Notes on the Pathological Effects of Alcohol.

Lewis A. Williams.
Chester.

Illustrated by microphotographs (of original sections made from Post-mortem Specimens) which are described at the end of the thesis.
The object of the following notes is to compare and contrast the various pathological phenomena exhibited in some of the chief organs of the body, produced by the ingestion of alcohol. The subject is of great importance, and of late years has been brought much into evidence by researches of many prominent observers. Clinically one is struck with the frequency of signs of irritative gastric disturbances, especially the vomiting in the morning, loss of appetite, etc., shown in patients suffering from the effects of alcohol either:

A. Taken in large quantities at one time — Acute — or

B. Taken in small quantities over very long periods — Chronic — The latter being the most frequent, and this not due solely to the inhibition of ardent spirits, but more often to the constant use, as beverages, of beer and wines.
Apparently the symptoms of gastric
disturbance reveal themselves earliest,
and long before we have any evidence
of hepatic trouble. Cirrhosis, etc.
and hence it is suggested to our
mind that certain pathological
changes must occur primarily in
the stomach.

On examining the stomach in chronic
gastritis caused by alcohol (as well
as by other irritative substances) we
find to the naked eye the mucous
membrane of the stomach is covered
with thick tenacious mucus.

On washing this away, the mucous
membrane appears red and swollen,
and contains primateform haemorrhages,
indicating inflammatory processes.

Microscopically, there is evidence
of round cell infiltration, increased
vascularity, thickening of the
mucous membrane, the thickening
being due to a sclerosis or increase
of the connective interstitial tissue
(fibrosis). And the essential gland
structure is seen to be altered, often becoming eroded or even disappearing altogether.

In some very chronic cases the thickening is often more marked and the vascularinity not so well marked, but in place of this are to be seen pigmented patches, giving evidence of former congestion and haemorrhages.

Occasionally small ulcers, haemorrhagic erosions are scattered over the surface.

The increase of connective tissue substance has been known to produce, especially in the pyloric region, a rough and wrinkled appearance; the increase of the connective tissue may take place both in the upper and lower layers of the mucous membrane, and in some cases this increase is so great that the walls of the stomach are greatly thickened, and the stomach itself diminished in size (Cirrhosis of the Stomach)
It is probable in comparing this evidence of profound gastric disturbance with the pathological appearances and clinical manifestations in cases of gastritis caused by the ingestion of other irritating foods and drinks, that the same immediate causes obtain in all these cases, namely:

a. Local irritation (direct) by the substance ingested.

b. Formation of poisonous bodies—poisons—formed by the abnormal fermentative processes occurring in the organ after the ingestion of such substances.

For example, gastric catarrh is very prevalent among the peasantry of Southern Europe where sour wines form important beverages. Sweet wines as used in this country are all acid to litmus paper, and dilute wines and spirits undergo acetie fermentation in the stomach, thus acting as acids
There is no doubt regarding the fact that if the stomach contents are excessively acid, especially if due to acidity produced by abnormal fermentation in the stomach following delayed digestion, that large and poisonous quantities of toxins (albumoses) must find their way to the other organs and tissues of the body.

**LIVER**

The changes produced by alcohol in the liver are several in number:

1. Fatty infiltration.
2. Fatty degeneration.
3. Cirrhosis, which may be:
   2. Multilobular
   3. Unilobular

The pathology of each will be considered; in each case the naked eye appearances, and then the microscopic
FATTY INFILTRATION.

The fatty liver is increased in weight; and, in extreme cases, it may be double its normal size; the organ is enlarged generally, rounded at the edges, and increased in thickness. Its consistence it is usually soft; and it has an opaque yellow colour. It is nearly always possible with the naked eye to distinguish evidences of the lobular distribution of the fat; and on looking closely we can distinguish the lobules mapped out in a most characteristic manner.

Microscopically, the liver can be seen to contain large quantities of fat, which appears first in the peripheral parts of the lobules, and from this it is inferred that it has been brought by the portal blood. This fat is deposited in the hepatic cells, at first as fine drops, but as more fat is added the drops...
grow in size, and as a rule the
drops of fat are much larger than
in fatty degeneration.
As the condition advances, more
and more of the lobule is affected,
and the infiltration may overtake
its whole extent. Even in extreme
cases however it usually preponder-
ates at the peripheral parts.
There is a tendency for each drop
of fat to gradually enlarge and
assume a considerable size; the
protoplasm of the cell being pushed
aside by the fat.
The changes which occur in the
lobule are somewhat as follows.
Fat globules appear in the liver cells
adjoining Glisson's capsule; these
globules enlarge and the protoplasm
of the cells diminishes in quantity;
the cells themselves increase in size.
The distended cells appear to
compress the capillaries in the outer
zone. The deposition of fat extends
to the intermediate and central zones.
and the capillaries and central vessels are compressed. In advanced stages the liver tissue closely resembles adipose tissue.

Prof. Seins Woodhead considers that we have in this condition an interference with the oxidation of the fat that is normally taken up by the liver cells, and an improper utilization of the fat that is brought by the portal blood to the liver cells; the accumulation of fat thus indicating impaired activity of the protoplasm of the cells.

**FATTY DEGENERATION.**

Occurs often associated with the former condition, but latter may occur singly.

The naked eye appearances are similar to the former. The liver being enlarged, softer in consistence than normal. On section with a knife the surface is distinctly greasy.
Microscopically the liver cells are shrunken and irregularly outlined, and contain minute fatty particles. This condition occurs in any or all of the zones of the lobules. The nucleus is not pushed on one side, and the rare small fatty granules do not coalesce as in infiltration. The protoplasm of the cells is atrophied and has undergone marked changes. It stains broadly except with acetic acid.

**Cirrhosis of the Liver.**

This condition is a chronic inflammation of the interstitial connective tissue and occurs homogeneously throughout the organ. Therefore the irritant is contained in the blood circulating in liver. And the name "the drinker's liver" indicates the fact that alcohol is commonly the supposed irritant.

It is said that the frequent taking
of undiluted spirits is the cause of the disease, but the condition has been produced experimentally by chronic poisoning with Phosphorus and Caustic acids; it has been met with in young children and

Prop: Greenfield Prop: Coats have recorded the condition occurring in cats.

In cirrhosis we have chronic inflammation of the connective tissue of the liver resulting in new formation of similar tissue. The interstitial connective tissue follows the portal vessels, forming a framework in which are supported the Portal Vein and its branches, the hepatic artery and hepatic duct.

