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"On the Etiology, Pathology and Clinical Significance of albumosuria and Peptonuria"
Introductory:

This is a subject which has engaged the attention of many Physiologists and clinical observers, and more especially within recent years. For the consideration of the occurrence of Albemoses and Peptone in the urine it will be necessary to trace the source and destiny of these bodies in the human economy before proceeding to discuss the pathology of the conditions known as Albemoseuria and Peptonuria, and their clinical value to the Physician.

It will therefore be the object of this thesis to attempt to bring together and summarise the various facts and observations which have been recorded concerning the relation of the Albemoses and Peptones to disease; to enumerate the diseases in which these morbid phenomena have from time to time been found; to point out the methods employed for their detection in the urine; and to refer to the results which have been obtained by their artificial introduction into the circulation. Finally we shall endeavour to arrive
at some practical conclusions regarding the value of these physical signs in the prognosis and treatment of disease.

II Physiological survey of the Proteids and the changes they undergo in the alimentary canal:

Proteids must be regarded as the most important class of foodstuffs, since they are indispensable both for the building up of our frames and as a source of energy.

It is customary to divide Proteids into various classes according to their solubility in water, their behaviour to heat, alcohol, and various other reagents.

They all however respond to certain tests, the most delicate of which is the Xanthoproteic test, which consists in adding strong nitric acid to the Proteid and boiling when the liquid or precipitate turns yellow; on adding ammonia the yellow liquid or precipitate turns orange.

The separation of the different classes of Proteids will be referred to later. At present the various classes will be enumerated and only those
two with which we are specially concerned will be referred to.
The classes, then, into which the Proteids are divided are the Albumins, the
Globulins, the derived Albumins, the Proteoses, the Peptones and the
cogugulated Proteids.
For our knowledge of the Chemistry of the Proteoses and Peptones we are largely indebted to Kühne and Chittenden
and Neumeister.
The Proteoses:—

These are the intermediate products in the hydration of Proteids, the final products being the Peptones. They are formed in the body by the action of the Gastric and Pancreatic Juices. They may be formed artificially by heating with water, or more readily by dilute mineral acids; Neumeister has however recently found that the albumose formed by the action of super-heated steam differs in a few minor reactions from those formed by acids or by Gastric digestion; he has called this amid albumose.
They are not coagulated by heat.
They are precipitated but are not coagulated by alcohol, never being rendered
insoluble, even after standing some weeks under this reagent: herein they agree with the peptones and differ from the albumins and globulins, the former of which are rendered readily insoluble, the latter less so, by this method. The individual bodies of this class differ somewhat according as they are formed from albumins (albumoses) or globulins (globuloses): the albumoses may however be taken as an instance of the class, and it is with them that we shall especially be concerned.

Three varieties of albumoses must be recognised and the subjoined table taken from Halliburton's Chemical Physiology and Pathology shows the reactions of these albumoses and also of peptone (vid. p. 5). It will be seen that Deuter-albumose is more nearly allied in its reactions to peptone than it is to the other albumoses. Proto and Hetero-albumose are often called the primary albumoses as they are the first products of the hydration of proteids.

Hetero-albumose differs slightly from the other albumoses in its reaction
<table>
<thead>
<tr>
<th>Variety of Protein</th>
<th>Hot and Cold Water Sol. e.g. 10%</th>
<th>Hot and Cold Saline Sol.</th>
<th>Saturated with Trace of MgSO₄</th>
<th>Saturated with (NH₄)₂SO₄</th>
<th>Nitric Acid</th>
<th>Copper Sulphate</th>
<th>Other Sulphates and Caustic Potash</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proto-albumose (in both)</td>
<td>Soluble</td>
<td>Soluble</td>
<td>Precip. Precip.</td>
<td>not precipitated</td>
<td></td>
<td></td>
<td>Precip. Precip.</td>
</tr>
<tr>
<td>Hetero-albumose</td>
<td>Insol. i.e. precipitated by dialysis from saline solutions in 65°C</td>
<td>Soluble</td>
<td>Precip. Precip.</td>
<td>not precipitated</td>
<td>Ditto</td>
<td>Ditto</td>
<td>ditto</td>
</tr>
<tr>
<td>Deuter-albumose</td>
<td>Soluble</td>
<td>Soluble</td>
<td>not precipitated</td>
<td>Precip. Precip.</td>
<td>ditto</td>
<td>ditto</td>
<td>ditto</td>
</tr>
<tr>
<td>Peptone</td>
<td>Soluble</td>
<td>Soluble</td>
<td>not precipitated</td>
<td>not precipitated</td>
<td>not precipitated</td>
<td>Ditto</td>
<td>ditto</td>
</tr>
</tbody>
</table>

It's alcohol, being partly converted into an insoluble product called dysalbumose.

**The Peptones:**

These, as we have seen, are the final products of the hydration of Proteids. The Protein remains no longer as such if hydration goes further. It is only recently that peptone has been separated from the albumoses and for this we are indebted to Wenslou who found that peptone, unlike the albumoses, was not precipitated by ammonium sulphate. This, T. Sidney Martin declares, is the only method by which peptone can be identified with certainty.
The foregoing table shows the more important reactions of peptone.

Pure peptone, freed from all other proteids and excess of salts by dialysis, precipitated by alcohol, and dried, hisses and foths with evolution of heat on being dissolved in water.

It will now be necessary to study the changes which the Proteids undergo in the alimentary canal.

The Proteids are firstly acted upon by the Gastric Juice and this has been found to be a more complicated process than was at one time supposed.

