Welcome medal in the History of Medicine - 1913.

Essay
on
The History of the Development of our Knowledge Regarding Secretion.

by
Karl F. Sonntag, M.D.

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Introduction. The secretions have always played an important part in the history of physiology and of pathology, and men's views about them have altered much in the passage of time. The ancients attributed life itself to their cooperation with some vital force. Today we are acquainted with many different secretions—both internal and external—and we regard them as interacting to promote harmony in the organism. Popular interest has been aroused in them at different times and the latest stimulus was the lecture given to the British Association in Dundee by Professor Schäfer in September 1912.

Many of the crude ideas of the ancients were due to their not recognizing the value of linking together physiological facts. They rather regarded the phenomena of life as being due to gods. They were also influenced to an undue extent by philosophy, and they only made progress after anatomy and physiology were freed from philosophy and...
joined together. Anatomy was kept back because the superstitions of the day prohibited the dissection of human bodies. Many anatomical facts were misinterpreted. Hippocrates and Galen, for example, considered that the glands were reservoirs for humours and effete materials.

Medical knowledge was retarded also by the lack of original investigators. Men put too much belief in the masters such as Hippocrates and Galen and simply copied them. It was only when Galen's ideas were overthrown by Vesalius, Bartholin and others that secretions were understood along with the other bodily structures and functions.

Nevertheless, the ancients founded many very ingenious theories which were extended more by speculation than experiment. It was only in the middle ages that these were overthrown. The reaction against them was strong
but the pendulum swung back later, and we are recognising today that the ancients came very near the truth in some things in spite of their crude ideas.

A historical account of the sectations can be divided into three periods. The first and second are most distinct but the second and third overlap to a certain extent.

The first period may be called the epoch of the humoral doctrines. Most of the phenomena of life were supposed to be due to humours which were produced or eliminated in the glands. It extends from the time when the schools of <NAME> and <NAME> flourished about four hundred years before Christ till the time of <NAME> in the year 1540 AD. It is marked by the two outstanding names of <NAME> and <NAME>.

The humoral period was followed
by what we may term the "Period of External Secretion". It extends from
the time of Vesalius in 1540 till the
year 1889 when Brown-Séquard
drew attention to the internal
secretions. Hippocrates and Galen
were overthrown and originality
entered into medicine. Different
observers studied the structure
and functions of the different
glands.

After the year 1889 we enter on
our third period or epoch of
Internal Secretion. The line of
demarcation between it and the
second period is fairly clear.
There is some overlapping however
for Claude Bernard and others
had glimmerings of internal
secretions as far back as 1841,
whilst Edkins, Starling and others
have worked at enzymes and
hormones since.

These three divisions of the subject
do not correspond exactly to the
divisions of the History of Medicine but they are very convenient for our present purpose.

Before the time of the Schools of Eras and 600 there were no true medical theories which could explain secretions. Many of the ancient races had mythical ideas, however. The Ancient Babylonians thought that everything was due to some god and the body juices did not escape. The blood was the body juice which was the foundation of life. This was based on their idea that one of the gods was decapitated and his blood was mixed with earth.

The Ancient Egyptians were in advance of the Babylonians for they had a dominating factor in their conception of life. The fluids of the body cooperated with the breath to form life.

The Indians thought that life was carried on independently of the soul by blood, phlegm, and bile.
Of all the people of the past the Chinese are specially to be noted for their ideas today are practically the same as they were in ancient times. Some of them were very peculiar. They thought that semen originated in the right kidney which they called the gate of life. Although they had no knowledge of internal and other secretions, they practiced homeopathy to a large extent.

The beginnings of theory regarding the body juices were the philosophical writings of Pythagoras and Empedocles of Agrigentum. Empedocles formulated the theory of the four elementary forms - water, fire, air, and solid. Upon it Hippocrates consolidated all humoral ideas into a definite theory. These four forms were dominated by two forces - an active or spiritual and a passive one called amorphous substance. The element which predominated gave every body its form.
of importance was that of Hippocrates of Cos who lived from BC 460 to BC 397. The actual books he wrote is uncertain but the most probable ones are collected into the so-called "Corpus Hippocraticum". In it there is a monograph on the glands and this is probably the first medical writing about them.

The glands were described as bodies of a loose spongy nature and a fatty yellow colour. Their tissue is not the same as that of other parts of the body because it is granular. They have many veins. When they are cut the blood which flows out is white and watery. When handled they feel like greasy wool, and if strongly pressed between the fingers, a juice oozes out which looks like oil and their structure is destroyed.

The glands are found in great numbers in the interior of the body; more numerous in the cavities than round the articulations. They are
found in all moist and sanguineous regions.

Some of these glands were for the purpose of attracting and taking up the humours that come from above, into the cavities, and others about those which are poured out into the cavities themselves or those which are expressed by the working of the joints. Thus they prevent superabundance of humours in the tissues.

The glands had an intimate relationship to the hairs. After the glands had attracted the humours, the excess of these fluids was led out by the hairs which grew as a result. In dry parts of the body hair and glands are not found.

The monograph described glands in the omentum and intestines. It said that the excess of moisture prevented the development of hairs in the same way as sodden ground hinders the germination of seeds.

The head has glands; the brain is a gland.
gland. It is white and divided into lobes like glands. It gathers together the humours in the head and distributes them to the extremities by currents. The brain is larger than all other glands and the hair on the head is longer than elsewhere.

The ideas described in the monograph give us a good conception of the ramblings of the physiologists of the time. They show that they were not lost for any theory which might explain facts which they could not understand.

Among his famous works on medical subject, Hippocrates will always be known for his humoral theory. Before his time, however, everything was explained as due to humours. Hippocrates consolidated all the facts into a definite form. The humours were supposed to circulate through the body and, if their course were obstructed, acrid or sour fluids broke out in
different parts. There were at first many
humours but after the time of
Empedocles of Agrigentum they
were reduced to four—blood,
phlegm, black bile and yellow
bile.

Hippocrates gathered together all
known facts about the humours
and arranged them systematically
into a definite theory. He based
his statements to a great extent
on the facts and fallacies of the
theory of Empedocles of Agrigentum.

He said there were four humours—
blood from the heart representing the
warm-moist quality; yellow bile
from the liver representing the
warm-dry quality; black bile from
the spleen representing the cold
dry quality and phlegm from
the brain corresponding to the
cold-moist quality. The humours
were renewed by means of food.
If the humours were not properly
blended or if one was in excess of
The others disease resulted. Each humour also preponderated at some season of the year—blood in spring, yellow bile in summer, black bile in autumn, and phlegm in winter. Diseases due to any abnormality of the humours were more likely to appear in the season in which the affected humour was predominant.

Nemjburger aptly sums up the ideas in the humoral doctrine in these words: "This fantastically-conceived scheme, comparing the character of the season with the salient feature of the body humour, was only a part of the analogy drawn between cosmic phenomena and organic forces. It possessed, however, empirical support in genuine observations upon the seasonal variations of disease."

In the writings of Hippocrates there are many peculiar conceptions of the uses of different organs and
secrections. We have already seen how
the brain was likened to a gland.
It collected, among other humours,
semen from the whole of the
body and sent it down the
spinal cord to the testicles.

After Hippocrates and his
famous School of Cos there came
many medical sects which all
had their own special theories.

Dogmatists. The first of these was the
Dogmatist School, so called by Galen.
It included the names of Theophrastus,
Polybos, Plato, Diocles and Aristotle.
All believed in humoral doctrines.

Desippos. Desippos laid much stress on
bile and phlegm. If they melted
and became fluid, lymph and
sweat were formed. If they became
firm by drying up, flesh and
fat resulted. Anomalies of bile
and phlegm gave rise to disease.

Philippos. Philippos, on the contrary,
regarded bile as the result but
not the cause of disease.
Plato said that the liver, which is smooth and shining as glass alters, by means of its sweet and bitter principles materials derived from the head. The spleen is related to the liver and absorbs impurities. Digestion is brought about by inspired fire. The intestines aid digestion by preventing the food from passing too quickly.

Diocles of Carystos was, according to Pliny, the greatest physician after Hippocrates. He described the cystic and hepatic ducts. According to him, nourishment occurs through the blood which is formed in the liver. When food is taken into the stomach it undergoes a putrefactive process which is brought about by inspired warmth. This constitutes digestion. Wastes are got rid of in the intestines, bladder, sweat and exhalations. The four humours were regarded by him as cardinal fluids and not as primary elements of the body. They were evolved from food.
The last of the Dogmatists was Aristotle, who lived from BC 384 to BC 322. He said that nourishment taken into the stomach undergoes coction under the influence of warmth and the pneuma. Wastes are got rid of by the intestines and then the food is taken into the mesenteric veins and converted into blood. The liver and spleen fix the vessels and aid digestion. The spleen draws moisture from the stomach. The gall bladder contains bile which is a useless excrement.