The new formation occurs in the great majority of cases only in these regions, that is to Say, in Glisson's capsule outside the lobules (Common or Multilobular Cirrhosis). Sometimes the connective tissue increases in amount between the
individual lobules (Focal or Unilobular Cirrhosis)

Multilobular Cirrhosis

The macroscopic appearances of the liver vary considerably. In the early stages the liver is enlarged, but later on it undergoes atrophy and distortion. The connective tissue contracts, and being irregularly distributed, the organ contracts irregularly. The surface of the liver presents various sized projections, consisting of the less affected hepatic tissue between the cirrhotic depressions, forming the hobnail appearance. These projections being fatty are usually yellow or brown and opaque. The edges of the organ are dragged in, making the organ appear more compact. It is hard to the feeling, and more tough to cut than normal. On the cut surface it may be possible with the naked eye to make out the grey connective
tissue with islands of opaque or pigmented hepatic tissue in it. Microscopic appearances
in the early stages the affected connective tissue is abundantly cellular like granula-
tion tissue, and the process of new formation is evidently similar in its details to that in other
chronic inflammations.
The newly formed connective tissue has a tendency to shrink, causing atrophy of the hepatic tissue; the contracting tissue isolates groups of lobules of various sizes. These areas of remaining hepatic tissue are gradually encroached on by the connective tissue. The atrophy of the hepatic tissue results from the cutting off of their blood supply, the contracting connective tissue causing the portal vessels to become narrowed. The hepatic artery is not much affected by the contraction; indeed it supplies
the active connective tissue, and there is a new formation of capillary blood vessels in connection with its terminal branches.

The destruction of the hepatic cells takes place to a large extent by fatty degeneration, and one can often see in the midst of the connective tissue, islands, representing hepatic tissue, composed of little more than collections of oil drops. The hepatic tissue is also commonly stained with bile pigment of a yellow or brown colour, and thus we may associate with destruction of the bile ducts by the contracting connective tissue.

Clifford Allbutt in his "System of Medicine" gives the following interpretation of the changes which occur in Cirrhosis.

"It may be taken as certain that they are produced by the action of alcohol entering the liver by the portal vein. But these interlobular..."
Changes are twofold. There is both a degeneration of the hepatic cells and a development of new fibrous tissue, and it is by no means certain whether either of these changes is dependent on the other, or whether both changes are concomitant effects of the alcoholic poison.

It has been argued that the hyperplasia of the connective tissue is consequent to a primary degeneration of the hepatic cells, and dependent upon it, that it is such a hyperplasia. In fact, as is known to occur around degenerate and disrupted structures in all parts of the body, and in favour of this view, that the cell degeneration is the leading cause and not the effect of the fibrous overgrowth, it is pointed out that although there is undoubtedly a high degree of pressure exerted upon the liver cells, yet no so much as the development of new vessels from the hepatic artery.
takes place step by step with the growth of the new fibrous tissue. The blood supply is still ample, and there is not that mechanical anaemia present which would be likely to cause such an extreme cellular degeneration.

On the other hand, if specimens of early cirrhosis are examined from cases in which death has occurred from some other cause, no doubt can be entertained that the interstitial change is essentially an inflammatory one, and that it has its starting point around the main branches of the portal vein at a time when the appearance of degeneration of the hepatic tissue proper is either scanty or absent. Consequently, though it is possible that the cell degeneration may in part be a primary change, and a direct result of the action of alcohol upon the cell, and though it is possible that this cell degeneration may play some part in the production
of symptoms. Yet it is quite out of proportion to the vast overgrowth of fibrous tissue.

The balance of evidence is strongly in favour of the fibrous overgrowth being a primary morbid change and it is certainly responsible for the chief symptoms of the disease.

Unilobular Cirrhosis:

The form of Cirrhosis known as Fine Cirrhosis or Unilobular Cirrhosis, though equally due to alcohol, is far less common than the other and presents many points of marked contrast with the preceding.

The liver is increased in size, reaching a size and weight far beyond anything met with in the Multilobular form. A weight of 5 to 7 pounds is common, over 10 pounds has been met with.

The surface is smooth, the capsule somewhat thickened, its normal shape is preserved, and no appearance of any tendency to contraction
The cut surface is smooth, and often where, as usually happens, jaundice has been present, the whole surface is yellow or olive green. The consistence is not so leathery as in the multilobular form.

Microscopically: newly developed fibrous tissue is seen throughout the organ, and this surrounds the individual lobules (Unilobular). And it may even invade the periphery of the lobules. In nearly all cases a remarkable pleures of bile ducts is seen embedded in the new tissue. In the neighbourhood of the Portal vein, that is, in the centre of the triangular interlobular space, where in health may lie seen one or two small bile ducts in transverse section, there are now seen one or more large irregularly-shaped spaces, lined with columnar epithelium. Near the margin of the lobule, and more especially in the new fibrous tissue occupying the interlobular tissue.
lie a series of smaller ducts, which tend to be arranged around, and parallel with, the edge of the lobule. And if these ducts the lumens is much smaller and the epitheliaum lower and more cubical.

From this system short lengths of duct commonly arise, which come off at right angles, pass straight to the edge of the lobules, and apparently become continuous with columns of hepatic cells. The lumens of these ducts are usually packed with detached cells in a state of active proliferation.

That all these epithelial-lined canals are in fact bile ducts, not mere double rows of hepatic cells in the new tissue, is shown by the fact that they can be readily injected from the hepatic duct, and they often show masses of inspissated bile in their interior.

The mode of origin of these new bile ducts is somewhat obscure.
It is possible, though not likely that they are, as is held by Chassot, a wholly new formation. Such a process would have no parallel in disease of any other organ. It has been maintained, again, that these ducts represent aced and are columns of liver cells derived from the peripheral part of the lobule which is invaded by the new fibrous tissue, that their epithelium consists in fact of liver cells degraded and converted into duct cells. This view receives some support from the arrangement of the ducts, especially of the short ducts, which run up to the margin of the lobule, where their cells become merged in those of the hepatic columns.

On the other hand, if this were the true explanation, we should expect that a transitional stage would be met with, in which the process of conversion of the highly organised liver cell into the biliary duct cell would be seen, but this is not the
case. At the junction of the lobule and duct, there are liver cells and duct cells, but no cells in a process of change from one form to another.

Cori has suggested an explanation which appears to be the most satisfactory; and the same view is held by Corts. It is as follows.

Where the liver tissue wasters from any cause and the lobule thus grows smaller, and its margin recedes, the biliary canaliculi which in health lie inside the lobule between adjacent rows of liver cells are laid bare to view. In health these canaliculi are minute tubes, formed only of a basement membrane, and it is to be supposed that as they are left bare by the recession of the margin of the lobule, the epithelium of the extralobular bile ducts multiplies and grows up to them, and tends to afford them a regular epithelial lining. In this way, many foets are
explained. First, the usual arrangement of these dexters becomes intelligible. Secondly, these dexters, though far more common in this form, occasionally occur under other conditions. They are not uncommon here and there in the multilocular form; they are common in the periphery of supplicative scars; they may be seen around tubercles in the liver.