Various experiments performed to simulate gastric digestion go to prove the necessity of the acid constituent of the Gastric Juice and the value of the ferment, pepsin, in supplementing the change. In due course it has been found that the proteid has passed through the various stages of hydration ending in the final formation of peptone. Beyond this gastric digestion does not normally go.

Hübner, in a paper already referred to (p.3) observed that there are two varieties
of peptone, a form which, by the further action of the pancreatic juice, is split up into leucin, tyrosin etc.; this he called heme-peptone; and a form which resists this action; this he called anti-peptone.

It is thus possible to speak of heme and anti digestive products.

An interesting question, which has been investigated by Neumeister, is whether each form of albumose has an "anti" and a "heme" variety, or are certain albumoses heme and certain "anti"?

His investigations lead him to believe that albumin consists of a "heme" and an "anti" component: as a result of the first stage of hydration the heme-albumin is resolved into proto-albumose and hetero-albumose; the anti-albumin into hetero-albumose and acid-albumin, the latter of which yields only anti-products.

Hetero-albumose results as the second stage of hydration, being thus nearer to peptone in its method of formation, as we saw it was in its reactions.

Proto-albumose yields heme-peptone,
The intermediate deuter-albumose being hemi; as it yields hemi-peptone.

Deuter-albumose yields both anti and hemi-peptone, i.e., amphi-peptone, the intermediate deuter-albumose being likewise amphi.

Lastly, the anti or acid albumin yields anti-peptone, the intermediate product being known as anti-deuter-albumose.

The pancreatic juice acts on proteids with much the same results as we have seen under the gastric juice but with certain differences; the more important are (a) trypsin acts in an alkaline medium; (b) pancreatic digestion is more rapid than gastric digestion; (c) the action goes further, inasmuch as hemipeptone is split up into simpler products, such as leucin, tyrozin etc; (d) the action of the pancreatic juice is rather to erode the proteid than to cause it to swell and become dissolved.

(e) The albumoses are more rapidly dehydrated, and thus converted into peptones, by the pancreatic than by the gastric juice.

The intestinal juice, per se, has no action
on Proteids; this has been amply proved by Masloff, who was the first to make use of antiseptics; by using Thymol or Salicylic Acid he found that the juice had no digestive action even on fibrin. This has been confirmed by Wenz.²

The results of earlier observers, therefore, such as Leube and Thiery were due to the non-exclusion of Putrefactive Bacilli.

Before concluding an account of the changes undergone by the Proteids in the alimentary canal, reference must be made to the part played by Putrefaction.

This is prevented from occurring normally in the stomach owing to the acidity of the gastric juice, which is antagonistic to bacteria. This fact has been satisfactorily determined by Harris and Tooth³.

Strass and Wurtz have found that the gastric juice is an actual germicidal agent.

Putrefaction always occurs, however, in the intestine, especially in the large intestine; the bile keeps the process in check, this indeed being one of its most valuable functions.
The antipeptone is decomposed with more difficulty than the hemipeptone by putrefactive agencies. The products of putrefaction include ammonia, sulphurised hydrogen, ammonium sulphide, volatile and fatty acids, amines, and amido-acids, especially leucin and tyrosin; indol, phenol, and skatol and cresol.

It is an striking fact that certain of the products of putrefaction are themselves antiseptics, especially phenol and cresol, and that if manufactured in sufficiently large amount, or if allowed to accumulate in the system, they would inevitably destroy the life of the microbes which produced them.

Bochard has, in this respect, advanced an auto-intoxication theory to account for certain diseased states, and although we cannot consider it as fully proven, it is an ingenious piece of reasoning and is founded on physiological principles. He considers that an absorption of poisonous alkaloids, which are normally formed in the alimentary canal and are normally excreted from the body, chief
ly by the kidney, may set up a condition of self-poisoning.
Leucin and tyrosin have been found to be produced by trypsin without
the agency of putrefaction; indol, phenol, and skatol, however, result
hastily from bacterial action; there is no doubt, however, that where put-
refaction is present the formation of leucin and tyrosin is much favour-
ed.

The obvious result of the complex changes we have been studying is to transform
the colloid and coagulable albumins into bodies which are capable of dif-
fusion through animal membranes. This property is possessed in a marked
way by the peptones, although some observers, such as von Wittich have
doubted their ready diffusibility. The albumoses do not possess this
quality to the same extent as do the peptones.

Before leaving the subject of the rela-
tion of the Proteids to the peptones it
may be well to refer briefly to what the
exact change consists in.

We have seen that the process is
one of hydration but is there not some
thing further than this which aids in assisting this transformation?

We know that the amido-acids, such as leucin and tyrozin, result from the decomposition of Proteids, and that the Peptones are intermediate bodies in their formation. Is it not natural, therefore, to assume that the Peptones are the first products of decomposition and that the transformation of Proteids into Peptones is not merely one of hydration but is also accompanied by decomposition?

If this is true, as there appears little reason to doubt, an important part in the process must be ascribed to the putrefactive organisms in the intestinal canal.

III. Absorption of Proteids from the alimentary canal.

Having traced the source of these bodies and having considered the changes which they undergo in the alimentary tract, their destiny must now be inquired into, so that we may be in a better position to understand those conditions, where through faulty processes in absorption, the albuminoses and peptone
may be excreted as such in the urine. We must recognize in absorption not merely a physical process but also a vital phenomenon.