After Aristotle we come to the famous School of Alexandria in which anatomy flourished to a great extent. Several medical sects existed and many did not believe in the humoral doctrines. Three names must be mentioned—Hephaestus, Erasistratus and Eudemos. They all paid much attention to the anatomy of secreting organs.

Hephaestus of Chalcedon flourished about 300 years before Christ. He
described lacteals, lymphatic glands, liver, salivary glands & pancreas. The nourishing force of the body
had its seat in the liver.

Erasistratus held that the liver formed blood. Spleen and the bile were useless.

Eudemus carefully described the pancreas.

After Eudemus we must pass over a period of two hundred years in which nothing new was added
to the knowledge of the secretion. No one did anything in the way of theorising till Asclepiades
who was born about the year 124 BC at Brusa in Bithynia. He held that the body is composed of atoms
which are combined to form tubular spaces or body pores endowed with sensation through them the body juices flow.
He said that digestion does not take place in the stomach because he never saw digested food in the vomitus
or in any stomach which he opened.
Asclepiades was followed by the Pneumatists. These considered that the liver was an organ of haematoxia. The blood was formed by inherent warmth acting on the nourishing part of the food. The spleen was regarded as a purifying organ. They also thought that the ovaries did not produce real seed but were analogous to the mammary glands in man.

After the Pneumatists we have to consider the immortal Galen whose influence is felt in medicine to the present day. Medicine was simply Galenism from his time to the middle ages. For our present purpose we must consider his work on semen, glands, digestion and humours.

Galen knew that semen was for reproductive purposes. Its active principle was unknown to him. From it the nerves, membranes, bones and veins of the fetus were formed.

He did not give a thorough
anatomical description of the different glands, though he may have been acquainted with the fluids secreted by a number of them. He was acquainted with the secretion of the prostate gland, the mucous and saliva in the mouth, the bile secreted by the liver, and the humour furnished to the intestines by the various glands. He thought the saliva was transmitted to the mouth by veins for he did not know the function of the duct of Hensen and Wharton. He termed the mammae glandular bodies. Although he knew all these secretions he did not think they were produced by the glands. He rather considered these structures to be reservoirs for effete materials.

Galen believed that there were three digestions in the body—stomachic, hepatic and in the organs. Food taken in is digested in the stomach, assisted by warmth from the four lobes of the
Ever and it enables four subordinate, organic forces to be carried on—attractive, fixative, alterative and excretive. Chyle arises in the small intestine and is conveyed by the portal circulation to the liver where it is converted into blood. The spleen acts as a purifier and withdraws from nourishment the thick earthy parts which go to form black bile. This passes by a duct to the stomach and then the intestines and it is got rid of in the faeces. The liver sends the blood to the heart and then over the rest of the body. Waste products are formed—excrements, black bile, urine and sweat.

Galen believed implicitly in the humoral teachings of those before him. The humours cooperated with the prænæ to form the essentials of the human body.

After Galen we come to a sterile period in the history of the secretions. Greek medicine was transmitted to the east—where the Arabsians got hold of it.
During the decline of Greek medicine, a period of nearly seven hundred years, only one name stands out — that of John Arcturian. — who lived at Constantinople between the 13th and 14th centuries.

Arcturian believed that all the functions of the body were dominated by spirits. The purest juice formed in the stomach from food is carried to the liver where it serves for the composition of natural spirits which are the instruments of the conceptional faculty of the soul. These are carried into the body by the umbilical vein. With this physiologist we end our first period and enter on the second one or the epoch of external secretion.

The second period in the history of secretion is noted for the overthrow of Hippocrates and Galen and the commencement of scientific medicine.

The first name of importance which
we have to consider is that of Andreas Vesalius who was the first to submit the views of Galen to anatomical research. He lived from 1514 to 1564. Even though he overthrew much of Galen, he upheld the latter's physiological teaching about the liver as an organ of secretion of the blood. He only denied assimilative properties to the portal vein. In his work he started a discussion on the liver which lasted for nearly two centuries. He was strongly opposed by many physicians.

His ideas were supported by Argentieri who tried to restrict the functions of the liver but without much success.

After them we must pass over a few years made notable by Harvey's discovery of the circulation of the blood to the year 1622 when Pasquale Aselli, the Professor of Anatomy in Milan, described the lacteals. This was the first blow struck against
the views of the ancients that the liver is an organ of haematoxia. The final blow was struck by John Pecquet, a student at Montpellier, who discovered the receptaculum chyli and its functions in 1647. He was supported by Bartholin and Glisson, but he was opposed by Nicoll, de Biles, and even William Harvey.

Bartholin extended Pecquet's teaching and his work was very important. He carried out many researches in other directions and his name will always be connected with the accessory duct of the submaxillary gland and the discovery of the vulvo-vaginal glands. This last discovery he shared with Duverney.

John Glisson, the other supporter of Pecquet, was a Professor in the University of Oxford. He recognised the property of irritability in living tissues and this had an important bearing on the secretions later on.
His ideas did not impress the medical world at the time as they were forgotten. Sixty years later they were revived by John de Goetze, who confused them with elasticity. Finally they were raised to absolute fact by experiments conducted by Albert von Haller in 1747.

The phenomena of irritability as described by these three observers were applied to the secretions by Theophilus Borden in 1751. He combated all previous chemical and mechanical ideas with which writers had been satisfied, and he attributed the secretions to the proper action of the glands which have specific tone and irritability.

While these researches on irritability were going on many important observations about the generative secretions were made by Fabricius of Aquapendente, Harvey de Graaf, Hahn, Leeuwenhoek, Buffon and von Haller. Their work was
be described later under the secretions of the generative organs.

The next name of importance is that of van Helmont who founded a medical system. After him, some several men who tried to explain all the functions of the body on some general principle such as chemistry, dynamics and animism. They have left no permanent facts of value to medicine.

Van Helmont had some peculiar ideas regarding digestion. He thought the stomach and spleen had omnipotence over the rest of the body and constituted the drum-virate. The archens or conscious soul resided in the pylorus where it supervised the other organs. There are six digestions. The first takes place in the stomach by the aid of an acid ferment supplied by the spleen; the second in the duodenum where the bile mingles with the
alimentary bolus and changes its acidity into volatile salt: the third
in the mesenteric veins where the
chyle is transformed into venous
blood called venous: the fourth
digestion is effected in the heart
by means of heat, agitation, and
a particular ferment which
causes venous blood to become
arterial: the fifth digestion takes
place in the brain where vital
spirit is extracted from arterial
blood: the sixth digestion consists
in the work of assimilation which
each part executes in appropriating,
by virtue of its innate spirit, the
aliment that is natural to it.
With the number seven nature
keeps a sabbath and rests.

Van Helmont was succeeded
by Sylvius de Leibö and Thomas
Willis who founded the medical
system called Iatro-Chymia
which tried to explain everything
by chemistry. Ferments and spirits
accounted for everything.

Francis de le Bo, called Sylvestre, lived from 1614 till 1672. He denied the presence of the archens described by Van Helmont. His description of digestion was good and came near the actual thing but he spoiled it by absurd descriptions of the juices concerned. According to him the food in the mouth is triturated and impregnated with saliva, a fluid with great fermenting properties. Then it descends to the stomach where it meets with the residuum of the last meal, a species of leaven favourable to digestion, by means of which it undergoes a second preparation. It is then passed into the intestine as a viscid whitish fluid. A little below the pylorus it is acted upon by bile, saliva, and pancreatic juice which constitute a triumvirate. The purest and most fluid part
then goes into the lacteals and the rest into the faces. Bile owes its virtue to an alkaline salt tempered by an oily volatile spirit. Saliva acts because it has an acid and volatile spirit entering with water into its composition. Pancreatic juice owes its activity to an acetous volatile spirit.

Willis. Thomas Willis, the contemporary of Sylvius, believed even more in ferments. He thought that chyle is extracted from food in the stomach by the aid of an acid fluid. He denied that the spleen supplies any ferment because no communication has been discovered between it and the stomach. The milky colour of the chyle is due to coating of saline and sulphurous parts mingled with the ferment essential to life.

After Willis the Jetro-Chemical system fell to the ground and it was replaced by Jetro-Mechanical doctrines. These tried to explain all functions of the body on dynamic
principles. It had two staunch adherents—Borelli and Baglivi.

