism it is possible to have similar results in man.

Hanot & the French pathologists have insisted that the form of Cirrhosis whose characters are a large smooth cirrhotic liver with jaundice, the form now spoken of as Hanot's cirrhosis is of infectious origin, though they have not been able to declare what is the microorganism causing the infection

No one has so far suggested that Common or so called atrophic cirrhosis is of microbic causation, The prevailing idea is that alcohol or other irritant by setting up a condition of chronic gastro-enteritis & mucous membrane of the upper part of the intestinal canal permits the absorption of toxic substances from the food these toxic substances taken up by the portal blood induce a surrounding chronic phlebitis with or without direct action upon the liver cells.

Adami states that during the last 4 years he has carefully

studied all cases of hepatic cirrhosis which have come to the post mortem rooms at the Royal Victoria Hospital In 2 cases in 1895 & 1896 he though he had gained cultures of a minute diplococcus but in a later case he was able to gain from an agar tube of the liver juice an extremely minute diplococcus staining with great difficulty & scarcely visible. He further states that he found in some sections of a Dr Abbott, on examining with $\frac{1}{18}$th inch immersion lens, a great number of minute microbes present as Diplococci with a slight halo round them, even smaller than those seen in Pictons cattle disease. They are very much smaller he states than the Diplococci of Pneumonia, Some were larger & more distinctly in the form of Dipo-bacilli Thus at the present time he would go so far as to say that in a certain number of cases at least of Lobnailed livers there are present in the liver, a minute micro organism resembling closely that found pathogenic in the infective cirrhosis of cattle, a form of which is present most frequently as a minute micro coccus but sometimes has a more bacillary appearance & which is thus to some extent polymorphous.

The development of the fibrous tissue in Cirrhosis

amilton" Journal of Anatomy & Physiology 1879 p 185

He believes that the greater part of the fibrous tissue in the cirrhotic tissue owes its origin to the liver cells themselves.

rice Guys Hospital Report XLII p 295 &c

He thinks it extremely doubtful that the greater part of the fibrous tissue in Cirrhosis owes its origin to the liver cells themselves. He has not been able to make out any connection between the fibrous tissue & the hepatic cells.

. J. Dreschfeld. Journal of Anatomy & Physiology 1881.

States that although he saw all the first changes in the liver cells described by Hamilton he has not be abe to satisfy ~~himself~~ himself as to the eventual conversion of the liver cells into fibrous tissue. In one of his cases. he states that the parenchyma of the lobule showed normal liver cells, atrophied cells & large masses of fat cells, throughout the greater portion of the lobule; at the periphery of the larger lobules & to a larger extent in the smaller lobules, the liver cells showed the nuclear changes, the proliferation, & the gradual change into biliary

canals, in other portions of the preparation the proliferating & many nucleated liver cells were seen to form spindle shaped bands, showing still the component cell elements, but somewhat compressed & elongated. These bands were seen in the circumference of the lobule, & also between tracts of more fully formed fibrous tissue in the inter lobular septa they were surrounded or compressed by fibrous tissue, but I have not been able to trace their conversion into fibrous tissue.

On the other hand even in this early cirrhosis the demarcation between the embryonic fibrous tissue & the liver parenchyma, except where obscured by the proliferating biliary ducts, was very marked & tracts of this tissue could be traced close to but still separate from the many nucleated liver cells quite into the lobule.

Furthermore, masses of embryonic cells were seen immediately around the inter lobular vessels & the tissue here seemed often of younger growth than that nearest the periphery of the lobules, which would not be the case if the theory that the fibrous tissue is formed from the liver parenchyma were the correct one.

One of the very marked features of Biliary Cirrhosis & which was well shown in the specimens which I have already described, was the formation of so called newformed bile ducts. I shall now give extracts from different authors on the subject.

Cornil. Archives de Physiologie (1874.)

He discovered & published his first work on the subject in 1874, he showed that they were met with in all forms of cirrhosis, but that it was in Hypertrophic cirrhosis that they were seen in greater abundance

MM. Charcot & Gombault. (Leçons sur les maladies du foie et des reins) Paris 1882.