The condition common to all these affections appears to be the destruction of the margins of the lobule by the pressure of some kind of necro-infection, and it is clear that the development of these dexters has no relation to a previous biliary obstruction, for they may be present in abundance in cases where there has been no suspicion of jaundice at any time, and from the brilliancy of their staining capacity we may conclude that the dexters are in active
Life and growth, and in this respect they stand in marked contrast with the degenerate liver cells into which they seem to merge. These epithelial cells are usually in a state of active multiplication, and by their numbers may even occlude the lumen of the smaller ducts, and in view of this it is possible to suppose that the common occurrence of jaundice in this form of cirrhosis is due to their occlusion by this means.

It has been asserted for many years that the cause of cirrhosis was the obstruction of bile ducts, and a special form "Biliary Cirrhosis" has been described. There are cases which have this origin, but there are many cases of biliary obstruction which have no such result. Biliary Cirrhosis forms a small proportion of the cases of Cirrhosis, and in the whole the disease seems to be haematojenous in its origin. Charcot used the term "Biliary Cirrhosis"
to indicate that the irritation extended from the bile ducts, and this form was distinguished in its causation from the haematogenous or venous, in which the irritation extended from the blood vessels. The Biliary form arising in connection with obstruction and inflammation of the bile ducts. Experiment has proved that obstruction of the bile ducts leads to an increase of connective tissue in the liver, and to a monolobular cirrhosis.

The ordinary alcoholic cirrhosis in the early stages may show considerable hypertrophy. The new formation may be monolobular in distribution, and there may be the most marked new-formation of capillary ducts.

In a case of liver disease, where the patient was addicted to alcohol for over two years, there was enlargement of the liver some six weeks before death, there were haemorrhages from the stomach and bowels, and marked ascites, but little or no jaundice. After death the
liver was found small, weighing 143 ounces, there was great excess of connective tissue and mononuclear in its distribution. The hepatic cells contained abundant fat. In this case the cirrhosis, although mononuclear, and at one period hypertrophic, was not connected with obstruction of the bile ducts.

The difference between the multilobular and the unilobular forms of cirrhosis appears to depend on the part of the Portal system upon which the injurious influence of the alcohol first makes itself felt. In the former the morbid change may be clearly seen to arise around the main portal vein, which lies in the triangular interlobular spaces or Portal canals. Thus producing the well known symptoms due to Portal obstruction, namely, Ascites, which is present in at least 80 per cent of such cases, and a condition of passive hyperaemia in which the stomach and intestines are maintained
followed by a constant and persistent catarrhal condition of the mucous membrane. The obstruction of the portal vein often leads to widening of the venous channels which form communication between the portal radicles and the systemic veins, in this way we may have great dilatation of the internal hemorrhoidal veins leading to piles.

The Spleen is nearly always enlarged and indurated.

Jaundice is ordinarily absent.

In the unilocular form there is evidence to show that the brunt of the damage falls rather on the small portal branches, which approach each lobule from all points at its periphery, and consequently the resulting new fibrous tissue is developed around each lobule, and by its encroachment upon the edge of the lobule an appearance of newly developed bile ducts may be produced, and in view of the packing of the smaller of these ducts with epithelial cells one can account for the common occurrence
of jaundice in this form.
There is little or no evidence of Portal obstruction. Ascites is entirely absent as a rule and the Spleen is generally not affected.

HEART.

FATTY INFILTRATION.

The normal heart is well known to present on its surface a certain amount of adipose tissue, this fat is beneath the pericardium, lying between it and the muscular substance of the wall; it is normally most abundant along the course of the coronary arteries, along the inferior border of the right ventricle, at the apex, and at the origins of the great vessels.

The amount of fat varies greatly in different individuals, but it may be said that the surface of the right ventricle and the greater part of that of the left are usually free from fat. Sometimes this fat increases greatly
both in superficial areas and in thickness, so that the entire Right ventricle may be covered, or the whole heart may be coated with a thick mantle of fat. The adipose tissue does not always confine itself to the pericardium, but frequently extends into the connective tissue lying between the muscular fasciculi in the proper muscular wall of the heart. The superficial layers of the muscular wall may thus be largely replaced by adipose tissue. It is not uncommon to find the proper muscular substance of the right ventricle largely replaced by adipose tissue, only a thin layer of red muscle appearing inside the thick layer of fat, and even this interrupted by areas of adipose tissue. Of course, in such cases there is great loss of the muscular power of the heart. The space occupied by the fat in the muscular walls of the heart must be obtained at the expense of the proper muscular substance, and
the question arises whether the atrophy of the muscles is the primary condition, or the fatty infiltration.

We have to take into consideration the fact that a fatty infiltration of an exactly similar character occurs in voluntary muscle, and is there associated with disuse of the muscle. In this case the loss of function is the primary condition, and the fatty infiltration the secondary, and so in the case of the heart we meet with fatty infiltration in cases where there is no general atrophy, and we may infer that atrophy and weakening of the muscle have been the primary, and the infiltration the secondary, condition.

Microscopically, the deep layers of the epicardium are seen to consist for the most part of adipose tissue, and this adipose tissue sometimes extends along the intermuscular septa, and some fat cells may be seen between some of the muscle fibres. The muscle fibres themselves
are not affected

FATTY DEGENERATION. This condition occurs very frequently in the heart, especially in its minor degree, and most recent observers have come to the conclusion that, as in the liver, the two conditions of degeneration and infiltration are often associated, though either may occur without the other being present.

Fatty degeneration of the heart shows itself in patches, so that the muscular tissue is seen to lie, as it were, flecked with pale spots or streaks. This is best seen on examining the muscular tissue from within, as it is easier seen through the endocardium.

The heart is generally flabby, fragile, and pale in colour, and usually dilated.

The microscope shows the transparent muscular tissue interrupted by opaque patches, in which no a
high power can be seen fat droplets in the muscular fibres. These fat granules are frequently arranged in rows, representing the original muscular fibrillae, and the contractile substance is obviously lost or converted into oil; the sarcous matter has undergone transformation. As a rule the fat granules appear first in the neighbourhood of the nuclei of the muscle fibres, the nuclei may be invisible or indistinct.