Alphonse Borelli who flourished about the year 1657 founded the doctrine of the dynamics of the body. Secretion, nutrition and digestion were brought about by pressure, evaporation, or transpiration. According to him digestion in the stomach is a simple titration which is sometimes assisted by a corrosive ferment. Secretions and nutrition were the result of physical laws acting on the humours. Humours and solids allowed part of their substance to escape by evaporation and transpiration and little spaces were formed at the places from which the particles were detached. The sanguineous globules, pressed with the violence of the heart and arteries, become engaged in the little lacunae. All the globules do not enter indiscriminately into all the interstices: each globule insinuates itself into a vacuole
whose configuration is analogous to its own: thus the osseous globules enter into the pores of bone only, fleshly globules into those of flesh, and membranous ones into those of membrane. Each tissue therefore receives aliment appropriate to it, is nourished and repairs its loss.

Borelli's ideas on the secretion of urine are in keeping with his other absurd notions. Blood is projected with force into the emergent arteries and comes in contact with the orifices of the sanguineous capillary tubes on the one hand and the orifices of the uriniferous canals on the other. Suddenly its molecules, united by simple apposition, separate as in passing through a sieve. The aqueous globules of the urine pass into the proper renal tubules whose configuration is the same as their own. The sanguineous globules insinuate themselves into the veins that
are conveniently disposed to receive them and cannot allow aqueous ones to pass. He concludes by saying that it is impossible for any magnetic force or ferment, placed expressely in the kidney, to separate sanguineous and urinary molecules from one another and dispose each of them in its appropriate reservoir.

Borelli and Bagliivi were followed by Stahl of the Animistic Theory and John Brown of the Brunonian Doctrine. They did not specially describe secretions so we may pass them over and consider Hermann Boerhaave.

Boerhaave, who lived from 1668 to 1738, drew his theories from a mixture of anatomy, physics and chemistry. His views were sound and his descriptions good. He described digestion as follows:

"Food is continually diluted with salva which flows unceasingly from the mouth and oesophagus into
the stomach and by the humours which transmit from the stomach itself. These are mixed and agitated with the rest of the food which has already been taken. Their intimate parts are moved by the action of the air which is ground up with it and all this is augmented by the heat of the organ. The effect of the concave part of the velvet tunic is to dilute, macerate, swell, attenuate, and produce the commencement of fermentation, putrefaction, rancidity and the solution of food and fit them for change into a nature similar to that of the humours of the body. Solid food, which is but slightly masticated, is digested by the contractile power of the stomach muscles and in some animals this is the sole process of digestion in the stomach.

While physicians were discussing
these medical systems certain observers were describing experiments carried out on the glands and their secretions. At present it is only necessary to enumerate them for their researches will be described fully later on. Many of these names will become less familiar to students in the future owing to the adoption of the Basel anatomical terminology.

In connection with the structure of the glands we must mention Müller (1836), Simon (1845), Kölliker (1847), Gooden (1845), Bowman, Carpenter, and Sharpey.

The secretions of the glands were obtained as far back as 1754 by Beaunier. His work was continued by Spallanzani (1729-1759), Stevens (1777), John Hunter, and Barlow. They all worked chiefly with secretions in the alimentary canal. In recent years we must mention Haidenhain (1878), Langley (1878), and Pavlov.
Of those who analyzed secretions we must mention Benelius (1779-1848), Mulder, Prout (1823), Beaumont (1825-1833), Müller and Schwann (1836), Bernard (1845), Blondlot (1846), and others of less importance.

The influence of the nervous system on secretion has been known for a long time. Actual secretory nerves were demonstrated by Bernard, Havitache and Ludwig (1851). Ludwig worked at the nerves to the salivary glands. Langley, whose work was published in 1878, also studied the same nerves. The effect of reflex action on the glands was described by Claude Bernard, Pavlov, and Hemmister.

The actual changes in the glands were surmised by Kölliker, Donders and others but it was not till the year 1878 when Haidenhain and Langley, working independently, settled the question for good.
discovery of hormones by Starling and Edkins in 1906. Since they published their researches on secretin in that year many hormones have been discovered.

Although our second period comes to an end in 1889, this discovery of Starling and Edkins forms a fitting termination to it. Our third period or period of internal secretions should really commence with Claude Bernard in 1845 but his observations were not accepted at the time. Brown-Séquard really commenced it by the publication of his book in 1889. Many of his ideas have been contradicted. He was quickly followed by Poebel who carried out researches on the testicle, Schäfer, Herring, Oliver, Howell, and others who have investigated most of the ductless glands very carefully.

In connection with the ductless glands, many experiments have been
performed to show their relation to carbohydrate metabolism and glycosuria. Baumann's isolation of isodthyine from the thyroid gland in 1895 started interest in the far-reaching effects of the glands on other parts. Bayliss and Starling followed with their discovery of hormones in 1906. Since then many physiologists have taken up the subject in relation to diabetes. In connection with the pancreas we must mention Pflüger, Rédon, and Forshoch, and Cohnheim. Of those who studied the relation of the suprarenal capsules it is important to note Blum, Herber, Forges, Elliott, Underhill and Glosser. The part played by the thyroid gland has been studied by McCurdy, Talia, Underhill, and MacCallum. The parathyroids were studied by Eppinger, Talia, Rudiger, Underhill, Milditch and Ott. Lastly, the pituitary gland, in this connection, has been
the subject of research by nearly every physiologist of the day.

At the present day we are noticing more and more, that the secretions of the ductless glands are correlated. This has been proved by Eppinger, Halla, Haller and others.

At different times popular interest has been aroused in the secretions and the latest was the Address by Professor Schäfer to the British Association in Dundee in 1912. Our latest medical summary was the Address in Medicine given by the late Dr. A. Gibson to the British Medical Association in the same year.

Such is an account of the history of the development of our knowledge of the general principles of secretion. Let us now look at the individual organs.
References.


The Salivary Glands

The salivary glands were first described by Herophilus of Chalcedon who lived about the year 300 BC. Their secretion was known to Galen who thought it was conveyed to the mouth by veins. He did not know the use of the ducts.

After Galen we must pass over many centuries till we come to Réaumur, Spallanzani (1729-1799) who carried out important experiments. They found that food which had been moistened with saliva was more readily acted upon in the stomach than food which had merely been wetted with water. In 1842 Wright saw the same thing in a boy who had a stricture of the oesophagus.

The analysis of saliva was carried out by Wright in 1842. It was the same as that of Frerichs Jacobowitch in 1850 and Jacobowitch in 1855. Wright drew up the following table:
<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Water</td>
<td>938.1</td>
</tr>
<tr>
<td>Pityalin</td>
<td>1.8</td>
</tr>
<tr>
<td>Fatty matter</td>
<td>0.5</td>
</tr>
<tr>
<td>Albumen</td>
<td>1.7</td>
</tr>
<tr>
<td>Muscle</td>
<td>2.6</td>
</tr>
<tr>
<td>Ashes</td>
<td>4.1</td>
</tr>
<tr>
<td>Loss</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1000.0</strong></td>
</tr>
</tbody>
</table>

**Milk**

Milk was likened to ptyalin to Lehmann, diastase, and Lehmann to albumen andcasein.

The ashes were analyzed by Enderlin in 1844. He said it was similar to the ashes of blood.

The presence of sulphydrazogen was settled by Prettkofer (1846), Strahl (1847), Bidder and Schmidt.

They could not ascribe any use to it, however.

The constant presence of iron was demonstrated by G. Harley.

The effect of the nervous system on the salivary secretion was first studied by Ludwig in 1851.

He saw the nerves running along...
with the vaso-motor nerve fibres. Haidenham in 1878 and again in 1883, described the different effects produced by stimulating the different kinds of nerve fibres. He concluded that the secretion of water is controlled by different nerves to the secretion of solids.

Langley saw that the conditions in the cat are different to those in the dog. He studied the different fibres by the method of painting ganglia with nicotine and thus blocking the different routes of impulse. He also described the so-called paralytic secretion which comes from the glands when the secretory nerves are cut across.

The process of secretion in the glands must be considered under two headings. The first is the histological and the second is the normal mechanism of secretion.
In connection with the history of the histological changes in the glands only two names stand out—Haidenhain and Langley.

Haidenhain studied the changes by stained hardened sections, but Langley observed the living cells before and after the secretory process had been in full swing. Both arrived at the same conclusion, namely that the resting cell is full of granules and these disappear from without inwards after activity.

The normal mechanism of secretion was shown by Pawlow to be reflex. Kemmeth and Huber also demonstrated this fact.

References:

The Stomach

The stomach has always been regarded as the organ in which important changes take place in the food. Many peculiar ideas have been entertained about it and these have already been described in the general history of secretion. Up till the year 1752, there was not much detailed work done on the stomach. Two theories held their ground till that year. The first regarded the gastric mucosa as a nervous layer and the second considered that the digestive changes in the food in the stomach were brought about by trituration by the muscular coat.

