Thesis

composed by

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# Contents

## Waxy Degeneration

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Waxy, Amyloid, or Lardaceous degeneration has been known to pathological observers for a considerable time; and the chemical composition of the waxy material, its reaction to various staining agents as well as its anatomical seats and distribution throughout the tissues and organs of the body, have been carefully studied by many distinguished investigators. Indeed, the chemical composition of the waxy, amyloid or lardaceous substance has been satisfactorily determined; and comparatively little requires to be added to...
to the present advanced state of knowledge regarding the clinical and histological aspects of the degeneration. Nevertheless, even at the present time, the picture of this degeneration is not a complete one; light still requires to be thrown on certain points, more especially in connection with the ultimate cause or causes of the affection, and the mode of origin of the waxy material in the tissues.

Hyaline degeneration, on the other hand, has only been described within comparatively recent years. A good deal has been written bearing directly or indirectly on this change. Several valuable papers embodying the results of careful research, have been published both in this country and on the continent, with the view of adding to our knowledge regarding it. Unfortunately, however, the descriptions given of this degeneration by the various writers on the subject do not, in many respects, coincide, and, consequently, our knowledge regarding it, still remains somewhat vague and unsatisfactory.
In studying any subject, it is well at the outset, to endeavour, as far as possible, to become acquainted with its history, in order to ascertain what has been previously thought and written on the matter. I shall, therefore, in the first instance, proceed to give a rough outline of the history of the Waxy Degeneration.

The more advanced forms of this degeneration have such well-marked and characteristic features as to make it extremely probable that the older pathologists had not allowed its presence to escape their notice. And, indeed, on looking over the works of some of the more renowned of the old medical writers, passages are met with more or less confirmatory of this opinion. Of course, in some of the cases about to be quoted from these writers, a certain amount of doubt and uncertainty hangs around the description; and the opinion formed, even after a careful perusal of them, is apt to run (it may be quite
quite unconsciously and unintentionally) in the direction most in accordance with the preconceived ideas of the party perusing. His mind being somewhat warped and biased, erroneous conclusions may very naturally be the result. And this is specially apt to occur when one endeavours to form an unbiased opinion as to the presence of this degeneration in an organ, merely from a short naked eye description, however faithfully given, such as we have in some of the cases from the older writers; this description being unsupported by any confirmatory evidence in the way of either chemical reaction or microscopical investigation. Accordingly, it will be understood, that, in tracing the history of this degeneration the views put forward in regard to the cases quoted from the older authors are only meant to be of a tentative character, and are not intended in any way to be dogmatic or affirmative.

Amongst writers such as Malfi and Bonetius whose works were published in the latter part of the
seventeenth, and the beginning of the eighteenth century, the spleen appears to have been the organ (judging from the descriptions given) in which this degeneration was principally observed. Thus we find Malpighi [Opera, London. MDCCI. XXXVI Tom. II pp. 111-112] devoting a whole chapter to a description of “certain bodies scattered throughout the spleen”, a careful perusal of which serves to point to the conclusion that this acute observer had met with at least one case of the special form of waxy spleen which goes by the name of “sago spleen.” In this chapter he notes “the fact that, in the spleen, those “bodies”, which, in his honour, are now named “Malpighian”, are with difficulty observed in man, but in disease they may swell up and become conspicuous, as in the case of a girl whose spleen he had observed post mortem, to have been “studded with clear conspicuous globules scattered about like bunches of grapes” – “ut in defuncta puella observavi, in qua globulis conspicuis racemation dispersis totus scatebat.” Bonetus
Bonetus (Sepuleretum MDCC. Tom. II p. 287, observation XCV) in a section devoted to a description of cases of "Tumour of the left hypochondrium from enlargement of the spleen" records a case corresponding, in all probability to the so-called "diffuse form" of waxy spleen. The case was that of a woman who had suffered for a long time from what Bonetus describes as "obstruction of the viscera" (diurna viscerum obstruente). The following is his post mortem report of the appearances presented by the enlarged spleen:—"Liones in cadavere defunctae invenimus tantae esse duritiei ut vix cultro cederet, nisi magna vi intruso. Inter secanum non dissimilis audibatur sonitus, quem in lignis spongiosis discisis animadvertimus et si clarissim loqui licet, et colore et duritie carnem fumo duitine induratum illin referebat, sive quod interceptis obstructisque vasis spleneticis exauruit, sive quod atro succo repletus nutritus que fuerit induratus."