At a late stage there is complete destruction of the muscle fibres and their replacement by fatty droplets.
Arteries

Atheroma

Consists in a more or less localized thickening of the internal coat of the artery, nearly always in the form of patches. These patches are hard, and in the earlier stages cartilaginous. The vessel is more rigid than normal, and in small arteries the vessels do not collapse. The calibre is also diminished by the inward projection of the patch. On cutting into a patch in either the aorta or a cerebral artery there is often an opaque yellow colour revealed in the deeper parts, and this is an indication of fatty degeneration. Often, too, especially in the aorta there is calcareous infiltration of the deeper parts of the patch. Microscopically it can be seen that the endothelium of the tunica intima is continued over the patch, and in nearly all cases it is readily seen...
that the patch is really a thickening of the internatal coat. The thickened intima is composed of dense connective tissue, which in the early stages contains many round, oval, and stellate cells. In a fully formed patch the structure is often somewhat indefinite, the tissue is indeed well obsolete, and as already indicated, fatty degeneration readily occurs, which usually begins in the deeper layers of the patch; the tissue breaks down, so that a cavity containing fatty debris is formed (atheromatosus abscess). The tissue superficial to the cavity may give way, and so expose the cavity, forming an atheromatosus ulcer.

The effects of atheroma are:

1. Narrowing of the calibre of vessels
2. Interference with the muscular contractility
3. Rigidity

The narrowing of the vessels in the case of small arteries, such as the arteries of the brain causes considerable interference to the circulation.
The loss of contractility also affects especially the smaller vessels. The rigidity and weakening of the wall affect chiefly the larger vessels, and are important factors in the causation of aneurism. For example take the case of the aorta. During the cardiac systole the aorta does not dilate, and at the end of systole it does not recoil. Thus the force of the elastic recoil is lost to the circulation, which in distant parts is apt to be stagnated. The result of this is hypertrophy of the left ventricle; and this hypertrophied ventricle, sending the blood forcibly into the rigid aorta, produces commonly a diffuse dilatation of the arch.

It has long been known that calcareous infiltration occurs especially in tissues in which the vitality is lowered. In the case of fatty degeneration, where of course the vitality of the tissue is greatly impaired, there is usually
marked evidence of deposition of calcareous matter. This is well seen in the muscular coat of the blood vessels, in which fatty degeneration of the muscle fibres has already taken place, and is especially well marked in alcoholics. Calcification has long been recognised as a sequel to fatty degeneration, and Prof. James Woodhead considers that this form of vascular disease has in alcohol one of its most important exciting and adjacent causes. Lime salts, phosphates or carbonates are deposited only in vitally inactive tissue, and under pathological conditions, especially in tissues that have undergone fatty or caseous degeneration wherever dead tissue is found, lime in an insoluble condition is deposited. Coats describes a distinct affection of arteries which he calls "fatty degeneration of the intima" and he says this must not be confused with atheroma. It consists of yellow markings, slightly raised above the
internal surface of the vessels, especially
in the aorta and pulmonary artery.
If a portion of such a patch be exam-
ined under the microscope, it will
be found that the condition consists
in a fatty degeneration of the cells of
the intima. The cells contain abundant
numbers of fine drops.
If the condition is advanced, the
intercellular substance becomes also
the seat of fat deposit. Sometimes
when the degeneration is very advanced,
the patch softens, and an erosion
forms which is very superficial and
must not be mistaken for the athero-
matous ulcers. and coats further
says that this condition is to be classed
in the same category as fatty degener-
ation of the muscular tissue of the heart.
NERVOUS SYSTEM.

Among the causes of toxic and multiple neuritis most writers include alcohol, for the reason that it is a product of the action of vegetable organisms closely allied to the bacteria, and so may be regarded as a toxic resulting from the action of microbes. The irritant being in solution in the blood acts on the whole nerves at once: the result of this irritation is inflammation and breaking up of the medullary sheath, and degeneration of the nerve fibres. There is also wasting of muscles in cases where the motor nerves are involved.

It is usually stated that spirit drinking is the commonest cause of alcoholic paralytic, but it is probable, judging from observations made at the Manchester Royal Infirmary, that the disorder is quite as often brought on by excesses in beer.

The results of necropsies in cases of
alcoholic paralysis shows that while
motoric changes are frequently found in
the brain and spinal cord, the most
frequent changes are in the peripheral
nerves, and there is now abundant
evidence in favour of a direct causal
relationship between peripheral nerve
changes and the peripheral paralytic
phenomena.
The changes in the nerves may involve
both the connective tissue and the nerve
fibres, but the latter always suffer
more severely. The condition then is
mainly one of parenchymatous neuritis,
perineuritis and interstitial neuritis being
absent or present to a slight degree only.
Hence to the naked eye the nerves and
their branches appear quite healthy.
In acute cases however, when there
has been acute inflammation of the
sheath and connective tissue the nerve
may appear reddened and swollen, or
at a later stage soft and pulpy. As
regards the distribution of these
changes in nerve fibres, the rule is that
they are most intense in the terminal branches to the muscles and skin, and become progressively less marked towards the larger branches, the trunk and anterior roots of the nerve are usually quite healthy.

In the diseased portions of the nerve the fibres are not affected equally; some may be quite normal, some may be slightly affected, and others may have undergone complete atrophy. These differences, as shown by Fleming, are largely related to the presence or absence of local occlusions in consequence of changes in the vessels.

The nerves of the limbs are principally affected, and the branches of the musculo-spiral and the anterior tibial usually suffer the most severely.

The muscles in connection with diseased nerve present changes similar to those of experimental neuritis; they are pale and wasted, and their fibres are reduced in size; all the fibres are not affected to the same extent. There are
changes too which appear to depend on some process other than simple atrophy, thus the connective tissue of the muscles may be profoundly altered, its overgrowth in some cases is so great that it looks as if there had been a primary fibrosis of muscle with a secondary atrophy of fibres. This interstitial myositis is chiefly found in cases of chronic neuritis, but it may appear in acute cases. - Two causes may be suggested.

1. That it is secondary to the irritating effects of the poison on the nerve branches
2. That it is primary and due to the action of the poison on the muscle itself.

The following observations on alcoholic neuritis are taken from Dr. R. A. Fleming's "Diseases of Nerves" in Albutt's System of Medicine.

Referring to Peripheral neuritis Fleming says that in this affection the toxin acting either on the fibres of the nerve, or directly on the capillaries in the nerve, causes not merely definite changes in...
the cells of the intima of the capillaries and small arterioles, but also small haemorrhages, oedema of lymph, and lymphoid cells, all of which most probably interfere by pressure with neighbouring nerve fibres, but further it is these same fibres, of which many must be vaso-motor, which are degenerated in an affected nerve in Forier-Kennett's. Moreover, they are more degenerated than any other fibres.

There is also strong presumptive evidence in favour of the degeneration of vaso-motor nerve fibres both in the central and peripheral ends of a divided nerve, wherever the fibres by such division have lost their function. Nerve fibres generally conduct impulses in one direction only; some to, and others from, the cells in the cord or brain; but although a fibre may thus conduct physiologically in one direction, for example, centrifugally, it does not follow that an injury or
irritant applied to reach a fibre will not seriously affect the cells to which the process belongs, and from which nerve stimuli pass.