They also agreed with this idea & admitted the proliferation of these duct as one of the principle characters of Hypertrophic Cirrhosis, but also noticed this proliferation in other conditions

Hanot & Schachmann. Hypertrophic cirrhosis with chronic icterus

H. de Physiol. 1887.

In the above thesis Hanot states that in the portal spaces one sees numbers of canals, formed by the apposition of a double row of cubical cells, highly coloured with well marked nuclei. These cells approach in such a manner as one asks himself if there is a lumen between them. These canals are sometimes straight & sometimes curved, they branch in the portal spaces & penetrate into the inter lobular

spaces but it has never been decided what the point of attachment is between the space between the hepatic lobule on the one hand & the bile ducts on the other, We have seen them in several sections taken from the periphery of the lobules & prolonged into the interior with the interacinous ramifications of the connective tissue Where the sections of these canals has been longitudinal & also transverse we have seen a very small orifice surrounded by 3 or 4 longated cells.

Breger like Charcot like Kiener & Kelsch have traced the proliferation of the duct quite into the interior of the lobules & believe that they are formed from hepatic atrophied cells.

Authors who have observed these newformed ducts in various affections of the liver

Wagner. Arch d' Heilk 1862 p 459.

Winiwarter. Wiener med Jahrbucher 1870 p 256.

Liebermeister Beitrage z pathol. Anat v Klinik der Leber Krankheiten 1864 p 38

Ackermann Virch arch 1880 p 435

Litten Charité annalen 1878 p 12

Breger Virch Arch. 1879 p 88

A. Tierfelder Atlas de Physiol 1876 p 6 3 2 et 7 7 1

Morin Dissertat. Lausanne 1876

Friedlaender Ueber. Epithelwucherung. u. Krebs Strasbourg 1877 p 46

Simmonds. Deutscher Arch f Klin Mediz 1880 p 23

Chrzonszczewsky Virch Arch (Potoff 1880 p 531.

These authors have observed them in various hepatic affections

Lenker Deutsch arch f ke med 1872 p 166.

Waldeyer Virch Arch 1868

Cornil Arch de Physiol 1872 p 402.

The latter have noticed them in acute yellow atrophy of the liver + in degeneration following phosphoras poisoning

Wangeldorf Deutsch Arch f ke med 1882 p 561

States that he has noticed this proliferation in all alcoholic cirrhosis + he has examined also found in Syphilitic cirrhosis, in cirrhosis which accompanys Tubercular peritonitis + in Hepatic atrophy due to pressure

Hanot

The frequency of these ducts of new formation in all hepatic diseases whatever may be their nature, Their direct connection with the bile ducts of the portal spaces + with the intralobular duct would rather lead us to consider them as old ducts put in evidence perhaps by the retcal. of the hepatic lobules + perhaps by the inflammation of the connective tissue in the midst of which they are found He asks whether there is going on in the small ducts a new formation or only the pre existing bile duct brought into evidence by the atrophy of the neighbouring tissues In a normal liver these duct are wanting + when Cornil

discovered them he advanced the hypothesis that the normal canals were rendered visible by the atrophy of the surrounding tissues

Cornil further states that these small bile ducts too fine to be distinguish in the normal state of the liver are brought to notice perhaps by the irritation which takes place in the diseased organ or perhaps by the breaking up of the hepatic cells between which they lie & which hide them but there remains an obscure point with to explanation. For in the normal state the extra lobular bile ducts are lined by cubical epithelium, whilst the intralobular ducts are reduced to the state of small openings cloked with flat epithelium of Lepros. . He thinks that the normal epithelium of the extralobular duct is extended into the intralobular ducts with which they are in direct communication

MM Charcot & Rauvier

They have examined the specimens of Cornil immediately ask if these canals were not derived by the budding of the extra lobular canals produced under the influence of chronic inflammation. If this hypothesis appears plausable in cases of slow development; it is difficult to admit it in the cases of acute Yellow atrophy, the development of which is too rapid for budding of this nature to have time to develope. The first hypothesis of Cornil

would appear to explain better the origin of these ducts

MM. Charcot & Gombault (Arch. de Physiologie 1876 p 290).