The changes through which the proteins have passed, from a colloid to a diffusible state, determine the physical part of the act, namely a diffusion through the walls of the vessels; but the cells concerned in absorption must be regarded as living, and on this account they have not merely a power of selection but also the capability of changing the substances which come in contact with them. This property is specially displayed in the absorption of the proteins.

It has been shown by D'Arcy Power that a certain amount of protein can be absorbed unchanged. After swallowing a dozen raw eggs he found egg-albumin in his urine. Most protein is, however, absorbed as peptone or as peptone and albumose. Yet how is it that these bodies can not be discovered in the blood, under normal conditions, even when the digestive processes are at their height?
Hofmeister, it is true, sometimes found in the blood of animals during digestion small quantities of heptone, and a few other observers had, before this, found traces of heptone in petrol blood, but these observations were made before the thorough separation of heptones was possible, by the use of ammonium sulphate. 

Hofmeister has employed this reagent and proved the absence of the albumoses and heptone from blood and lymph, even during the most active periods of digestion. He is seconded by such men as Pflug, Malpighi, and Gyereghi and Adamkie, Wies, although they differed as to where the changes took place. The portal blood has been found to be as free from albumoses and heptone as the hepatic blood; the liver cannot therefore take part in this change. Where then do the albumose and heptone go to?

Does the blood effect a change in these bodies?

Schmidt-Melheim and Fane inclined to this view, since a solution of heptone injected into the blood died?
heared from the blood in a few minutes. If the blood has this power it can only
be within the vessels, as shed blood
has not this destructive action on pep-
tones.
What part may the white corpuscles
take in combining with the peptone?
These are all points not thoroughly
elucidated yet.
Neumeister could not detect the
presence of albumenoses and peptones
in the blood by chemical means after
injection, although he recognized their
presence by their action in rendering
the blood uncoagulable.
We are left with the hypothesis
that the change from the albumenoses
and peptone into the Proteids of the
blood must occur during the actual
process of absorption.
Probably both the epithelial and lymph
cells are responsible for this dehydra-
tion; but this, as we have already
said, can only be an hypothesis.
This view is favoured by experiments
which shew that the stomach and
bowels, recently removed from an
animal, can reconvert peptone into
the proteids of the blood.
One more piece of evidence may be adduced in this connection. M. Phol's has shown if a solution of peptone be placed in contact with pieces of mucous membrane removed from an animal recently killed, and then be artificially circulated through a frog's heart, it has the power of keeping it beating, which it had not before being brought into contact with the mucosa. Here we may believe that the solution of peptone has been transformed into the blood proteins. We must however bear in mind the great effect produced by minute doses of salts on the frog's heart, as pointed out by Ringer, which detracts from the value of such an experiment as this.

It must be noted that these experiments bear only on the physiological side of the question as to where the peptides become regenerated into the blood proteins. It would be more satisfactory were we able to obtain chemical proof on this subject. One can therefore only suppose that the peptone is reconverted into protein in the mucous membrane of the digestive tract; and that it is a vital
process has been shown by Hofmeister to be probably the case. He took the stomach of a recently killed animal and divided it into two symmetrical halves by incisions in the greater and lesser curvature; one half he threw into boiling water, the other he kept in water at 60°C. for a few minutes before placing it for two hours in a temperature of 46°C. The amount of peptone in both halves he found to be the same. A temperature of 60°C. kills the living animal cells but not the unorganised ferment. The conversion of peptone into proteid must therefore be brought about by the vital actions of the surviving cells. We may quote one further experiment which agrees with Hofmeister's results.

Salvioli cut out of a recently killed dog a coil of small intestine, with its piece of mesentery attached. One gramme of peptone in solution (10ccms) was placed in the intestine, and the ends closed. Then a current of warm defibrinated blood, diluted with a solution of common salt, was injected into a branch of the mesenteric artery and was allowed to flow out again.
by the corresponding vein, the collateral vessels being tied; marked peristalsis was set up.

After the current had lasted for four hours the contents of the bowel were examined and were found to consist of about half a gramme of coagulable albumin, with mere traces of peptone. No peptone was found in the blood which had been making the circuit. Peptone added to the blood, however, beforehand, was always found unaltered at the end of the experiment. From this the peptone evidently seems to disappear in the intestinal wall on the way from the intestinal contents into the blood.

It is probable that the reconversion of peptone into the blood proceeds within the intestinal wall is not by any means a complete one, and therefore we must suppose, in spite of the inability to detect it, that part of the peptone passes into the blood: if this is so, as Hofmeister would have us believe, what happens to this peptone, and why does it not appear in the urine as we
shall find it does, when introduced artificially into the blood?

It is probable that the peptone absorbed from the intestine as such, behaves differently from that which reaches the blood from other sources.

Hofmeister considers that the peptone which has reached the blood from the bowel is contained not in the plasma but in the leucocytes. If this is true we can then account for the inability of the observers we have already referred to, to find peptone in the blood: they merely examined the plasma.

We know that pus cells contain peptone and we shall have more to say about this at a later stage.

This theory is also based upon the finding of peptone in the spleen, where leucocytes occur in large numbers; again leucocytes are found in considerable quantity in the adenoid tissue of well-fed dogs; in hungry and fasting dogs they are much diminished in number.

Peptone has been found in the uppermost layer of blood-clot, where the
Leucocytes are most abundant 1-2
of per cent of blood. Lastly Pohle 3 has found the number
of leucocytes to increase during the
digestion of proteins but not during
the digestion of the other classes
of food-stuffs: this leucocytosis, he
has further shown, proceeds from
the bowel wall.