Whether nerve fibres conduct away from the cell or towards it, the cell itself appears, often only temporarily, but sometimes permanently.

The changes found in the cell include, alteration in size of the cell itself, change in the position and size of the nucleus, in the number and size of fibre's granules, and other modifications. Changes which may be temporary or permanent.

Hotchk and Horsley prove by experiments that nerve fibres appear to conduct electrical currents in the direction in which they usually carry nerve stimuli, and that currents passed in an opposite direction meet with considerable resistance.

To: Judson Barry (Allbutt's System of Medicine) describes Multiple Symmetrical Peripheral Neuritis and he says that the commonest
cause of the disease is a chemical poison, and it is important to recognize firstly that the action of the poison is not necessarily limited to the peripheral nerves; on the contrary, there are frequently indications that it has impaired the functions of other parts of the nervous system, and secondly, that the name 'Peripheral neuritis' does not imply that the abnormal condition of the nerves upon which the characteristic symptoms appear to depend, is due to the direct action of the poison, and is entirely independent of changes produced by the poison on the central nervous system. In other words, lesions of the peripheral nerves do not necessarily constitute the whole anatomical substratum of the disease, but are its most conspicuous features. Of the older observers Graves favoured the view that certain forms of generalised paralysis depend on disease, not of the brain or spinal cord, but of the nervous cords themselves. In one passage
Graves asks the question. May not the decay and withering of the nervous tree commence occasionally in its extreme branches? And may not a blighting influence affect the latter while the main trunk remains sound and unharmed.

It is very clear that in most cases of Peripheral Neuritis the cause of the disease is some Rheid of poison, and some of these poisons may be enumerated: namely, Lead, Arsenic, Mercury, Phosphorus, Silver, Alcohol, Ether, cyanide of Carbon. It may also be caused by the microorganisms which produce specific diseases, or by their products, for example, those of diphtheria, influenza, typhoid, pneumonia, erysipelas, gonorrhea, syphilis, and septicaemia.

The symptoms of peripheral neuritis at the different stages of the disease indicate that irritation of the nerves is present in the early stages, and symptoms indicative of destruction of nerve tissue are
present in the later stages. Thus in the early stages we have, on the motor side, muscular spasm and cramp; on the sensory side, shooting pains, paraesthesia, and cutaneous and muscular hyperaesthesia. In the later stages, paralysis and anaesthesia are predominant.

It is difficult to explain the variations in the distribution and character of the symptoms met with in this disease.

The frequency of the action of the poison on the brain is shown by the prevalence of psychical phenomena; the extent of its action on the spinal cord is not easy to define, and with regard to changes found in the nerves, pathologists are not yet agreed how far such changes are primary, or how far they are secondary to minute lesions in the cord. In other words, to see the central nervous system exercise any influence on the distribution and character of the symptoms presented by Peripheral neuritis, and are variation...
in the motor and sensory phenomena to be explained by difference in the selective action of the poison on nerve fibres, or on the ganglionic cells which preside over their nutrition.

There are three probable ways in which a limitation of changes to the peripheral nerves may be explained:

1. The poison selects and attacks those parts solely and predominantly.

2. It primarily attacks nerve cells, and as a consequence those portions of the nerve fibres which are farthest removed from their influence undergo degeneration, namely, the peripheral.

3. The poison acts with equal intensity on nerve cells and nerve fibres, the former recover, but the latter, having been robbed of vitality for a time, have lost resisting power; and degeneration already started, easily progresses.

Two distinct substances are said to enter into the constitution of a motor cell — namely, a chromophile or
chromatic substance which takes up basic colouring matter, and an amorphous fundamental substance which presents no affinity for colouring matter. The chromatic substance, called also Kinetoplasma, is represented by a number of granules, arranged for the most part around the central nucleus, and also in rows along the cell border. They are prolonged as slender rods into the protoplasmic processes or dendrites of the cell, but do not occur in its axis cylinders. The latter is a prolongation of the achromatic amorphous substance called also Trophoplasma, which in the cell body binds the chromatic granules together.

The researches of Marinesco and others have proved that when the axis cylinder is diseased, as in Peripheral Neuritis, certain changes take place in the Kinetoplasma. The chromophile granules disappear partially or wholly, and the nucleus
Instead of being in the centre approaches the periphery of the cell. If the lesion of the nerve fibres be slight and curable, the chromatic substance may regain its normal characters, but if the lesion be severe other changes set in. The fundamental achromotactic substance disintegrates, both in the axis cylinder and in the cell body, and the whole neuron becomes atrophic.

These changes then are secondary to lesions or disease of nerves. Do they differ from primary changes in the nerve cell due to the action of some poison directly upon it? Marinesco believes that a difference may be distinguished, and he says that when anaemia of the cord is produced by temporary ligation of the aorta there is a dissolution of the chromophile elements, and in addition to this the trophoplasma quickly disintegrates, vacuoles are produced, and ruptures occur in the protoplasmic processes. It is this precocious
disintegration of the tropho-plasma
which Morinesco regards as particu-
larly characteristic of primary lesions
of the nerve cells.

The chief value of these researches is
the proof they afford that minute
changes in nerve cells are very
common in cases of neuritis, and
that many of them are secondary to it.

They show that while nerve fibres
depend for their vitality on nerve cells
the condition of the cells is influenced
by that of the fibres; not only may
central changes lead to peripheral
lesions, but the latter also in turn
may initiate lesions in the nerve centres.

It will be granted that a predominance
of pathological changes in peripheral
nerves is evidence that they have
been specially selected by a
particular poison, and if this be
admitted, it is logical to infer that
cases exist in which these facts are
attacked alone, the neurons themselves
presenting no affinity for the particular poison.
The pathological refection is probably mainly due to the Rea of poison and to its dose, but partly also to antecedent weakness of the part of the neuron which is attacked.

Further, it is to be noted that Coeptis act, not only on nerve cells and nerve fibres, but also, in many cases, on the vessels supplying them.

The careful investigations of Fleming show that degenerative changes in weakened nerve fibres are greatly expedited by local effusions depending on vascular conditions. He has found in cases of alcoholic neuritis effusions particularly well-marked around the arterioles, and capillaries, in the endoneurial septa, and often between the nerve fibres and the perineurium, and separating the inner lamellae of the perineurium. The occlusion acts injuriously by compressing the nerve fibres in its neighbourhood thus causing degenerative changes in them, not merely.
at the level where it occurs, but also to a greater or lesser extent peripherally. The effusion was always accompanied by changes in the walls of the vessels and these vascular changes become better marked as the nerves were traced peripherally. Fleming believes that the greater the interstitial effusion, the less the chance of subsequent recovery.