We have in this description several indications pointing more or less strongly...
strongly to the presence of waxy degeneration:

1st. The chronic course of the disease.
2nd. The increase in size of the spleen.
3rd. The increase in consistence of the organ.
4th. The general appearance of the cut surface—described as resembling both “in colour and consistence, flesh hardened a considerable time by smoke.”

Numerous subsequent writers on this subject have adopted terms somewhat similar to the above in describing the waxy appearance in organs; and it appears to me that the description here given is so characteristic as to leave little doubt that we have to deal with a case of waxy disease of the spleen. Such being the case, we may look upon Bonetus as the first to make use of the expressive term “smoked flesh” as descriptive of this change. And we shall see that other medical writers used this as a favourite expression to describe the same affection.

Morgagni, also, seems to have been acquainted with the diffuse form of waxy spleen and he quotes Abraham
Abraham Vater as having previously described the same change. In his great work [De sedibus et causis morborum 1761. Tom. II. Liber III; Epist. XXXV. p. 68] Morgagni relates an interesting case of enlargement of the spleen associated with an ulcer of the left leg. A woman, twenty-eight years of age, of slender build, married, but sterile, suffered from an enlarged spleen which was perceptible to the touch, and from fever. She was anaemic and had had amenorrhoea for two years. Soon after cessation of menstruation an ulcer made its appearance on the left leg, at the side of which ulcer an abscess formed, and after a time, opened externally, discharging a quantity of pus. Instead of healing this abscess remained open, and continued to discharge pus. It is noted that during what would have been a menstrual period this abscess became swollen and irritated and discharged a much larger quantity of pus than at other times. Early one morning she was suddenly seized with symptoms pointing to obstruction of the pulmonary artery.
artery, and died within an hour. At the post mortem, the spleen was found greatly enlarged, and weighed eight and a half pounds. In commenting on this case Morgagni mentions the fact that the occasional association of enlargement of the spleen with ulcers of the legs had been pointed out in Tom. I. Epist. xxx., p. 34; and that this same connection between ulcers of the legs and enlargement of the spleen had been observed even from the most ancient times. In proof of this latter statement, Morgagni goes on to quote from the Prorquatetica the following passage: "Those who have an enlargement of the spleen and hæmorrhages, but not an ill smell of the breath, will have foul ulcers of the tibia."

This case is extremely interesting as well from a clinical as from an historical and pathological point of view. Unfortunately, the naked-eye appearance of the enlarged spleen is not given. Nothing is said as to the colour or consistence of the enlarged organ; but from a careful consideration of the clinical history of the case, an

idea
idea may be formed as to the probable nature of the enlargement. There is a history of chronic fever, anaemia, amenorrhoea persisting for two years, and the presence of a chronic suppurating sore of the left leg which discharged a quantity of pus. Whether this latter was simply cutaneous or connected with diseased bone is not very evident from the description given. The presence of long continued suppuration is of itself however an important predisposing cause of waxy degeneration; and this would be rendered still more probable as the cause of the enlargement of this spleen if, in addition, as is not incompatible with the history of the case, one or other of the bones of the leg had been affected. Therefore from these considerations, I am inclined to regard this as a case of waxy degeneration affecting the spleen.

However this may be, we have in Tom II. Liber V. p. 498. the record of a case of enlargement of the spleen the description of which points much more clearly and distinctly to the waxy
waxy change as the cause of enlargement. The patient in this instance was a man who had suffered from symptoms resembling phthisis, whose lungs, post mortem, showed nothing at all morbid, but whose spleen was enlarged, very hard and heavy being composed of a dense substance which Abraham Vater had compared to a "gammon of bacon somewhat hardened by smoke." "Aliquando autem," writes Morgagni "e contrario mon in lienis tumore occurrit dolor, sed in lateris sinistri imo parte ad dorsum vergente," "ut in viro qui cum praetera pluribus aliis symptomatibus, phthisim mentione," "tibis, frisset, conflictatus, nihil denique in pulmonibus quod vitiosum esset," "post mortem estendit, sed lienum grandiorum, durissimum, et valde gravem, quippe ex densa compactum substantia quam Abi. Vaterus (Dissert. de scirrhus Viscer) cum dissecto petasone porcino," "fumo leviter indurato comparavit."

The naked-eye characters of the enlarged spleen in the above case are set forth with such clearness as to leave little doubt that we have here to deal
deal with well marked waxy degeneration of the organ. And the quotation from Abraham Vater would naturally lead one to conclude that even at this time the naked eye appearances of this degeneration were fairly well recognised. The comparison of the waxy material to the appearance presented by "smoked ham" is likewise interesting in view of the description given above by Bonetus and of that given subsequently by Rokitansky and others in their delineation of this change.