What happens to the peptone that
we have seen is probably contained
in the leucocytes and has been brought
thither from the intestine 9.

We know that it is not normal
ly excreted in the urine and it
does not disappear in the blood, as
has been experimentally shown 3. We
can only imagine that it passes into
the tissues from the capillaries,
as is surmised by those who have failed
to find it in the blood of the cows
feeding veins, when it has been
found in arterial blood during
digestion.

We may suppose that it becomes chan-
ged and excreted from the body, ta-
king part in the general metabolism.
This can however be merely hypothet-
cical, so far as our present knowledge
goes.
The source and the destiny of the albumoses and peptones has now been sketched, to have the way for an inquiry into the etiology and pathology of their occurrence in the urine.

\[IV\]

The conditions in which albumonuria and peptonuria have been described as occurring:—

It is only quite recently that the albumoses have been satisfactorily separated from peptone, and many cases, described as cases of peptonuria, have probably been cases of albumonuria, the proteid most likely to be mistaken for peptone being, as we have seen, deuterous or secondary albumose. Peptone was first described in the urine by Gerhardt. To Kühne and Chittenden, whose papers have already been referred to, we are largely indebted for our present knowledge of peptonuria and albumonuria.

In a large number of diseases peptone and albumose have been described as occurring in the urine. In several fevers peptone has been found in the urine, typhoid, typhus, variola, scarlet fever, mumps, erysipelas, measles, in general acute diseases, acute rheu...
matism, tuberculosis, scurvy. In empyema, cancer of the liver and intestines, catarhal jaundice, para
metritis, apoplexy, etc.
Schultzen and Reiss record a case of phosphorus poisoning where peptone was present.

Maixner records a case of empyema pneumonia with peptone in the urine.

Regarding the albuminoses, Jones was the first to describe a case of albumosuria; hetero-albuminose was probably the form of albuminose he found. His case was one of osteomalacia. Kühne has since found it in the same disease and others too. Hoppe-Seyler found it in some cases of kidney atrophy. Plassas found it in the urine of people rubbed with petroleum. Bortel found it in a few cases after severe exertion.

Gowers has found it in a case of glycosuria.

Deuteroproteose is sometimes found in the urine; indeed, many cases in former times described as cases of peptoneuria were really cases where this form of albuminose was present.
Albumin and peptone are also found in the urine in many other conditions where no explanation has been forth coming, such as various skin eruptions, in some nervous diseases, cerebral hemiplegia, or psychoses. Proto-albumin has probably yet been found in the urine.

We may find albumin or peptone in the urine in cases of chronic nephritis where some of the albumin has been changed into these bodies. The serum-globulin, which may be present in albuminuria, may also be likewise changed, in this case probably into hetero-globulose.

It will thus be seen that albuminuria and peptoneuria have been described in a large number of diseases, diseases which appear to have no common pathology to explain their occurrence, in many instances, at first sight.

It will now be necessary to point out what is known as to the pathology of these symptoms, and to attempt to explain their occurrence in, at any rate, some of the numerous diseases above mentioned.
IV. Pathology of Albumoscuria and Peptonuria

Uria:

Very little information has been forthcoming of a definite nature to explain the occurrence of these morbid phenomena, and in discussing their pathology we must rely on conjecture to a considerable extent. There are three possible sources of albumoscuria and peptonuria. In the first place, they may be derived from the gastro-intestinal tract; secondly, it is possible that they may arise in the blood itself, and thirdly, morbid conditions in the tissues may result in their formation and excretion in the urine.

In considering their derivation from the intestinal tract we are at the outset beset with a difficulty; for we do not really know the precise change by which the albumoses and peptones are regenerated into the proteids of the blood; in other words, the exact physiology of the process has not yet been revealed.

We have to be content to say that the change takes place during the actual process of absorption, that the
gastric and intestinal mucous mem-
- braces affect the change, and that
- the change is a vital one.
- If, then, we do not know precisely
- how the change is brought about,
- it is not easy to formulate deviations
- from what normally takes place.
- Faults may arise in connection
- with the absorption process, and
- these may come about in many
- different ways.
- By an excess of heptone being formed,
- we can understand that the 'equilib-
- rium' of metamorphosis, so to speak,
- might be put out of gear, resulting in
- either the excess of heptone or possibly
- even all the heptone being absorbed,
- more or less unchanged. Again, by
- faulty chemical processes, the al-
- bromes might fail to be completely
- hydrated, and be absorbed either
- at the primary or secondary stage
- as such.
- It is quite reasonable to suppose that dis-
- eases of the stomach or intestine, such as
- inflammation, degenerations of various
- kinds, or malignant disease, might
- so interfere with the vital ac-
- tion of the cells concerned in the
metamorphosis as to render them more or less functionally inactive; as a result of such a condition, absorption, ceasing to become a vital act, might become merely a mechanical or passive process.

Even where there is no organic lesion in the gastric or intestinal mucous membrane, it is possible that function may modify the process of the metamorphosis of peptones materially, for there can be little doubt that the vital action of the absorbing cells is completely regulated by the nervous system. Reflex inhibition of the action of these cells, therefore, such as might arise from mental emotions of various kinds, or even from unsuitability in the quality or the quantity of food ingested, in fact, all causes of functional dyspepsia might. We may argue, allow of peptone, or even of the albuminoses, being absorbed more or less unchanged.