In conclusion, some of the main pathological features of peripheral neuritis may be summarized as follows:

1. The chief cause is a chemical poison.
2. The poison affects all parts of the nervous system, though to a very unequal degree in different cases; partly because the nature of the poison varies, and partly because individual portions of the nervous system present varying susceptibilities in different persons. It may indeed be safely assumed...
that sometimes the peripheral nerves are solely implicated, while it is probable that particular filens, motor, sensory, or vaso motor may be picked out by special poison. In many cases however there is evidence that the brain or cord or both may be attacked together with the nerves.

In order to study the relation of alcohol to the tissues in disease it is evident that we must if possible determine the action of minute doses of alcohol upon healthy protoplasm, and whilst it must not be assumed that substances that exert a toxic action upon one Reid of protoplasm necessarily exert a similar action upon another, we may take it for granted that should alcohol be found to exert deleterious action upon many Reid's of protoplasm other than that of the human subject it will in all probability exert some
toxic action upon our higher protoplasm, especially if we find that it causes any disorder of its functional activity.

It may be well therefore to mention a few facts and observations that have been noted as to the action of alcohol upon what may be termed the lower protoplasmic, vegetable and animal.

The effect of alcohol in lowering the vital activity of protoplasm has from time to time been carefully noted and recorded - and in the minds of those who have worked on this subject, there appears to be little doubt that even the first developed and therefore most stable functions are materially interfered with, or in some cases, altogether removed.

Logiel and Gerard (The Scientific Valuation of Alcohol in Health, 1909) both maintain that alcohol seriously slows down ameboid movements of the leucocytes of the blood, first causing sluggishness
and then, if the action of the alcohol be continued long enough, or in sufficiently strong solutions, completely abolishing such movements.

It has for some time past been accepted that the protoplasm of certain plants reacts to narcotics much as does animal protoplasm.

Ridge (Alcohol and Public Health, 1893) has demonstrated that even a one per cent solution of alcohol interferes seriously with the germination of cress seeds, and he further showed that the production of chlorophyll, a substance which may be said to correspond to the haemoglobin of the blood, is markedly interfered with by the use of even small quantities of alcohol. In the case of the geranium, both growth and chlorophyll production are seriously affected. Two cuttings from the same plant were placed under, as far as possible, nearly similar conditions, one was fed with one per cent of alcohol
every other day, the other with water only, and after six weeks, the one that had received the dilute alcohol was only about half the size of the other, and was a delicate sickly plant.

Neither fresh water medusae nor the water flea can survive long in the presence of even small quantities of alcohol—1 in 4,000 of water—though they remain perfectly active and well in ordinary water. Ranber (quoted from Woodhead) has noted the effect of alcohol on a great many plants and animals, and he found that alcohol acts as a definite protoplasmic poison upon all forms of cell life upon which he experimented: that plants become shrivelled and pale, that animals become intoxicated, and that those that live in water soon die—Perch placed in a 2 to 4 percent solution of alcohol rapidly become intoxicated, fall to the bottom
and die. The crayfish placed in a two per cent solution succumbed in a single day. Thus the justifiable contention is that all protoplasm, whether the basis of animal or plant life is deleteriously affected by alcohol.

In all text books on pathology alcohol along with such substances as ether, phosphorus, and other toxic agents is assigned a place as an active agent capable of and actually engaged in producing fatty degeneration. Whilst as one of the most important toxic substances giving rise to an increase in the amount of fibrous or cicatricial tissue in the blood vessels and certain of the visceral organs, it is also given an important place as a pathogenic factor. Moreover alcohol is now brought into line with certain of those poisons produced by the lower vegetable organisms as a protoplasmic poison, which combining...
rapidly with oxygen that is brought to the tissues, appears not only to take up the oxygen which the tissues should be allowed to utilise, but also to interfere with the powers of these tissues to take much oxygen as is left. So great is this oxygen hunger of alcohol that the oxidation of the fat and carbohydrates taken into the body is interfered with in a most marked fashion. The respiratory oxygen is seized upon by the alcohol with which it enters into combination and is thus prevented from combining with protoplasm. The metabolic, nutritional, or building up processes are interfered with, whilst there is also serious interference with the secretion of waste products from the protoplasm with its imperfect activities.

In connection with the first part of the process—the building up of the tissues—we have in the presence of alcohol two sets of conditions induced, neither of them normal.
The first of these manifests itself in an excessive accumulation of fatty or adipose tissues under the skin, and a similar accumulation of fat in the interstitial tissue of the heart wall near the epicardial surface; in the liver cells, especially in the peripheral zone of the lobule; and in the connective tissues. The cells in these various positions become enormously loaded with fat, and giving rise to that extreme adiposity that often characterizes consumers of alcohol, especially of beer.

It should be noted however, that in all these cases there is, as a rule, not only no corresponding increase in the growth of other tissues, such as muscle, liver cells, and the like, but there may be an actual wasting, atrophy, or diminution in these tissues often accompanied by impaired functional activity.

In the second place there is a far more important metabolic change
that this mere progressive accumulation of fat, there is an actual degeneration of the higher protoplasmic substances, fatty material being formed at the expense of the higher protoplasm; abnormal metabolic processes are set up, which lead to the destruction of protoplasm, in an increased elimination of nitrogen, and in the accumulation of fatty degenerative products in the protoplasm of important cells and tissues.

It is sometimes assumed that this fatty degeneration is the result merely of want of food, a factor which undoubtedly plays an important part in the production of this condition, but in alcohol poisoning this is not the case, for fatty degeneration in a very advanced form may occur in stout people in whom there is extremely well marked fatty infiltration of the connective tissue and liver cells.

We have in fact in this coexistence
Of infiltration and degeneration one of the most characteristic features of alcoholic poisoning, or of poisoning by substances similar to alcohol.

This fatty degeneration of the protoplasm of the more highly developed or specialized cells is well seen in the muscle fibres of the heart, and in the liver cells, both of which afford the best illustrations of fatty degeneration met with in the post-mortem room.

It is a curious fact that the distribution of fatty degeneration in alcoholics is very similar to that which obtains in cases of diphtheria and other conditions of bacterial poisoning, so that we must admit that alcohol produces the same changes as do bacterial products.

W. J. Kerr, writing on the effects of alcohol on the liver ("The Effects of Alcohol upon the Liver" 1895) comes to the conclusion that alcohol when taken in considerable quantities and
for any length of time may cause extensive cirrhotic changes in the liver, but that this is not invariably the case, and that in a certain proportion of cases the organ seems to escape any marked cirrhotic changes, but even in those cases in which cirrhosis is not produced, marked degeneration occurs in the protoplasm of the liver cells proper.

In an examination of the changes in the liver cells of a series of animals, rats, to which alcohol was given, there was vacuolization in certain cases and "in many cases of long-continued administration extensive fatty infiltration of the cells was found" accompanied apparently by those changes that are supposed to be the result of a true fatty degeneration.