They ligatured the Common bile duct & in the midst of the alterations which were produced they both observed a rich network of bile ducts with cubical epithelium in certain parts of the periphery of the lobule & they were led able to state

1. A direct communication between the cells & the ducts The hepatic cells are progressively atrophied up to taking the appearance of a bile epithelial cell.

2. An anastomosis of one of these extra lobular duct with an interlobular one. all these ducts having besides a cubical epithelium

MM Charcot & Gombault thought that the coming together of the preexisting canals would only enter into the production of the phonemoma as a secondary element & wondered if these canals became a transformation of the interlobular canals, ignoring the origin of them by budding. As to the part played by the epithelium which lines these ducts of new formation they hesitate between two ideas

1. Whether the formative contation of the ducts provided by the epithelium was propagated from one place to another

2. The transformation on the part of the hepatic

cells themselves.

This latter hypothesis has rapidly gained ground & MM Keener & Kelsh proclaim it as an undeniable fact.

MM. Keener & Kelsh (arch de Physiolog (1876 p 777)

In a thesis on the newformation of Bile ducts they state that they have studied the newformation of bile ducts in 6 cases of Interstitial inflammation of the liver, associated with various alterations in the parenchyma, Adenoma, nodular Hypertrophy, diffuse inflammation & In several of these preparations one sees in the lobules swallowed up in connective tissue the cellular bridges replaced by small columns which are only other bile passages & which have a strong tendancy to become large. one follows them continuing the into the canals with fragments of hepatic columns left by the cirrhosis & The transformation of the hepatic cells into bile cells is progressive & would be prepared by the proliferation of the hepatic cells, accompanied by the atrophy of their protoplasm.

Klebs. states that the small ducts are only formed from the ved hepatic changed cells.

Charcot (arch de Physiologie) 1876. p 471.

In this he states that he adopts the ideas of Keener & Kelsch

Broeger

He also pronounces in favour of Kiener & Kelsch in cases of interstitial inflammation of the liver but admits that these ducts have various methods of development according to the different hepatic diseases in which they are formed.

1. Made at the expense of the hepatic cells, he believes that the liver cells become smaller & atrophic & arrange themselves in longitudenal rows which by simply leaving a lumen between the rows of cells would form biliary canals.

2. By the dilatation of the inter & intra lobular ducts

MM. Charcot & Gombault

They exclude any other method of development of the ducts outside of that of the transformation which takes place in the hepatic cells, after having established anatomically, the transformation of the hepatic cells, they examine the modifications undergone by the diverse elements of the liver & they show that the lobules are able to undergo not one but several alterations

In their sections they are able to state

see over

1. That certain lobules have been equally atrophied by the hyperplastic Connective Tissue which does not retain a trace of it

2. That certain other lobules have undergone pigmentary degeneration have finished up by being absorbed

3. That others & the greater number are transformed into Bile ducts

The authors do not state if around the degenerate lobules they have seen any bile ducts but the facts are numerous which answer affirmatively this question

T. J. Dreschfeld (Journal of Anatomy & Physiology. XV. 1881. pp 74 pp 75

States that he has had no difficulty, especially in the case of early cirrhosis & of fatty liver. To trace the proliferating biliary canals to the liver cells He says that he has noticed in his specimens at first a proliferating process in the liver cells of the peripheric part of the lobule; the nucleus of the liver cells enlarges to a considerable extent & takes the staining better than the nucleus in the ordinary

liver cells; then there are seen liver cells with two, four, or even more nuclei; next we have an endogenous cell growth from these nuclei; liver cells are thus seen, increased in size & longitudinal or oval in shape, filled with small cells each having a distinct nucleus & a small amount of protoplasm & resembling in appearance the cubical epithelium found in the nets of new formed biliary ducts close to the periphery of the lobule; & lastly, the direct connection of these proliferating cylindrical masses with small biliary ducts, already possessing a lumen, & lined by small epithelial cells, was seen, giving at first sight an appearance as if the biliary ducts terminated in club shaped blind extremities, as was described by Waldeyer in a case of acute yellow atrophy of the liver. I have no doubt that the formation of biliary ducts by atrophy of the liver cells described by Frieger & others, also occurs, & indeed in cases of mechanical obstruction of the biliary duct, I have seen an appearance much resembling that described by Frieger

These two modes of formation must likely correspond to two different pathological processes

1.