That such has not yet been proved to be the case speaks very highly for the wonderful way in which the stomach and intestine do their work.
We cannot but admire the manner in which the poisons produced in our alimentary canal, for as we shall see later on, the albumen and peptone, in sufficient quantity, act as violent poisons, are normally prevented from being absorbed as such into the circulation and thus doing us damage. When these bodies are allowed to pass through the gastric and intestinal mucosa unchanged, then it is that we have one source of peptonuria and albuminuria. The theory already brought forward might serve to explain some cases of chronic dyspepsia with dilated stomach where peptonuria has been found, and also some cases of malignant disease in which, as has already been pointed out, it may occur.

Can this theory of the absorption of the albumen and peptone more or less unchanged, serve to explain some cases where chronic dyspepsia is associated with anemia, toxic headache and constipation, these bodies acting as poisons in the blood?
The chief argument against such an hypothesis would lie in the fact that albumoscuria and peptonuria have not, so far as we know, been described in this class of cases; but the detection of these bodies in the urine has only lately been perfected. Although, so far, this conjecture has nothing to support it from the clinical point of view, yet it is permissible.

We shall consider later on the question as to the possibility of these bodies, which have been absorbed into the blood, being destroyed there, and, on this account, not being able to be detected in the urine.

Let us next turn to the tissues as a source of albumoscuria and peptonuria; we shall find that most of the cases that have been described have been referred to morbid conditions in the tissues. In this connection we must remember that Hofmeister and others believe that during digestion some of the peptone is absorbed unchanged, probably extremely little peptone
passes into the blood as such, and therefore this may be eliminated as a source of peptoneuria under normal conditions. An interesting question may arise with regard to this unchanged peptone; does it vary in amount even under normal conditions and if it does vary, what are the limits, and how is the quantity kept within those limits? If we grant that some peptone does become absorbed unchanged, then it is extremely likely that this quantity may be so increased as to give rise to the excretion of peptone in the urine. When we consider the tissues as a source of the alburenes and peptone we are supposing that the gastro-intestinal tract is doing its work and that these bodies are undergoing their normal metamorphoses.

Under what circumstances, then, may the alburenes and peptones be formed in the tissues? This is the key to the pathology of alburenesia and peptoneuria derived from this source. Hofmeister has, as we have seen, referred to the affinity shown by peptone
towards the white blood corpuscles, for he considers that the peptone absorbed from the alimentary tract is contained in this element of the blood, and not in the serum.

When, as a result of inflammation, or more especially of suppuration, disintegration and death of the leucocytes takes place with formation of pus, then it is probable that the cell-proteids, which are identical with or closely allied to the blood proteids, are converted into albumoses and peptone.

Just as this action took place in the stomach and intestine in the presence of a ferment, so it is reasonable to suppose that the same process may occur in the tissues. What is the exciting cause here? We may suppose that the change may be set up by bacteria contained in the pus, or else by ferment, possibly allied to the digestive ferments, set free by the disintegrating and dying leucocytes.

This is the most plausible theory which has been brought forward to account for their presence in pus.
Albuminases and peptone have been described in pus by several observers. Eichwald was the first to describe their occurrence in pus. Hofmeister has also done work in this connexion. Sir Sidney Martin has, however, shown that the methods adopted by these workers were not entirely trustworthy; he considers that the only reliable way to detect these bodies is to place the pus under alcohol for several weeks, dry and extract with water. Albuminases and peptone remain in solution, the other proteids becoming coagulated. Halliburton considers that the albuminases and peptone are often found in pus in considerable quantities. Here again we find these bodies in the pus corporcles, not in the liquor puris.

If then pus contains or may contain albuminases and peptone, we have a clue to their presence in many of the diseases where peptonemia and albuminemia have been described as occurring.

We may probably go further than this and say that even in cases where there is not actual pus formation,
but where a great cell disintegration takes place, there we may have the formation of these bodies.
Hence we may include not only such cases as abscesses, empyema, puerperal inflammations of such serous membranes as the peritoneum, but also diseases where we know a great cell-disintegration takes place, such as phthisis, malignant growths, pneumonia, the specific fevers and phosphorus poisoning, in which, as we have seen (p. 22) it has been described, and indeed, all or nearly all those cases in which we have seen it may be present.

How can we account for the presence of hetero-albumose, known as Bence Jones' albumin, in the urine in cases of osteomalacia? The pathology of this disease is very obscure, but from the synonym it has received, mollities ossium, we gather that a large disintegration of the osseous tissue takes place, the bones becoming gradually decalcified, so that here again the theory holds good. It would be difficult to say why we have here an excretion of albumose.
and not of peptone.

In such cases as the ones we have been considering why should we have both albumenoses and peptones formed? We must probably look on the formation of the albumoses as a stage towards the final formation of peptones as we do in digestion; the complete change depending on the activity of the bacteria concerned in the process.

Once again we can account for the occurrence of these bodies in cases of glycosuria (Gowers) and in cases of severe exertion (Gerstel), which result in increased metabolism, and therefore more or less cell disintegration.

It would be interesting to bear out Gerstel's observations by examining the urine of men engaged in severe manual labour such as blacksmiths, navvies etc., with a view to ascertaining if the cell disintegration, dependent on their work, resulted in the formation of and excretion in the urine of the albumenoses and peptone.

We can hardly believe that peptone and
albunmoses result in every case where cell disintegration occurs, even when in large amount; or else peptonuria and albunmosuria could not fail to be far more common than they are. We can only say that when excrated in the urine there is either a probability of pus formation or great cell disintegration in the body, that is to say when we have reason to believe, as we usually have, that their derivation is from the tissues.