Kerr further states that "we know that alcohol is not only consumed giving off heat etc., then rising up
some of the oxygen really required for the combustion in the tissues and organs of fats, sugars etc derived from the blood, but also retards oxidation of the tissues by preventing the red blood corpuscles giving off oxygen (Fleuret, Breton). The consequence being a storage of fat in the organs" and his conclusion is that "the effects of alcohol are most frequently and principally seen in the parenchyma, the most common change being deposit of fat in the liver cells."

J. M. Cowan ("Fatty degeneration of the myocardium" 1902) who has taken great pains to determine the part alcohol plays in the production of fatty degeneration concludes from his own observations that "alcoholism seems to display a distinct part in causation, a fact which agrees with the clinical knowledge of how badly such cases bear acute disease. Cardiac failure
always ensuing at an earlier period
than one would anticipate, and in
sunning up the cause of fatty degener-
ation he speaks of the presence of a
noxious agent in the general blood
stream or in the lymph channels of
the heart as being one of the most
important of them.

It is now recognised that alcoholism
is one of the main causes of fatty
degeneration with or without fatty
infiltration of the heart muscle.
Alcohol appears to exert a definite
toxic effect on the protoplasm of the
heart muscle, as the result of which
nutrition of the protoplasm is so far
interfered with that marked degener-
ative changes of a fatty nature are
brought about in this regularly
and periodically active muscular
tissue. It is evident, from the
account of work the heart has to do,
that the whole of the metabolic processes,
whether of bringing up and absorbing
nutrient material, or of secreting
waste products should be kept as normal as possible, and if the assimilating or secretory powers are in any way interfered with, these must necessarily be a loss of the margin of reserve power with which fortunately, the heart seems to be endowed, but which inevitably must come to an end at some stage if any great strain is made upon it.

It may here be well to draw attention to the way in which this reserve may be encroached upon. There can be little doubt that in most cases alcohol increases the rate of the action of the heart, and in this way must necessarily cut short, however slightly, the period of rest between each contraction of the muscle. In this way the period allowed for getting rid of waste material must necessarily be diminished, if waste materials are excreted from the heart muscle as they are from the voluntary muscles.
There appears to be sufficient evidence at our command to warrant us in believing also that alcohol exerts a definite influence in interfering with the assimilation of nutritious substances that are conveyed to the heart by the blood and lymph, whilst in addition we have the direct toxic action of the alcohol on the tissues of the wall of the heart. We have thus an increased amount of work, diminished assimilation, an accumulation of waste products actually blocking the lymphatics, in any case acting in conjunction with the alcohol continuing to occur a distinct and direct poisonous effect upon the active tissues of the heart muscle.

We have therefore, with the increased amount of work, and the corresponding drain on the margin of reserve, no increase in the amount of nutrition, with the inevitable result that the reserve must ultimately become...
exhausted.

Fatty degeneration of the protoplasm of the more highly developed or specialized cells, then, is seen to great advantage in the muscle fibres of the heart, and in the liver cells. Here this condition is by no means confined to those tissues in what we may call fatty degeneration is well seen. A somewhat similar condition is present though in a much less marked degree, in the other tissues of the body, for example, it may often be demonstrated as occurring in the muscular coat of the walls of blood vessels, resulting in the conditions of fatty and calcareous degeneration previously described.

One of the most difficult problems with which the pathologist and the physician are faced is that connected with the part played by alcohol in determining the cause nature of the vascular changes brought
about in alcoholism, both acute and chronic.

There can be little doubt however that each form is associated with a special series of lesions and that the importance of the lesion depends in great measure upon the tissues affected. The more highly and late developed organs and tissues apparently being more affected in cases of acute poisoning. The lower and less highly developed tissues appearing to react more distinctly in chronic cases.

To this general statement, it is however necessary to add a certain qualification, for it is found that, as in all cases of poisoning by protoplasmic poisons, in addition to the highly developed tissues, those organs that are kept most continuously at work (e.g. the heart) are specially affected by the acute process.

It will be found also, that this
localization is a specially well-marked characteristic, as regards the blood vessels. In the acute process the delicate endothelial tissues of the blood vessels and perivascular lymphatics undergo comparatively rapid degenerative changes, owing to the passage of considerable quantities of toxic substances through the walls of the delicate capillaries. The poisonous substances thus coming into direct contact with the protoplasm of the cells, interfering with their nutrition, and thus both primarily and secondarily, with the nutrition of the surrounding tissues, rapid degenerative change occurring not only in the endothelial cells of the vessels, but also in the parenchymatous tissues of the organs in which they run. These changes in most cases being accompanied by the formation of greatly increased amount of formed fibrous or connective tissue
In chronic alcoholism, on the other hand, where the amount of toxic irritant poison coming along the vessels is comparatively small, and in dilute solution, it will be found that the endothelial cells are, as a rule, not so markedly affected as are those cells which normally give rise to the production of connective or cicatricial tissue, when they are submitted to continued or intermittent irritation.

In cases of chronic alcoholism, the slight but prolonged irritation gives rise especially to a thickening of the subendothelial layer of the intima and of the connective tissue of which the tunica adventitia is composed, though along with this we have, in the case of the medium sized vessels, not only an increase of the connective tissue between the bundles of muscle fibres, but as the result of the enormous amount of new tissue in the intima and
adventitia, a marked interference with the vascular supply of the media. The result of this is that the muscle fibre with its nutrition already impaired by alcohol, undergoes a further degenerative process, resulting in fatty degeneration, and ultimately in calcification. This fatty condition of the media corresponding to a certain degree with the previously mentioned change in the heart muscle.

Of one thing in connection with chronic alcoholism most clinicians and pathologists are satisfied, that in patients suffering from this condition, death from cardio-vascular disease is more common than among any other class of patients. Moreover, it is more generally recognized by both physicians and physiologists that the exhibition of alcohol invariably leads to a dilatation of the smaller vessels, especially capillaries. This dilatation being due probably not to increased
activity of the vaso-dilatator nerves, lead to a paralysis of the vaso-constrictors. Here again, arguing from analogy with what takes place in other muscles with which the nerves are intermittently or continuously paralyzed, we should expect to find along with the diminished activity of the muscular or middle coat of the vessels an impairment of its nutrition and consequently some atrophy or even degeneration of the muscle fibres, one is not surprised therefore to find that fatty degeneration followed by calcification of the middle coat is very frequently met with in patients who have succumbed to chronic alcoholism. Wherever there is marked degeneration of tissues, there is usually some replacement of the more highly organized tissues by tissues of a lower type -- connective tissues in the blood vessels, moreover, where the nutrition of the various coats is
carried on through the agency of the vasa vasorum common to all three, no one coat can be affected without the others being to a certain extent involved, for example, in certain forms of kidney disease, in which the tunica intima becomes thickened and we have a condition of what is known as "endarteritis obliterans" the tunica adventitia is invariably more or less involved. the middle coat also becomes more fibro cellular, the muscular tissue gradually undergoing concurrent atrophic changes.