The polygonal depressions seen to the naked eye on the inner surface of the stomach walls were described first by Dr Sprott Boyd of Edinburgh. Freidrichs discovered the peptic cells and Kolliker (1861) described the peptic and mucous glands. Brinton in 1861 detected the presence of small lymphoid masses like Peyer's patches. These discoveries helped to dispel the idea that the mucous membrane is a nervous layer.
The theory that digestion in the stomach is due to trituration was first disproved by Réaumur in 1762. He made animals swallow sponges with strings attached by which he could withdraw them. He showed that food outside the stomach can be affected just as inside by the fluid in the sponges. He also showed that trituration in the gizzard of fowls is analogous to mastication.

Spallanzani (1729-1799) carried out similar experiments both on animals and on himself. He enclosed different foodstuffs in perforated receptacles which were ultimately passed in the stools. He proved that trituration in the stomach is very slight for some of the wooden containers were extremely thin and fragile and also cherries and grapes, even if very ripe were passed unbroken.

Stevens made experiments on a hussar who exhibited himself as a stone swallower. He made him swallow perforated silver balls containing foodstuffs and he studied the changes in them. Live leeches and worms were found to be dissolved like incinurate.
objects. He found that raw foods suffered less than cooked ones and the more finely a substance was divided the more easily was it digested. These experiments proved that some secretion acted upon the food in the stomach. The post-mortem action of this fluid on the stomach wall was studied by John Hunter and Carrell.

Our true knowledge of the gastric juice dates from the work of Prout in 1823. He saw an acid fluid secreted during digestion and he analyzed it in the rabbit, hare, horse, calf, and dog. He said free unsaturated muriatic acid is present in no small amount. The source he thought was the sodium chloride of the blood which gives up chlorine in the stomach and leaves sodium in the blood to be carried to the liver.

Two years later Prout's work received some proof at the hands of Beaumont. Beaumont made experiments from 1825 to 1833 on a young man named Alexis St Martin who had a gunshot wound
wound in the abdomen through which changes in the stomach could be observed. He saw that, immediately after food entered the stomach, the vessels of the mucosa became injected and the colour of the lining changed from pink to dark red. From the surface there distilled a colourless viscid fluid with an acid reaction. Any foreign body, even the smooth bulb of a thermometer in contact with the wall excited the flow of this fluid. During fasting the surface was covered with a little viscid mucus, occasionally slightly acid. Beaumont described the fluid as clear, transparent, and odourless. The taste is saltish and like thin mucilaginous water slightly acidulated with muriatic acid. It diffuses in water, wine, or spirits and effercesces with alkaline carbonates. It coagulates albumen, is powerfully antiseptic and checks putrefaction in meat. When
pure it keeps for months but if it is mixed with saliva it becomes putrid in a few days. Dunglinson analysed it and found muriatic and acetic acids, phosphates and muriates of potassium, sodium, magnesium, and calcium.

Many physiologists then sought to thoroughly analyse this fluid and the influences which bring about its secretion. The analysis falls into two classes—the acid and the organic matter.

The Acid of Gastric Juice was the subject of much discussion before its nature was finally settled. Beaumont, Poult and others described free muriatic and acetic acids but doubt was cast on their statements. Blondlot\(^{(4)}\) said the acidity is due to biphosphates of lime but this statement was severely criticised. He got no effervescence with alkaline carbonates. Melsens and Dumas\(^{(5)}\) said Blondlot worked with too dilute fluids for they found that
iceland spar corrodes in the juice, a thing which only free acid can bring about. They did not deny the presence of dihydroxy phosphate of lime. The presence of free acid was settled and the next thing was to find out what the acid was. Bernard and Barreuil (6) carried out many experiments which also disproved Blondlot's statements. They thought lactic acid was the essential one and food has no influence on its character. Phosphoric acid is also present. P.D. Thomson (7) also thought lactic acid was the important one.

Lehmann (8) saw both lactic and hydrochloric acids. He got the hydrochloric acid from the stomach contents of a diabetic patient to whom he gave an ipecacuanahb emetic and he obtained lactate of zinc crystals from a cat. Liebig found hydrochloric and phosphoric acids. Chevreul, Leuret, and Basseigne all detected lactic acid. The true cause of the acidity being hydrochloric
was finally settled by Bidder and Schmidt in 1851.

The animal matter in gastric juice was described first by Dunglisson. Schwann and Müller called it pepsin in 1836. Bidder and Schmidt analysed it in 1852. They gave it the formula C_{53}H_{67}N_{17}O_{22}S. It was extracted from gastric juice by Pekelharing in 1902.

The milk-curdling properties were first described by Boerlinus, a Swedish chemist of Westerlösa who lived from 1779 to 1848.

The influence of the nervous system on the secretion of gastric juice was studied by Beaumont upon Alexis St Martin. Bernard\(^{(9)}\) shewed that digestion instantly stops when both vagi are cut, but he did not observe that digestion can recommence later on.

Reid, Hübner, as shown by Reid, Hübner, and Ravitsch. In 1860 Bernard\(^{(9)}\) found that stimulation of both vagi...
increases the flow of gastric juice and stimulation of the sympathetic stops it. Similar results were obtained by Pavlov in 1902 and by Hornborg in 1904. These last observers saw that secretory fibres were contained in the vagi. They proved it by preventing food from entering the stomach after mastication.

The actual changes in the cells of the gastric glands were described by Haidenhain and Langley in 1878.

Lastly we must mention the discovery by Bayliss and Starling of a hormone in 1906, called gastric secretin. It is secreted into the blood by the pyloric glands and it excites the flow of gastric juice.

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The Intestines

The history of the intestinal secretions is more a history of the glands in the wall of the alimentary tube with their products. The bile and pancreatic secretion are to be treated separately.

The glands of Lieberkühn were first described by Brunner in 1686. They were not mentioned generally till Lieberkühn discovered them in 1782. He said they only occur in the small intestine but Boeck (3) pointed out their existence over the whole extent of the large intestine. The use of their secretion was not known till recently.

Biddel and Schmidt thought it dissolved albuminous particles but Lehmann, Freichs and Brinton did not. In recent years Cohnheim discovered erepsin and its activating influence on trypsinogen (1901) and Pavlow (1902) detected enterokinase in the duodenum. Bayliss and Starling in 1906, from an elaborate series of researches detected prosecretin in the
Brunner's Glands were discovered by Brunner in 1686. He thought their secretion was of the nature of pancreatic fluid. Kölliker said, however, that they secrete an alkaline mucus which has no action on coagulated albumen.

Peyer's Glands were described by him in 1677. They should be called Crew's Glands because Nehemiah Crew mentioned them in an essay in 1676. Their secretion was the subject of much discussion at first. Some thought they gavethosesmell. Later on they were supposed to be a form of secreting gland of a closed type. When the contents were mature the cell wall and part of the mucus over it gave way and the material was discharged into the intestine. The remains of the gland then disappeared. Kölliker started a reaction against these ideas by stating that the glands are analogous to lymphatic glands. His views were confirmed later by Brücke, Hux, Recklinghausen, Vranchow, Frey, and Mardenbain who detected canals in the glands.
References:

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The Pancreas.

The pancreas has a double action to be studied. In the first place we must consider the history of its external secretion and in the second we must consider its internal one.

Hippocrates. The organ was first described by Hippocrates and

Eudemos. Eudemos, two anatomists of the Alexandrine School who lived about the year 300 BC. It did not get much attention till the time of

Claude Bernard in 1849. In the same year

Stannius described its existence in fishes, a fact previously doubted.

Claude Bernard's experiments are classical. He made an incision into the abdomen of a dog of sufficient length to allow him to draw out the duodenum and head of the pancreas. Into the larger of the two pancreatic ducts he tied a silver tube and he replaced the organ but left the tube projecting through the abdominal incision. To the canula he fixed a rubber bag. The operation was performed on dogs which were fed and allowed to fast for some time. Between half past seven in the morning and five o'clock in the afternoon he obtained four and...
a third drachm of fluid or nearly half a drachm per hour. Next day inflammation had set in and the secretion was more copious but its consistence was diminished and its properties changed. If the experiment was performed at the height of digestion the fluid was less in amount but its quality was good. If the bowel had been exposed to the air for some time the quantity and quality of the secretion were both altered. Bernard described carefully both normal and abnormal secretion. He found that the secretion is the same in all animals.

Levret and Lassaigne analysed the secretion and found that it contained an animal matter called pancreatic and certain salts. It was like that of saliva but no sulphuretanogen was found. Bernard thought the action of the juice was due to pancreatic.

The part played by the pancreas in amylaceous digestion was described by Bouchardat and Sandras in 1845.
They thought the secretion of the intestinal mucosa helped but the bile did not.