There are many points of interest in connection with the pathology of the formation of albumoses and peptone in the tissues, but we must refer to one, namely the possible part played by these bodies in the production of fever.

It cannot be said that the pathology of the fever process is yet fully agreed upon. There is no doubt that the immediate cause of the heat generated in fever, lies in the increased blood and tissue oxidation, which signifies that rapid metabolism is going on. Now we have seen that where there is rapid metabolism there we may find albumosuria and peptonuria.
It is an enticing theory to assume that the microorganisms which are associated with nearly, if not with all, the different fevers with which we are acquainted, act on the tissues, setting free or giving rise to the formation of peptones and albumoses; that the consequent cell disintegration with the formation of these bodies produces the rise of temperature, the rise being in proportion to the dose of albumose and peptone.

When considering the results of the artificial injection of these bodies into the circulation we shall see how much ground there is for such an hypothesis.

To account for the cause of the temperature rise in what is commonly known as traumatic or waste prod-uct fever, which is believed to be aseptic in character, we may argue that as a result of the 'aseptic tissue necrosis', which results from the injury, the albumoses and peptone are formed by a ferment (the fibrin ferment?) and act as we have already conjectured.

A most interesting fact has been record
...ded which lends some probability to this view, namely that peptain and trypain, when introduced into the circulation, can cause this type of fever: this we believe they do by depotentising the tissues.

One more type of fever may be referred to, namely hectic. The conditions under which we are liable to have hectic fever developed are those in which it has been pointed out that albumoses and heptone may be formed in the body and excreted in the urine.

We know that albumoses and heptone act, when introduced into the circulation, by producing a rise of temperature, and therefore we have ground for assuming that they may so act when manufactured in the tissues.

How far they may account for the other phenomena of the hectic state we have not yet evidence to show.

Martin, in the paper already quoted, believes that the fever which accompanies suppurative processes is often, at any rate in part, produced by the
entrance of these substances into the circulation.
Lastly the blood itself must be considered as a possible source of the albuminoses and peptone.

There is however little or no evidence to show that albuminuria or peptonuria may arise from the formation of these bodies in the blood, as there is to prove the dependence of these symptoms on their derivation from the tissues.

That the albuminoses and peptone must circulate in the blood before being excreted in the urine is obvious, but at any rate, in by far the larger number of cases, the alimentary canal or the tissues, or possibly both, must be regarded as their source.

Yet we may argue that the bacteria may act on certain elements in the blood, viz. the proteins, transforming them as in the case of the cell-proteids in the tissues, into albuminoses and peptone; if this does occur, the change would probably take place under the same conditions as govern the formation of these bodies in the tissues.
It is more probable, however, that the action of the blood towards albumoses and peptone is a haemolytic rather than a homogenic one; and this conclusion is based upon the comparative infrequency of albumousia and peptonuria, when contrasted with the frequency and variety of those diseases in which these bodies have been described as occurring in the urine.

This can in great measure be accounted for by insufficient and inaccurate analysis of the urine in those diseases where we might expect to find these bodies, were a systematic and accurate search made for them.

Yet it is hard to believe that the occurrence of albumousia and peptonuria in the urine is proportioned to their absorption into the blood from the alimentary canal or from the tissues in disease.

In considering the changes undergone by the proteins in the alimentary canal, we saw that one of the actions of the pancreatic juice was to change part of the peptone, namely
the hemi-peptone into simpler products, such as leucin, tyrozin etc. (Other products are asparaginie acid, ammonia and proteinichromogen).

Why, we may ask, should not this change occur in the tissues, or even in the blood? If the agent is present which can transform the cell protoids and even the blood protoids into all bromones and peptone, why should not the change go a step further? We know that putrefaction is not necessary for the formation of leucin and tyrozin, although their forma-

As it is not possible that the hemi-

peptone formed in the tissues is in whole or in part further acted upon by the agent which produced it, while the antipeptone resists this change and is excreted in the urine?

Or, to go a step further, it may be suggested that where heptonuria occurs, there the peptone is present as antipeptone, whereas in many cases, where we should expect to find heptonuria, we fail to do so, for only hemipeptone has been pro-

duced, and has been broken up into
simpler bodies, which we cannot detect in the urine. Such a theory as this might account for the absence of peptoneuria in some cases, e.g., chronic abscesses, where we know peptoneuria may occur, and, expecting to find it, we fail to do so.

An objection to such a suggestion is the absence, in most cases, at any rate, of leucin and tyrozin, and those bodies into which hemipeptone is split up, from the urine in those cases, where, expecting to find peptone in the urine we failed to do so.

It is highly probable however that leucin and tyrozin have some relation to the excretion of peptone in the urine, for tyrozin and peptone have been found in at any rate one morbid state in the urine together, namely in acute phosphorus poisoning, where we know a great cell disintegration takes place.

It is probable that the morbid anatomy of the liver in cases of acute phosphorus poisoning closely corresponds with that of the liver in 'acute yellow atrophy' or 'malignant jaundice,' where we know a prominent feature in the disease is the occurrence of
leucin and tyrosine in the urine.