In chronic alcoholism the changes set up in the muscular coat are almost always accompanied by an increased formation of fibro-cellular tissue in the adventitia and intima, and it is here that it becomes necessary to take into consideration the other factor previously mentioned — the irritation of endothelial and connective tissue.
cells by the dilute solution of alcohol circulating in the blood vessels and in the lymphatics naturally we should expect that any changes set up in this way would be most marked in the terminal branches of the arterial system, and that the large vessels would be comparatively slightly affected; but when it is borne in mind that the walls of the large vessels are supplied with blood by delicate arteries and capillaries, and that in connection with these we have a lymph circulatory system, we are in a position to understand that the connective tissue changes in the walls of the blood vessels may modify most profoundly, not only their structure, but also their contracting and resisting power. These changes in the vessels are after all to be looked upon merely as a special manifestation of what may be called the connective tissue
group of changes, and probably are as Prof. Sirius Woodhead points out, the result of two very different sets of conditions. First, of a proliferation of the endothelial and connective tissue cells in and around the lymph sinuses, and connective tissue spaces; and secondly, of the accumulation of waste products, or even, in some cases, of tissue debris, consequent upon which, there is an invasion of the affected tissue by leucocytes, a condition almost invariably followed by further proliferation of the connective tissue cells. The stages of this process are well illustrated in the changes that take place in the liver. At one scheme, the acute process, we have numerous leucocytes, and a gradually increasing number of larger connective tissue cells appearing in the portal spaces. Whilst at the other scheme, there is met with the chronic
Polylobular Alcoholic Cirrhosis. "Hot nail, or liver drunken liver," in which the fibrous tissue occurs in many cases to be formed almost without any increase of the connective cells. In this chronic form of alcoholic cirrhosis we find that just as in the vessels the muscular coat disappears as the fibrous tissue is increased in amount, so here, the liver cells become atrophied, undergo fatty degeneration and fatty infiltration, and in some cases disappear altogether, as the fibrous tissue advances, and gradually invades the parenchymatous tissue. Whether this fibrous tissue formation is going on in the heart, in the kidney, in the liver, or in the blood vessels, or in the sheaths of the nerves, the process is essentially the same, and must be associated with the changes in the lymphatics already referred to.
In conclusion the question of predisposition to disease, and loss of immunity against certain infective diseases caused by alcoholism, will be referred to Keirin. (Hans Wollhead) made experiments on animals with very small doses of alcohol. He took as his dose for each animal an amount of alcohol proportionate to that given as a nutrient substance or medicine, or both in a dermatinum at Dares. This worked out to about 14 or 6 minims per pound of rabbit and be used the alcohol in a well-diluted form. In some cases its exhibition was continued over periods of weeks or even months before he commenced his experiments, and he continued its use for some time after the experiments had been going on. The also carried on a series of experiments on animals to which doses large enough to produce acute poisoning were
given. He used
1. Anthrax Bacilli
2. Tubercle Bacilli
3. Tetanus toxin.

For (1) Susceptible animals, such as rabbits, he used "first vaccine" (Antser),
whilst for the more resistant animals
dogs, fowls, and pigeons, he injected
a highly virulent culture.

(2) Tubercle bacilli in a glycerine
emulsion diluted with normal and
saline solution to 1 in 1000 and
1 in 10,000, giving a definite
quantity of each of these diluted
emulsions.

(3) Tetanus toxin, of which the
lethal dose could be easily measured.

As the result of numerous carefully
designed, and well-executed experiments,
he comes to the conclusion that
alcohol, whether introduced subcutaneously,
or by the stomach, induce in the animal body a
considerably increased susceptibility
to artificial injection or poisoning.
by the above organisms and toxins.

The view now being most universally held is that though alcohol in some cases of itself acts directly to produce the above mentioned phenomena by circulating as alcohol in the blood, it often and more generally affects the organs indirectly by causing diminished and delayed digestion followed by marked fermentative processes by which processes toxins, closely allied to the albuminoids, and also to the toxic bodies produced by the growth and development of pathogenic organisms in the system, are formed, and which being carried by either the lymphatic or the blood stream to the various organs, produce the various pathological changes above described. With regard to the liver changes the most general opinion is that
It is more than probable that the main cause is the specific and irritative one, and analogous to that produced by Phrennie poisoning, the metallic poisons and Typhus etc.

There is also reason to believe that the true Alcoholic Carbons (Multilobules) the order proceeds is as follows:

1. The fibroid or Carbothic change is primary and is followed by

2. The worked change in the liver cells themselves.

The pathology of alcoholism then is important in so far that alcohol brings about the changes described in these notes, that it gives rise to degeneration of nerve, muscle, and epithelial cells, that it causes an accumulation of waste products in the tissues by interfering with oxidation and with secretion and excretion.
direct and indirect, and that it induces a proliferation of the lower forms of tissue, often at the expense of the higher tissues. Bearing these points in mind we are able to understand what an important factor alcohol is in many of the processes of disease both acute and chronic. Whilst we find also that it interferes directly with the production of immunity against specific infective disease.
Liver. Fatty Infiltration. x200

Liver cells contain globules of fat which have coalesced in some cells, forming a large globule which displaces the protoplasm and nucleus.
Decrease in protoplasm.
Decrease in size of cells.
Diminished space occupied by capillaries.
Liver. Fatty Infiltration (advanced).

x 200.

Increase of fat deposit and in the size of the droplets.

Close resemblance of liver tissue to adipose tissue.
Liver - Fatty Degeneration. x 200.

Liver cells shrunken, irregular and containing fatty particles. Nucleus not pushed to one side.

Fibrous bands, causing atrophy of included liver cells. Liver cells closely packed with diminished capillary spaces.
Dense fibrous tissue formation
Livers cells generally atrophied
The fibrous tissue often isolating individual cells
Heart. Fatty Infiltration X 50.

Deep layers of epicardium composed entirely of adipose tissue, which also passes into the heart wall. Fat stained black with osmic acid.
Heart. — Fatty infiltration x 400.

Muscles fibres q'heart with fat globules seen between them.
Heart — Fatty Degeneration X 400.

Fibres in longitudinal section
Minute fat granules grouped round and obscuring the nuclei, chiefly at the poles of the nuclei and also following the lines of longitudinal section.
Cerebral Vessel - Atheroma x27.

Thickening of inner coat, laminated fibrous looking - not uniform around vessel.
Small spaces in outer part of thickened inner coat.
Elastic lamina ruptured.