The action on fats was the subject of much discussion about the time of Claude Bernard who said that the chief office of the pancreas is to emulsify fats. He always found fat in the stools when the pancreatic duct was ligatured. He tried experiments with other animal juices and he found that none of them could act as pancreatic juice does. Lenz and Fresenius showed, on the contrary, that other secretions in the intestinal canal can emulsify fats. They tied the pancreatic duct and fed the animals on milk and fat and they found the lacteals filled with milky chyle. Fresenius also tied the small intestine below the pancreatic duct and injected oil into the lower part of the bowel and he saw chyle in the lacteals. Bernard, however, tied both pancreatic ducts in the dog and he saw limpid fluid in the lacteals.

As regards the action of the pancreatic juice on albumens, many of the early
observers—Freyhls, Bidder and Schmidt—denied the existence of one. Corvisart, however, in 1859, stated that the juice converts albumens into peptones just as readily as gastric juice does. Harley and Danilewsky supported his views but Brinton opposed them. He said there was no specific action on albumen and any change, in vitro, was due to decomposition. In this statement Keferstein agreed. Corvisart replied, upholding his original thesis in 1862 and Schiff together with others recognised the truth in it. After the time of Corvisart and Schiff it became a recognised fact that the pancreatic juice can convert albumens into peptones. The next stage was the discovery that amino acids and bases also result. Lastly in 1901 Bohnhein, having discovered the enzyme, showed that typhic digest is not the last stage before absorption.

The history of the process of secretion
in the pancreas has three stages. The first was the discovery of the changes occurring in the cells by Haeckel in 1878. He showed that they are the same as in the salivary and gastric glands. The second stage commences with the work of Dolin'sky. Dolin'sky in 1895. He saw that acids in contact with the duodenal mucosa excite the flow of Populski's pancreatic juice. Populski saw that this effect is still produced when the vagus and splanchnic nerves are cut. It was left, however, for Bayliss and Starling to show the true significance of this fact. They proved that one of the so-called hormones is at work. The acid acts on the duodenal mucosa and converts a substance, called pro-secretin, into secretin which passes into the blood and stimulates the pancreas to activity.

The third stage was the demonstration of the effects of the nervous system.
on the secretion by the pancreas by Pavlov in 1902. Many before him had unsuccessfully experimented in this direction. He found that you may stimulate the vagus nerve, which controls pancreatic secretion, in the chest or in the abdomen. In the latter case the splanchnic nerves must be divided to let vaso-constrictor fibres degenerate. As in the case of the gastric glands there is a long latent period.

The internal secretion of the pancreas is very important and the history of its discovery and properties is very interesting. It begins with researches carried out in 1889 by von Mering and Minkowski. These experimenters showed that extirpation of the entire gland causes diabetes mellitus. They also demonstrated that this is not due to the loss of the external secretion.
or to interfere with the nerve connections but they are due to the withdrawal of some influence exerted through the blood or the lymphatics. Even a small part of the gland, left in situ will prevent the appearance of the glycosuria.

These experiments aroused great interest and physiologists came to look upon the Islets of Langerhans as the agents concerned. Islets ligatured the pancreatic duct and found that the glandular tissue atrophied but the Islets don't. Subsequently Opie, Isler, Kerzog, and others reported disease of the Islets in diabetes.

In spite of these discoveries all the attempts to prove the existence of the internal secretion failed by the administration of extracts and sera, failed so men were at a loss to explain matters.
Pflüger suggested that the organ supplies its internal secretion, so rapidly to the blood, that there is only a small amount in the gland at once. Yorebach and Heron supported this by experiment.

Lastly we must mention an accepted theory of diabetes which Cohnheim was formulated by Cohnheim in 1904. It states that the internal secretion of the pancreas cooperates with juices from the muscles. If anything interferes with their harmonious action diabetes mellitus results.

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The Secretions of the Liver

The liver has dominated medicine more or less since the beginning of theories and ideas about it have undergone a great change. We must study the history of the secretory apparatus, the bile, and the glycogen.

In connection with the secretory apparatus we must first mention (1) Kiemann who, in 1833, described the smallest biliary ducts commencing within the lobules by a close network. He supposed the cells line the ducts.

In this view he was supported by (23) Kronenberg (1844), (24) E.H. Weber (1844), (28) Backer, (26) Retzius (1860) and (23) Beale (1856). Another theory stated that the cells are packed between the ducts and vessels and they discharge their contents by temporary communications. The theory was believed in by Handfield Jones (1846), (27) Heue (1846), (28) Kölliker (1860), and Brinton. Many of the so-called ducts were artefacts produced by injections but the presence of...
proper canals was demonstrated by Budge (1850), Andrejevic, Hjorth, and Frey (1866). Lastly, Chroonszekwsky, in 1866, managed to inject the bile ducts and he got the injection also into the liver cells. Thus he showed that the cells empty their contents into the ducts.

The Bile

The bile was one of the humours of the ancient physicians. Two varieties of bile were described by them—yellow and black. At present we are concerned with yellow bile, for black bile was formed in the spleen. Yellow bile gave rise to acute disorders running a rapid course such as erysipelas whilst black bile caused chronic disorders such as mental disturbance. These ideas held sway till the destruction of Galen's teaching. As is usual, when any ideas are overthrown, men went to the extreme opposite position.

Paracelsus thought excess of bile could not cause disease because he
Van Helmont also considered that bile could not cause disease. He differed from Paracelsus in the fact that he thought bile was the very balsam of life and not a waste material.

This change of opinion about the pathogenicity of bile did not last long for Sylvius again said that bile can cause disease such as jaundice. He proved that jaundice is due to excess of bile in the blood. This doctrine was the beginning of a number of theories and discussions about jaundice.

Two theories were much debated by physicians. The first one considered that the liver filtered the bile from the blood and jaundice was due to interference with the function of the organ. Its supporters — Glisson, Morgagni, Boerhaave, and Van Swieten — had to give way to Marx, Eller, Werlhof, Selle, and Reil.
who upheld the second theory. This one argued that jaundice was due to obstruction to the excretion of bile. Saunders demonstrated the passage of bile into the blood. These theories left some forms of jaundice unexplained so some physicians—Darwin, Andral, Mayo, Robson, and Budd—thought that bile is due to changes in the blood itself, and jaundice was a blood disease. Grant assumed that the yellow material which gave the colon to blood serum was bile and biliary diseases were due to abnormalities of this substance.

Reil upheld this view in 1782 but he altered his ideas in 1792 when he said that the changes in the substance are due to increased activity of the liver. In 1786 Schötte renewed Grant's views in a paper describing Malignant Fever on the Coast of Senegal. Dietl also attributed the cause of jaundice to an increase
of the elementary constituents of the bile in the unhealthy juices of the body. Senac thought the red matter of the blood was bile and yellow bile was a product of its decomposition. Breschet agreed with this in 1821 and Dubreuil also in 1826.

A fourth theory of jaundice was mentioned by Deyme in 1804 and Gaullier in 1811. It stated that the yellow matter in jaundice is secreted by the skin and the liver takes no part in the process.

The chemistry of bile has been the object of much investigation. The reaction was carefully studied by Bidder and Schmidt in 1862, and Groupes and Besanex in 1863. Before that time it was usually described as alkaline. They pointed out, however, that it is neutral when fresh. On decomposing it is first acid and then alkaline.

The early analyses of bile were made by Berthollet, Groupes and Besanex, Mulder.
Bötinino gave the analysis as:

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>904.4</td>
</tr>
<tr>
<td>Bilin with fat and pigment</td>
<td>80.0</td>
</tr>
<tr>
<td>Mucin</td>
<td>3.0</td>
</tr>
<tr>
<td>Salts</td>
<td>12.6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1000.0</strong></td>
</tr>
</tbody>
</table>

Bilin

He described Bilin as a substance which taurine readily splits into hydrochlorate of ammonia and fellinis and cholinic acids. It is modorous and has a saltish bitter taste. The sweetness is due to glycerin derived from fatty matters. It is soluble in water and alcohol but not in ether. It is neutral and can combine with acids and bases.

Taurine

Taurine is a substance crystallizing in hexagonal prisms. It is soluble in 16 parts of water. The formula is C_{72}H_{44}O_{6}S_{2}.

The sulphur was described by Redtenbacher.

Fellinis and cholinic acids are very similar. Their barium salts differ. If boiled for a long time with hydrochloric acid diplopini (Bötinino) results.
The pigments in bile were both described by Beralius. He named them cholepyrhoxine, which is yellow, and bilifulvine or biliverdine which is green.

The views of Beralius were strongly upheld by Mulder but they were opposed by Streecker, Demarçay, Demas and Liebig. They said bile is a solution of a soda salt combined with cholic and urcholic acids. Lehmann called these acids glycocholic and taurocholic respectively. In addition to these substances, Goetz, Beanes, found copper salts and oxides of iron.