In the one case we have to do with active proliferation & new formation of biliary canals

2.

we have to do with a gradual change of the liver cells into bile ducts, due to atrophy of the cells by compression of the surrounding fibrous tissue

icate + Richaud (Arch de Phys 1880 p 303)

They describe a biliary cirrhosis in rabbits where the biliary ducts were the seat of parasites. They also trace the proliferation of the biliary canals from the liver cells, which undergo active nutritive changes + show fusion of protoplasm with proliferation of nuclei; small circular masses of embryonic cells are thus formed, which by the disappearance of the centrally situated cell + the change of the peripheric cells to epithelial cells, form thus biliary canals

I have found myself in all my specimens except one or two great numbers of these so called bile ducts. In two of them No 3634 4813 it is very plainly seen that these so called bile ducts arise from the hepatic cells. in 813 these ducts are seen in the lobule itself taking the place of the atrophied liver cells.

Summary.

It is very plainly seen in my specimens that in obstruction of the ducts when it is complete, be it due to Biliary Calculus. (Concretions) Inflammation or the presence of parasites, the result is the same namely that the ducts beyond the obstruction become dilated & filled ~~with~~ in the early stage with bile, if this obstruction persists, then you get Stagnation & Staining of the tissues with bile, producing what is known as Icterus of the liver. In one specimen there are present under the capsule extravasations of bile, the condition being know as Biliary apoplexy. When the obstruction has been of long standing & the bile capillaries between the cells are seen to be dilated & filled with bile granules. This dilitation of the bile ducts is seen best in the portal & inter lobular spaces. this being due to the lax nature of the tissues in which they lie. As a result of this stagnation the bile vessels become inflammed their epithelial coat become swollen & the cells proliferate; at a further stage, you see in the specimens the epithelial coat detached & thrown into folds. By this time the inflammation has also extended to the fibrous coat of the ducts producing thickening & later this inflammation extends into the cellular.

tissue in which the ducts lie producing the condition known as Pericanalicular Cholitis + As a result of this inflammation of the duct, an exudation takes place into the ducts + in one of my micro-photographs shows the duct filled with a fibrinous substance + In this inflammatory exudation which is seen in the ducts you see numbers of leucocytes + degenerated epithelial cells, the latter cells seen often in the specimen to completely occlude some of the smaller ducts + other ducts are seen to be filled with inspissated bile + In the case of Distomatosis you will see in the microphotograph the great thickening in the walls of one of the large ducts, the epithelium has been shed + its place is taken by layers of a fibrinous material

In none of the specimens except those which had been infected by micro-organisms did the ducts contain either muco-pus or pure pus. but in the specimen showing multiple abscesses, one of the abscesses is seen to be directly connected with a duct which contained granular material, muco pus epithelial cells in various stages of degeneration + great numbers of the micro organism (Staph Pyogens.) the latter being the infective organism which I believe had caused the abscesses + In this + other specimens, one sees around the minute bile ducts great clusters of round cells, these were seen to be situated on one side of the duct.

& some of these masses showed necrotic centres & were in my opinion the commencement of minute biliary abscesses.

As a result of inflammation in the bile duct extending into the cellular tissue we get Peri angiocholetis, this is characterised by the formation of new connective tissue, which tissue some authorities say is formed from the pre existing connective cells & others state that some of this newformed connective tissue is formed from the hepatic cells, the latter I have not been able to see. The condition of the liver in which there is this newformed connective tissue is spoken of as Cirrhosis of the liver. & the form of cirrhosis which is seen in most of my specimens is called Biliary cirrhosis, that is that the cirrhosis is secondary to the inflammation in the duct. In some of the cases this newformed connective tissue is seen to be greatest around the bile duct in the portal & interlobular spaces. produced the form of monolobular cirrhosis but as the inflammation has extended to the small ducts, connective tissue bands are seen to be prolonged from the interlobular bands into the lobule itself & later still between the hepatic cells, separating & surrounding the cells themselves, as a result of this pressure on the cells & their nutrient blood vessels by this connective tissue, we get the hepatic cells atrophied & in various stages of