One might argue, therefore, that in certain diseases of the liver, characterized by great parenchymatous degeneration with disappearance of the liver cells, peptone may be found in the urine; but where it is absent, then the bodies formed from its disruption would replace it. It is a curious coincidence, however, that, so far as we know leucin and tyrosin have not been found, at any rate at all frequently, in poisoning by other agents such as arsenic, antimony, alcohol, or even in malignant disease of the liver, where the morbid anatomy of the liver corresponds to a greater or less extent in its broader features, namely the destruction of the liver cells, with that of acute phosphous poisoning, although peptonuria has been described in malignant disease of the liver and in catarhal jaundice, and not improbably in other organic liver diseases. The clinical side of this question requires investigation; it will then be possible to decide if there is any practical evidence to support this hy
Detection of the albuminoses and peptone in the urine:

In considering this subject we require to bear in mind that the albuminoses and peptone may all be present or may be present separately. A systematic method of analysis is therefore necessary. A table of the reactions of the albuminoses and peptone to various reagents already seen shows the essential points in which they differ chemically and many of these reactions are made use of in separating them from the other proteins and from each other in the urine.

The albumin and globulin and hetero-albuminose must first be separated before deuter-albuminose and peptone can be tested for. (Protos-albuminose has not been described as occurring in the urine and may consequently be ignored in this connection.)

If we take a test tube and fill it 2/3 full of urine and heat the upper part of the urine, and a cloud appears, we know the cloud is due to one of the
causes, either the cloud is due to coagulable albumin, phosphate or to hetero-albuminose being precipitated. Martin shows that if we continue to heat the urine to boiling point, the hetero-albuminose disappears. By now adding a small quantity of acetic acid we dissolve the phosphates and the insoluble albumin remains.

The exact temperature at which hetero-albuminose becomes precipitated varies from 43° to 50° C; serum albumin or globulin are precipitated at from 70° to 95° C, and phosphates close to the boiling point.

The confirmatory test for hetero-albuminose is a characteristic one; nitric acid added carefully to the cold urine gives a precipitate, which dissolves on heating, and reappears on cooling, once more redissolving on again apply heat.

The detection of serum albumin and serum globulin, which must be coagulated, if present, before proceeding further, need not now occupy us. It has already been pointed out that until lately deuterous albuminose and peptone were indistinguishable.
These two bodies behave so similarly to reagents that the only way to distinguish them is to shake clear urine in a test tube with solid neutral ammonium sulphate. If the urine gives the reactions we are about to refer to, and also a precipitate with this reagent, we know deuter-albuminose is present. When no precipitate results, and the other reactions are obtained, peptone is present and true peptonuria is therefore present.

There are, as has just been said, certain reactions, which are given alike by deuter-albuminose and by peptone.

The biuret reaction (a drop of dilute solution of copper sulphate with excess of caustic potash) gives in both cases a rose-red colouration. Diluted Helmy's solution may give the same reaction. This is not a very delicate test, as small quantities of these bodies may not be able to be thus detected. Copper sulphate alone gives no precipitate with deuter-albuminose or with peptone, while hetero-albuminose is precipitated by it.
Lastly the reaction of deuterio-albumose and peptone to nitric acid must be referred to. The former gives no precipitate unless excess of salt be present, while peptone gives no precipitate under any circumstances. We have hitherto referred to clinical analysis of the urine so far as the albumoses and peptone are concerned.

In order however to separate the albumoses and peptone from the urine we have to make use of alcohol and the process requires one month, or preferably two or even three months for its completion. By adding ten times the volume of alcohol to the urine we precipitate all the proteins. At the end of the time above stated, pour off the supernatant alcohol, evaporate the remaining alcohol at 140° C., and add water. The albumoses and peptone enter into solution.

After faintly acidifying the solution with acetic acid, saturate fully with ammonium sulphate and filter off the resulting precipitate. This contains the albumoses, the filtrate the peptone.

After again saturating the precipitate with ammonium sulphate, redis
- Solving with water, acidifying with acetic acid and saturating with common salt, we separate the primary from the secondary albumoses. To separate the peptone from the filtrate already mentioned, the solution is evaporated to a small bulk, the crystals of ammonium sulphate are removed by filtration, and baryta and, if necessary, barium carbonate; the sulphate of barium thus produced is filtered off to the filtrate alcohol is added which precipitates the peptones; the precipitate is then washed with alcohol and ether and dried, and, if required, weighed.

This is the process, briefly described, for the separation and, if necessary, the quantitative estimation of the albumoses and peptone in the urine.

Observations on the results obtained by the introduction of the albumoses and peptone into the circulation:

This part of the subject is closely related to the pathology of albuminuria and peptoneuria, in fact it belongs to pathology, constituting the experimental pathology of these morbid phenomena; it has been thought, however, advisable to consider it separately.
The results which have been obtained from the injection of albuminoses and peptones into the blood are valuable in enabling us to bring forward, in at any rate a small degree, evidence to support some of the conjectures which have been already brought forward.

It has been shown by Schmidt-Mulheim and Dano that, if a certain quantity of commercial peptone, such as Witte's or Grube's, say about 0.3 gramme per kilogramme of body weight, be injected into a dog's circulation, and the animal, then killed by bleeding, the blood will be found to have lost the power of coagulating. They found this inability to coagulate lasted about 3 hours.

It is curious that this was not found to occur in the case of the rabbit.

This action of peptone has been disputed by Politzer, who considers that commercial peptone is impure. He believes the results referred to are due to the albuminoses, especially to hetero-albuminoses, contained in the impure peptone, and that pure peptone has little or no such effect.
Pollitzer has gone further than this in pointing out that the albumones may delay the coagulation of blood already shed. Some ferments have been shown to act in the same way.