In recent years analyses of bile have been made by Copeman, Pfeffer, Balf, Balch and Hahnemann. They all agree in the main facts with the older physiologists. The only important additions are cholesterin and lecithin.

Many experiments have been performed to prove that bile is not merely an...
excretion. They were all performed by making a communication between the gall bladder and the stenil and ligaturing the common bile duct.

Schwann of Rowan did this work as far back as 1814. His researches were carried out on dogs, most of which died after severe constitutional disturbance.

Blondlot took exception to Schwann's technique for none of his animals died but they never regained their original state. His contention was that Schwann's external opening tended to close and the bile underwent decomposition. He fixed a cannula into the gall bladder instead. Schwann then reconsidered his results and made new experiments which led him to the same conclusion as Blondlot. Bertelius and others had previously noticed that only a small proportion of the bile secreted went into the faeces.

All these experiments demonstrated the fact that bile is not merely an
Liesegang concluded that the bile is absorbed from the intestines into the circulation where it meets oxygen from respiration to form carbonic acid and generate heat. This was the beginning of our ideas of the circulation of bile salts.

The presence of the gall bladder as a reservoir of bile shows that this secretion has some effect on digestion. Sir Benjamin Brodie said it precipitates white chyle from chyme. He tied the common bile duct and saw the faeces filled with clear instead of milky fluid. Tiedemann, Smelmi, Todd and Bowman came to the same conclusion.

The bile in the foetus has received its share of attention. Simon showed that meconium contains all the elements of bile. Frenchiès analysed meconium and drew up the following table:
Biliary resin 16.6.
Cholesterol, oleic, margarine 16.4.
Epithelium, mucus, salt and pigment 69.0
100.0

Bilir is absent, however. In his views he was supported by Berzelius, Grup-Bessenher, Pettenkofer, Bidder and Schmidt.

Glycogen

The internal secretion of the liver is glycogen. Its presence was demonstrated first by Claude Bernard in 1853. He showed by precise experiments that glycogen is always formed in the liver, even when the diet is entirely nitrogenous. This glycogen is converted into sugar which passes into the blood where it takes part in metabolic processes. Lehmann and other celebrated anatomists confirmed his view. Davy, on the other hand, said that this conversion only takes place after death and the
sugar during life goes into the
intestines. Harvey and Sharpey
experimented on Pavy's lines but
their results confirmed those of
Bernard. Studium, working
independently, came to the
same conclusion.

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The Spleen

Although there is no internal secretion connected with the spleen, it is necessary to describe the connection of the organ with certain theories of the ancients. It was the seat of the so-called atrabilary matter or black bile.

Galen thought black material accumulated in the spleen as a result of the formation of bile and it could produce obstructions and enlargements of the abdominal organs. Various symptoms resulted.

This theory was upheld by most medical men. Van Helmont and Sylvius made slight modifications in it. Boerhaave and Van Swieten thought that, owing to certain morbid influences, the fluids of the blood were condensed and the solids became black, fatty, and earthy. Ultimately, this became black bile. Kämpf added several substances to it.
The first to demonstrate that the so-called black bile was really pigment were Reil and Hensingr. (3) But their information was not accepted for Vogel (5) again described black bile. He was followed by Lancisi, Billard, Bright, Stewardson, and others who described black bile in the organs of patients after death. The fact that pharyngeal matter is pigment was settled by Weckel, Virchow, Heschel, and Planet.

An interesting paper on the function of the spleen was published by Gray in 1854. It won the Astley Cooper Prize of that year. In it he supposed that the Malpighian Bodies secrete a protein into the veins. He also described the generation of blood corpuscles in the pulp.

References:

8. Wright. Reports of Medical Cases. 1831.
The Kidneys

The kidneys have always been regarded as organs for the excretion of waste products from the blood. An additional property was considered by the ancient Chinese who thought the right kidney secreted semen.

Asclepiades considered, however, that the urine went to the bladder in the form of vapour without passing through the kidneys. Here the vapour was condensed.

With the exception of these two peculiar conceptions the kidneys have always had their proper functions allotted to them.

In connection with the structure of the secreting elements we must mention Malfighi (1669); Bellini, after whom the tubules were first named; Bertini; Ferrein; and Henle.

The actual processes concerned in the secretion by the kidneys are summed up in two words—mechanical and secretory.
The first theory which was formulated was the secretory one which was formulated by Bowman in 1842. It is usually called the Bowman-Haidenhain theory. It stated that water and inorganic salts pass through the glomeruli whereas urea and other substances are secreted by the cells lining the convoluted tubes.

The mechanical theory was proposed by Ludwig in 1844. Its contention was that everything passed through the glomeruli and the water of the urine is absorbed in the tubes.

Around these two theories a storm battle was fought. Haidenhain injected methylene-blue into the blood and saw it in the tube cells. Fuchs injected acid fuchsine and saw the red staining in the tube cells but not in the glomeruli. Haeckel ligatured the renal artery in the
frog. In that animal the artery supplies the glomeruli only. He injected urea into the blood and the renal portal vein conveyed it to the tubular epithelium.

These views and many others disproved the mechanical ideas of Ludwig and confirmed the teaching of the Bowman-Hardenhain Theory.
The Urine

The reaction was fully studied by (1) Bence Jones who found that it was most acid just before meals and its acidity gradually diminished till six hours after meals. Liebig (2) said the acidity is due almost entirely to acid phosphates.

The specific gravity was stated by (3) Prout to be, on an average 1020 and by Becquerel as 1017. Tables have been drawn up by Christie (4), Becquerel, Day (5), and Golding-Bird (6). The healthy range was fixed by Prout as 1015 in winter to 1025 in summer. According to Watson it may rise in disease to 1060.

The analysis of urine was carried out as far back as the time of Berekelius who mentioned many of the solids and gave their amounts. According to Prout the figures were too high because he said Berekelius worked with too acid urine. The following is the
Analysis of Prouit, Beagureel and Golding Bird:

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>967.0</td>
</tr>
<tr>
<td>Urea</td>
<td>14.230</td>
</tr>
<tr>
<td>Urea Acid</td>
<td>4.68</td>
</tr>
<tr>
<td>Colouring matter, meaux</td>
<td>16.167</td>
</tr>
<tr>
<td>Animal matter</td>
<td>16.167</td>
</tr>
<tr>
<td>Sulphate</td>
<td></td>
</tr>
<tr>
<td>Sodas</td>
<td></td>
</tr>
<tr>
<td>Potash</td>
<td></td>
</tr>
<tr>
<td>Lime</td>
<td></td>
</tr>
<tr>
<td>Orthophosphate</td>
<td></td>
</tr>
<tr>
<td>Sodas</td>
<td></td>
</tr>
<tr>
<td>Magnesia</td>
<td></td>
</tr>
<tr>
<td>Ammonia</td>
<td></td>
</tr>
<tr>
<td>Chlorides</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td></td>
</tr>
<tr>
<td>Hyposulphate of soda</td>
<td></td>
</tr>
<tr>
<td>Fluoride of potass</td>
<td></td>
</tr>
<tr>
<td>Silica</td>
<td>Traces</td>
</tr>
<tr>
<td></td>
<td>1000.000</td>
</tr>
</tbody>
</table>

Urea

Urea of ammonia or artificial wine was discovered by Wöhler. Prout estimated that the amount in twenty-four hours wine was nearly half an ounce. Thudichum considered that figure too low. Vogel and Neubauer believed it should be an ounce. The variations brought about by...
diet were first studied by Lehmann. He found that more is present if the percentage of meat in the diet is higher. Becancourt saw that men secrete more than women and middle age is the time when most is present. According to Becquerel, an increase of urea follows an increase in the amount of wine. The source of urea was studied by Lehmann, Prout, Bischoff, and Rassagie.

Uric Acid was known for a long time under the name of lithic acid because it entered into the composition of urinary calculi. Golding-Bird said it is replaced by urea in birds. Thudichum estimated that the average daily excretion is eight grains. Prout thought it was in the form of ammonium urate in urine because one part of uric acid is only soluble in two thousand parts of urine. Hence Jones
showed that the sodium chloride in urine makes the ammonium urate more soluble. The source of urates being the combination of uric acid with the salts in the blood was shown by Liebig. Prout settled its formula as C_{10}H_{4}N_{4}O_{6}.

**Hippuric Acid**

This acid has been known to occur in the urine of herbivora as a soda salt from very early times. Liebig first showed its presence in the urine of man. Weissmann estimated its amount and compared it with uric acid. Its relation to benzoic acid and the fact that benzoates are excreted by as hippuric acid was first shown by Ure.