degeneration, we also sees other changes as the result of this pressure by the connective tissue we see the dilatation of the interlobular veins due to pressure on the vessels inside the lobules; this obstruction to the flow, resulting in dilatation of the veins, must also if persisting for some time cause degeneration of the walls & this would account for the great infiltration of the tissue observed in some of the specimens with blood cells. In one case the vein is seen to be in a state of thrombosis, this being probably partly due to the inflammation having extended from the bile ducts to the vein causing phlebitis & this together with the slow circulation might easily result in thrombosis The arteries also show inflammatory changes in some of the specimens this I attribute to be due, more to some poisonous substance circulating in the blood. (In many of the specimens I think the blood being over charged with bile is the cause of the slight inflammation seen in the artery) than to the inflammation having spread from the bile duct, but the latter has had something do do with the thickening of the fibrous coat of the artery which is seen in some of the specimens x.

One of my specimens is a case of Hypertrophic cirrhosis, a special form of cirrhosis described by Hanot & others, &

my observations in this case quite coincide with those of Hanot, Charcot & others, except that in a few of the lobular cells I found small fatty granules, a condition which Hanot says never occurs in a true case of Hypertrophic Cirrhosis therefore I am bound to think that the case which I examined could not have been a true case of Hypertrophic cirrhosis as described by Hanot although otherwise fatty changes may be present although to no great extent.

One is struck on examing cases of Biliary Cirrhosis, especially that form know as Hypertrophic Cirrhosis, by the presence of duble rows of small cells, the so called newformed bile duct. These are also present in other affections of the liver besides Biliary Cirrhosis. There has been several theories as regards the formation of these so called newformed bile ducts but in my observations I am convinced that they are formed from atrophied liver cells. In the specimens 3534. & 813. they could be traced into the interior of the lobules, taking the place of the hepatic cells.

List of authorities referred to in this Thesis

Achermann. Virchows Archiv 1880 p 435

Brieger Virchows Arch. (1879 LXXV p88. + 85 + 93)

Beale Trans. Path Soc. 1889. & L p 337.

Charcot. Leçons sur les maladies du foie et des reins Paris 1882

Charcot & Gombault, Arch de Phys. et Pathol. 1876.

Cohnheim Translation by McKee / London. 1888-90

Cornil Journ. de l'anat et de la Physiol XVIII. Paris 1882.

Dreschfeld Some points in the histology of cirrhosis of the liver. Journal anatomy & Physiology 1881. p 74 &c.

Frericks Disease of the Liver 1861. Vol ii

Gerhardt Changes in livers after ligation of the bile duct A. f. exp. Pathol. XXX 1892

Hanot & Schachmann Hypertrophic cirrhosis with Chr Icterus. A de Phys. 1887

Homén. Influence of ligation of the bile ducts on biliary infection 1894.

Hanot. These de Paris 1876.

Hamilton. The development of fibrous tissue from the hepatic parenchyma Journal of Anat. & IV. 1879

Hayem Hypertrophic cirrhosis A. de Physiol VI. 1874

Kelsch & Kiener. Affections paludéennes du foie. Arch de Physiol normal. et. Pathol. 1879 normal p 185

Kelsch & Vanechoucq. Contribution à l'histoire de la cirrhose hypertrophique du foie Arch de Phys. normale pathol. 1881 p 800.

Legg. Ligation of bile duct St Barth Hosp Report IX London 1873

Litten Cerrhosis of the liver, Munch med Woch 1890

Lancereaux & Lackerbauer. Anatomie Pathologique

Mayo Robson Diseases of Gall bladder & ducts

Murchison Diseases of the Liver 1885 p 145 &c

Nicati & Richaud Biliary cirrhosis in Rabbits Arch de Phys VII 1880

Price Hypertrophic Cirrhosis, with remarks on the Pathology of Cirrhosis Guy Hosp Report. XLII p 295

Smith. Acute Biliary Cirrhosis Brit J. 1894

Saundby Note on the morbid Anatomy of Hypertrophic Cirrhosis Trans Path Soc. 1879. XXX p 307.

Sabourin Biliary abscess Le progrès med 1884

Thierfelder Ziemssens Cyclopoedia of Medecine (Trans) X p 1860

Ziegler. Special & General Pathological Anatomy. 1897.