A further action of the albumones and peptone on the circulation is to markedly reduce the blood pressure: this was shown experimentally in the case of the dog, even producing coma and death, the albumones again being the chief factors in these results. The action of these bodies in producing fever when artificially introduced into the blood has been already referred to, but a dose too small to cause a marked fall of blood pressure with coma may produce a marked rise of temperature. And this may occur in rabbits, whose blood is not affected as is the dog's

Peptone injected into the blood rapidly appears in the urine as such.

Deuter-albumenose is excreted as peptone, being probably transformed in its passage through the blood into peptone, the final stage of hydration. It is possible that the change may...
occur in the act of secretion, especially if there should be any free acid present, for it has been found in large amount in the urine of carnivorous animals, but unless the free acid be present, the further hydration of deuter-albumose will not take place by this agency.

Proto-albumose and hetero-albumose have in the same way been found to undergo a further stage of hydration, occurring in the urine as deuter-albumose.

It seems curious that the process should stop short at this stage and further experiments are required to substantiate these results and explain them.

We may believe that the albumoses and peptones that are absorbed from the intestinal canal or tissues, or perhaps from the blood itself, and are excreted in the urine, undergo similar changes in excretion, or preparatory to excretion, to those we have seen following upon the artificial entrance of these bodies into the blood.

How can the coagulation of the
Blood be explained that has been found to result experimentally, and is it possible that this may occur in man as a result of the absorption of albumoses and peptone?

This is a question which is full of interest but we have not much light on the subject.

The most likely theory that has been put forward is that the peptone and probably the albumoses to a greater extent, act by inhibiting the activity of the fibrin ferment and thus retard or even arrest the coagulation.

A poisonous constituent has been separated from many peptones, being formed during the digestion of fibrin by artificial gastric juice; this is called peptone-totonic, being one of the ptomaines. It has been found to be rapidly fatal to frogs and rabbits, producing paralyseis and insensibility. May this alkaloidal poison have any action in thus inhibiting the activity of the fibrin ferment, or indeed in causing any of the other results already alluded to?

With regard to the fall of blood pressure, it must be assumed that
These bodies act, probably by means of a ptomaine or ptomaines derived from them, on the vasomotor centre in the medulla, inhibiting its action. Probably these phenomena are only caused by large quantities of the albumoses and peptone, and consequently we do not see these symptoms in cases of albumosuria and peptonia in man, where the amount absorbed is too small for their production. This does not, as has been mentioned, apply to the production of fever, however. Therefore, we find the results of the injection of these bodies into the blood tallying with these dependent on the absorption of the albumoses and peptone from the body. This, then, is a piece of evidence which goes to support the view already expressed that albumoses and peptone, especially when they occur in suppuration, play an important part in the increased heat production, constituting the fever process. The question may once more be raised as to how far this is dependent on the albumoses and peptone themselves on the one hand and
on toxins developed by these bodies on the other?
We have now examples of several diseases in which toxins are developed in the system by bacteria, which produce the general symptoms of the disease: the best examples probably of such diseases are diphtheria, tetanus and anthrax.

It is highly probable that the toxic action of the albumoses and peptone, when in sufficient quantity in the blood, is due to an alkaloid or alkaloids secreted by these bodies, and to such toxine or toxines must be attributed the various morbid phenomena we have enumerated.

The value of albumosuria and peptonuria in the diagnosis, prognosis and treatment of disease:

What is to be gained from the practical point of view, and this, after all, is of the most value to the physician, from the discovery of the albumoses and peptone in the urine? Are we in a better position to treat disease and to save life when we have discovered the existence of albumosuria and peptonuria?
It must be admitted that the answer to such questions as these is not yet very encouraging.

We have seen the diseases and morbid states under which these bodies may exist in the urine.

There is no doubt that the most important evidence of their presence in the urine is the existence of a large cell disintegration, and probably also a breaking down of the proteins apart from this, going on in some cases to suppuration.

In all cases of suspected cell disintegration and suppuration, therefore, the albuminoses and hydrophobes should be looked for in the urine: in such cases their presence or absence may be taken as a standard of the latency or activity of disease, especially where they have been present at one period, and have disappeared under treatment.

Thus in a case of advanced hip joint disease or in phthisis pulmonalis in its later stages, the presence or absence of these bodies in the urine would aid us in the often very difficult task of formulating a prognosis.
The presence of albuminuria and peptonuria may aid us in arriving at a diagnosis in some obscure cases of suppuration, and inflammation of a suppurative type. Examples of such conditions are suppuration inside the skull arising under various conditions, where the diagnosis is not clear. Again in cases of pneumonia going on its abscess of the lung a sudden occurrence of peptonuria would, where this complication was suspected, strengthen the suspicion: a pleural effusion may become purulent; here again, peptonuria in the urine would, if it were required, assist us in diagnosing this change.

Even although it may be argued, and with truth, that we are not much better for discovering these symptoms, yet it is only by observation of symptoms in disease, and their correct interpretation, that advance in the science of medicine can be made; and we cannot tell how long it may before the albuminoses and peptones may be found to play a most important part in disease and their occurrence...
in, or absence from, the urine be of
the greatest importance in the diag
nosis, and even in the prognosis of
disease.

Any one, therefore, who observes
these phenomena and is able to
correctly estimate their value, is con
tributing materially to our know
ledge.

With regard to the treatment of
cases presenting these physical
signs, we recognize that they are
the symptoms of serious pathological
conditions and treat the disease in which they are present; for
we cannot attribute any symptoms
to the presence directly of those sub
stances in the body as yet.

Their presence may however direct
our attention more especially to
the conditions under which we
believe they arise, conditions which
otherwise might have been ignored,
or held to be of little consequence.