**Uric Acid**

Animal Substances

The so-called animal extractives were studied by Liebig and Kekulé. Liebig detected creatin and creatinines and described them...
Sugar has been detected in small amounts by Lachem, Bruce-Jones, and Pavy.

References:
The Secretions of the Male Generative Organs.

I. The Semen

Many peculiar ideas regarding the semen have been held by physiologists and they have undergone a complete revolution.

The Indians believed that the semen united with the menstrual blood to form the embryo. Both of these conjugating elements arose from chyle.

The Chinese thought the semen arose in the right kidney which they called the "Gate of Life".

Alkm siden carried out experiments on this secretion. He combatted a prevailing theory that the semen came from the spinal cord. He killed animals after the sexual act and he found that there was no diminution in the amount of spinal substance.

Hippocrates and the humorists...
believed that the semen was a humour, which was gathered from different parts of the body into the brain whence it descended, via the spinal cord, to the testicles.

**Aristotle** said that semen, which is a mixture of fire, water, soul, unites with catamenial blood to form the embryo.

**Galen** considered that generative functions were the same in both sexes from his studies in comparative anatomy. The semen passes into the womb and unites with a female semen. From the semen arose skin, nerves, muscles, and vessels. The semen from the right testicle in man generates males and the left females.

Such was the ideas of the ancients which prevailed till the sixteenth century, when they were overthrown with many other views.

De Graaf(\(^1\)), whose name will always be connected with this part of physiology,
was the first to prove that the theories of Hippocrates and Galen concerning generation were pure imagination. He removed the right testis of a rabbit and let it cover a female and young of both sexes. Resulted. The same thing followed when the left testis was removed from another rabbit. This destroyed the notion that each testis generates one sex of embryos.

After his discovery, physiologists were divided into classes which speculated, each in its own way, about the origin of the embryos. One sect called animalculists had the proper notions. They thought the semen contained some active body which united with the ovum.

In the year 1677 the views of the animalculists were confirmed. Hamme, who was a pupil of Eewenhoek, drew the latter's attention to the spermatozoa but the master did not understand them. He got
and still retains the credit of having observed them, however. The division of the spermatozoon into head, neck, tail, filament and membrane was made by Heneage Gibbes.

The function of the spermatozoa was undecided till Spallanzani proved that they are essential factors in fertilisation. Their origin from the cells of the testis was demonstrated by Kölliker in 1841 and Goodall in 1856.

The internal secretion of the testicle was first described by Brown-Squard in 1889. He suggested that the extract of testicle might prove of value in cases of atrophy, senility, impotence etc. His statements gave rise to much discussion.

Poehl who was the second investigator isolated a substance called spermmin from testicular fluid. He gave it the formula C_{5}H_{14} N_{2} and he said it was the active substance which brought about the good results obtained by
Brown, Séquard.

Both and Pregel said that the injection of testicular extract causes increased muscular energy. They upheld their contention by means of ergographic tracings.

Dixon, on the other hand, said the only thing he observed was fall of blood pressure. The beneficial effects stated by others were due to suggestion.

Walker found that the injection of the extract does not check the general effects and the prostatic atrophy which follow castration.

It was with the experiments of Bonin and Ancel in 1903 that we became acquainted with the origin of the internal secretion of the testis. These observers ligatured the vas deferens. They found that the glandular tissue of the testis atrophied but the interstitial cells did not. Consequently they concluded that the internal
secretion comes from these elements. They found that an extract made from these cells counteracts the general effects of castration.

(12) Togee, in the same year, found that transplantation of the testes into another part of the body prevents constitutional disturbance following castration.

(13) Shattuck and Seligmann ligatured the vas deferens and saw that no evil symptoms resulted.

The most conclusive proof of the presence of an internal secretion were was given by Miesbann in 1905. He observed that a castrated frog does not develop the characteristic pad which appears on the hand in the breeding season. If he castrated the frog and transplanted the testes elsewhere in the body, the pad developed on the hand as usual.
4. Godard.
Cowper's Glands

These glands were also discovered by Méry.

The use of their secretion has not been properly settled. Kölliker said they secrete ordinary mucus which is not of any importance. Hyrtl said it is used to lubricate and protect the urethra. Nagel(1) said they are not purely seanal glands but Schneidemühl(2) said they are for they atrophy after castration. Griffiths(3) and Gley(4) shewed that they are analogous to the prostate gland in some animals. Stilling(5) stated that the epithelium undergoes certain changes in cattle.

In spite of these researches we are ignorant of their true function but time may settle this.

References:

The Vesiculae Seminales.

The views concerning the function of the seminal vesicles have undergone a change. At first they were regarded as reservoirs for storing spermatozoa. Now they are regarded as secretory organs. The turning point between the ideas was the statement of John Hunter that they are not purely reservoirs.

Kayser upheld Hunter's views in 1889. There were several supporters of the storage function. Amongst them we must mention Richet who carried out experiments for this purpose. He injected water into the vas deferens and some passed out at the urethra and some was (2) retained in the vesicles. Meckel and (3) Soubert observed sperm remaining alive for some time in them.

The adherents to the secretory theory are numerous. (4) Rode removed a testis from an animal and saw fluid accumulate in the corresponding.
Semenial vesicle so he proved that the fluid does not come from the testis. Stilling observed the same fact.

The composition and character of the secretion were studied by Nyström, Fürbringer, Sobotta, Kanthin, Camus and Gley. It is a thick, glairy, albuminous substance consisting chiefly of globulins. Its power of clotting was first demonstrated by Kataké.

Now we regard the secretion as an essential element of the semen for Steinach showed that the absence from semen diminishes the latter's fertilising power.

References:


4. Lode. _Beiträge zur Physi der Samenblasen._ 1895.

5. Stilling. _Viechow's Archiv._ 1884. xcviii.


11. Steinach. Pflüger's Archiv 1894. lvi

The Prostate Gland.

The fact that the prostate gland has a secretion was known to Galen. He did not know its use, however.

The secretion was analysed by Poehl in 1898, who described it as a slightly acid, neutral, or slightly alkaline, viscid fluid containing proteins and salts. Burschmann, Bottcher, Charcot and De Bovis all described granular, amylloid, and crystalline bodies in it.

Several theories as to its use have been propounded. An early theory supposed it supplied nutriment to the spermatozoa. Sturbringer, Steinach, and Walker thought it stimulated the spermatozoa, but Ivanoff...
said it had no such effect for spermatozoa can live and fertilize ova without it.

Serralach, Pares, and Griffiths (3) all thought the prostate gland yields an internal secretion which controls the activity of the testes and regulates the process of ejaculation.

References:

4. Storace. Pflügers Archiv. 1892
6. Serralach Pares. CR de la Soc. Biol. 1xii. 1898
The Ovaries

The ancients had many crude conceptions about the ovary. They did not know they produced ova.

Before Galen's time the semen was supposed to unite with menstrual blood to form the embryo.

Galen thought they secreted a spermatic liquor in copulation so he called them female testicles.

Such was the knowledge transmitted through the middle ages till the sixteenth century when proper medical knowledge began in this direction.

Fabricius D'Aguapendente made the first experiments to determine the part played by each organ in the act of reproduction. He killed pullets after coition and saw that, among the little yellow grains composing the ovaries, on enlarged and became more vascular and was detached and became an egg.

At a later period Harvey obtained the same results in bitches and he stated that the female element in reproduction
is a germ.

De Graaf made more precise experiments on rabbits and the substituted the word ovary for female testicle. He also described what will always perpetuate his memory—the Graafian Follicle.

The mammalian ovum was discovered by von Baer in 1828 and the fact that it is a single cell was settled by Gegenbauer in 1861.

The actual process of formation of the ovum in the ovary has been the subject of much brilliant work. In 1867 Pflüger showed that certain tubular growths of cells, recognised in 1838 by Valentin, developed into the ova and epithelial cells of the Graafian Follicles. The true changes and significance of these elements was first settled by Waldeyer.

At the present day much attention is paid to the internal secretion of the ovary and we recognise
that the entire character and habits of woman depend greatly on the activity of her ovaries. In fact the specialists in gynecology on the Continent say that love is the result of the internal secretion. Although the ancients did not know of ovarian secretion they had similar ideas about the psychology and physiology of woman.

Hippocrates wrote some very remarkable facts in his work on the female constitution ("epi τῆς γυναίκος φύσεως"). Aristotle, Archelaus, Galen, and Albertus Magnus all described how the female organs influence the body.

In the middle ages similar facts were mentioned in the works of Boireau, Hafftentz, Marie Clement, von Humboldt, and Busch. John Hunter, in 1780, first demonstrated in the case of a pharam, that peculiarities of the plumage are dependent on the ovaries. His animal developed male plumage in old age, when the ovaries had atrophied.
After his paper appeared, other observers – Gurney (1866), Darwin, Kehr (1878), Brandt and others – reported similar conditions and many experiments produced them artificially.

This set of observations led others to transplant ovarian tissue – Knauer, Grigoroff, Ribbert, Rubenstein, Carmichael, Marshall and Jolly – to see if the organ produced its effects from a distance. Most of the experiments yielded positive results.

A third evidence was given in the reports of effects produced by administration of ovarian substance per os or per cutem. Brown-Séquard was the first to do this. He found that extract of ovaries was not as powerful as extract of testicles. Reaton de Camboulac, Jentzer, Bentner, Carmichael and Marshall supported his views.

References:

2. Gegenbauer.
10. von Humboldt. Sexual Differentiation.
The Corpus Luteum.

The first to show that the corpus luteum is a ductless gland was Pernant. He supposed that it has an internal secretion which acts in the same way as ovarian secretion and its absence brings about children.

Regard and Policard upheld Pernant's views for they said they had seen droplets of secretion in the cells of the corpus luteum. They also believed in Pernant's theory that it prevents ovulation during pregnancy, a fact supported by Beard and Sanders.

A theory regarding the corpus luteum, which is generally recognised, was first brought forward by Born. It states that the internal secretion helps in the attachment of the ovum to the uterus. Fraenkel proved this experimentally. He stated that ovarian secretion really comes from the corpus luteum and he demonstrated that it has a great influence on the safety of the developing ovum in the early
months of pregnancy. Marshall and Jolly (6) extended many of Fraenkel's discoveries. They found that the early removal of the ovaries and corpora lutea terminates pregnancy. They also explained that in cases in which ovariotomy was performed in women in the early months, without terminating the pregnancy, the failure was due to some piece of ovarian tissue left behind.

Lastly we must mention the theory of Loeb and others, that when there is excess of luteal secretion, the ovum has extraordinary burrowing powers. The cells of the syncytiotrophoblast grow through the uterine wall and deciduoma malignum results.

References:

The Pituitary Body.

Much of the obscurity connected with the pituitary body in ancient times was due to its remote anatomical position and the difficulty in performing experiments upon it. It was first thought to discharge mucus through the nose, hence the name. Later on it was supposed to be the seat of the soul and it was called "L'Organe Enigmatique" by van Schuchten. Scientific interest was raised in it, along with other ductless glands, by Brown-Séquard in 1889.

Schäfer was the first after Brown-Séquard to take up the study of the gland. In 1894 he published the results of a series of experiments on it conducted by himself and J. Oliver. He showed that blood pressure rises after an extract of the gland is injected intramuscularly and the effect is the same as that produced by suprarenal extract.
(1) Howell took up the study of the gland when Schäfer and Oliver drew attention to it. In 1898 he showed that the rise of blood pressure is due to something in the posterior lobe of the gland. Schäfer confirmed this later.

The study of the pituitary body now became a practice by the leading physiologists and numerous results were published.

(2) Cjvov and Leven, in 1898, demonstrated on the heart that pituitary extract strengthens the heart and lessens its action in a manner identical to that of digitalis.

(3) The most interesting action on the kidney, the one which has received most attention is that on the kidney. Schäfer and Magnus and later on Schäfer and Herring proved that the extract is strongly diuretic and the active substance is contained in the posterior lobe. Schäfer administered gland substance by the mouth and
diabetes resulted. In 1909 Pal, and in 1911 Campbell and Cow performed the blood vessels with pituitary extract and saw the renal vessels dilate and saw the renal vessels contract along with other vessels of the splanchnic area.

The relation of the internal secretion of the pituitary body to carbohydrate metabolism has been the subject of many papers. The existence of glycosuria and the fact that diabetes often causes death in acromegaly has long been noted. In 1910 Caselli showed that destruction of the posterior lobe of the gland causes diabetes whereas destruction of the anterior lobe does not. Caselli observed the same fact when he partially destroyed the anterior lobe and totally removed the posterior.

Hanselmann and Hooley found slight glycosuria in two out of seven removals of the entire gland. Borchardt, Otto and Scott...
showed that glycosuria follows the intravenous injection of boiled extract of the body. Goetsch, Cushing, and Jacobson found that injections of the posterior lobe lower the sugar tolerance of normal animals and, if given in large enough doses, will cause transient glycosuria.

Lastly we must note the fact observed by Schäfer and McKenzie that the extract is a powerful galactagogue.

References
7. Caselli. See Ott.
The Parathyroid Bodies.

They were discovered by Sandström in 1880. Their value was not appreciated till the results of thyroidectomy were described. It was seen that removal of the thyroid gland was not fatal. Gley demonstrated that the animal dies if these bodies are removed as well and the symptoms are those of tetany. Moussau, Vassale, and Generale confirmed this. These results proved that some internal secretion is given out by these glands.

MacCallum and Voeglini thought the secretion regulates calcium metabolism because the symptoms of tetany can be removed by the injection of calcium salts. As in the case of the other ductless glands, these bodies are known to influence carbohydrate metabolism. Ephringer, Tallo, Rudinger, Underhill and Ott all showed that the effect is the opposite of that of the thyroid gland.
The Thyroid Gland

The thyroid gland was first supposed to be an organ for the formation of blood. Later on it was believed to secrete something necessary for the nutrition of the brain. Still later it was considered, by Simon, to act as a diverticulum for the cerebral circulation. Simon also held the same ideas as recently as 1878.

As in the case of the other ductless glands, the clinical phenomena resulting from their disease or removal preceded the discovery of the active principle in their secretion. Gull, Ord, and Charcot had all described goitres and myxedema, and Murray and Victor Horsley had given thyroid substance with success before we knew anything of importance of the secretion of the gland.

In 1889 Brown-Séquard drew scientific attention to the thyroid gland and in 1895 Rammann...
isolated a substance, called

todothygin or thyroidin, from an
extract of the gland. He said that
was the active principle and,
since his time, physiologists have
come to the same conclusion.

Recent experiments have shown
that the thyroid gland is connected
with carbohydrate metabolism.

McCurdy and Salta have shown
that thyroidectomy raises the
animals sugar tolerance and it
is extremely hard to produce ali-
mentary glycosuria in them.

Salta showed that adrenalins
does not produce glycosuria also.

MacCallum shewd that glycosuria
after excision of the pancreas is
diminished by thyroidectomy.

The most recent contribution to
our knowledge of this gland is the
fact that the internal secretion
cooperates in some mysterious
way with the internal secretion
of the ovaries and testicles.
The symptoms of myxedema, goitre, and oedema demonstrate the importance played by the internal secretion of the thyroid. They show that the active principle governs the higher functions of the brain. According to Gley they can be summed up in the following sentences: "Le génie et l'exercice des plus hautes facultés de l'homme sont conditionnis par l'action purement chimique d'un produit de sécrétion. Que les psychologues méditent ces faits!"
The Suprarenal Capsules.

The first to draw attention to the suprarenal capsules was Thomas Addison who described a train of symptoms resulting from disease in them in 1856.

In the following year Brown-Séquard showed that death rapidly follows if the glands are removed and the symptoms which appeared before death were the same as those of Addison's Disease.

After this observation a period of thirty nine years elapsed before anything else was added to our knowledge of these organs.

In 1895 Schüfer and Oliver and in 1896 Cybulski and Symonowicz discovered that these bodies secrete a substance which slows the heart and raises blood pressure. The medulla seemed to be the source of this material. It was found especially in the adrenal vein and it was found to increase in amount when the sympathetic nerves were stimulated. (Dreyer). This seemed to point to the fact that the
gland is influenced by secretory fibres. The active principle contained in
the secretion has received several names such as adrenaline, suprarenin, epi-
ephrine, and hemisine. In its nomenclature we must mention Abel, Albrecht,
Takamine and Stolz-Dakin.

The suprarenals have been studied with reference to glycosuria. In 1901
Blum showed that the injection of an aqueous extract of the glands causes
transient glycosuria. In 1907 Herber demonstrated that glycosuria results
if the capsules are massaged. Also adrenaline injections cause it and
intensify the glycosuria in depancreatized dogs. Porges, on the contrary, found that
the sugar in the blood and the glycogen in liver and muscles are reduced
when these bodies are removed. Elliott
Underhill and Glover demonstrated
that the internal secretion acts on
the glycogen storhouses through
the sympathetic system. The contained
glycogen is thrown out as lactose.
and the storage capacity is diminished.

References:

1. Addison. Disease of the Suprarenal Capsules. 1863.

In studying the history of secretions we are
struck with the importance they have
always played in regulating the life
of the organism, and as time goes
on we shall probably discover that
they have a more far-reaching
influence than ever was dreamt of.