In 1825 Dr. Matthew Baillie (Vol. II. p. 232, by Jas. Wardrop) makes note of enlargement and hardness of the spleen commonly considered a \textit{Scirrhus}. "The spleen," he writes, "is sometimes much harder than natural, and at the same time is generally a good deal enlarged. It is occasionally enlarged to five or six times its natural size, and it then forms a tumour very capable of being distinguished by an examination in the living body. When cut into, the natural structure seems to be preserved, except that it is much more compact or solid than it ought to be."
This state of the spleen is commonly considered as a scirrhus; but its structure is not similar to scirrhus in other parts of the body, and its real nature is probably at present not fully understood. When the spleen is in this state, water is sometimes accumulated in the cavity of the abdomen."

As regards the kidney, the same author writes, under the title "Scirrhus of Kidney": "I have once seen the kidney converted into a hard uniform substance, somewhat intersected by membrane, in which the natural structure of this gland was entirely lost. The kidney was at the same time very much enlarged in its size. This alteration of structure I should call scirrhus, because it exactly resembles scirrhus in other parts of the body."

Baillie also describes a condition of the liver, where it is very hard in its substance. "There is a state of the liver not at all uncommon, when it is much harder than natural, and when cut into, exhibits no peculiar structure. Upon the surface of livers thus changed, there is not uncommonly a thrice
appearance of membrane, disposed somewhat in a radiated form, and the lower edge is bent a little forwards." Baillie believed this to be the first step in the progress towards the formation of the common tuberculated liver, as he had sometimes seen very small tubercles formed on a part of the surface of such a liver "exactly of the common sort." This condition of the liver he sometimes found accompanied by "an incipient ascites."

It will be observed that Baillie here describes what may be regarded as in all probability a waxy degeneration of the spleen, liver and kidneys. The alteration in the structure of the spleen consisted in what was evidently a recognised pathological condition at the time when his work was published; for he says "this state of spleen is generally considered as a scirrhus." Whilst he regarded the change in the liver as not an uncommon one, the condition of the kidney was observed by him once only. Admitting the waxy nature of the changes Baillie here describes in the liver, spleen, and kidneys.
kidneys, we may consider him as the first in this country to point out post mortem appearances in each of these two organs, which may be regarded as waxy in their nature. Thus far we may give him credit; although it does not appear that he discovered any connection between the disease he describes in the spleen, and that occurring in the liver and kidneys.

In 1832 Dr. Hodgkin in a paper read before the Medico-Chirurgical Society of London on July 10th and 21st, and published in the seventeenth volume of the Society's Transactions (p. 68 et seq.) described a series of cases illustrating some morbid appearances of the absorptive glands and spleen. In case III we have the description of a morbid condition of the spleen which may be regarded as essentially corresponding to the waxy change. Dr. Hodgkin includes this case along with those presenting the typical features of the disease in connection with the history of which his name will ever be honourably associated; yet its essential characteristics were altogether different.
It was that of a man named W. Burrows, aged about thirty years. Admitted into the hospital on the 26th Sep. 1829, under the care of Dr. J. Morgan, suffering from scrofulous ulcers in the axilla and neck, along with general cachexia. Previously he had had symptoms of secondary syphilis, and was supposed to have taken large quantities of mercury. He died on the 27th Nov. 1831, having had ascites for four months before his death.

Post Mortem:—Body extremely emaciated. Along with other changes noted, the spleen was found about twice its natural size, and unusually firm. On section it appeared “dense, rather dry, and dark-red in colour, but homogeneous”. Its substance was “generally pervaded by numerous minute, translucent bodies, somewhat resembling incipient miliary tubercles of the lung, but considerably smaller than these generally are.”

We have in this case a history of secondary syphilis, with ulcers of the neck and axilla of a scrofulous nature, accompanied by general cachexia and extreme emaciation, and the presence of
of ascites, which made its appearance about four months previous to the death of the patient. These all point to the degeneration of the spleen as waxy in its nature; and this opinion is further strengthened by the post mortem appearance of the spleen. Seeing there is no history of any glandular enlargement we may, therefore, conclude that this is not a case of lymphadenoma, but that it is a case of waxy disease.

Up to this period (1832), as we have endeavoured to show, the more advanced forms of waxy degeneration had not escaped the observation of pathologists. We look in vain, however, in the writings of the authors quoted above, for the evidence of any distinct advance in regard to this degeneration. In 1761 Morgagni and his contemporaries seem to have known quite as much of the nature of the change in question as Hodgkin and his contemporaries in 1832.

In 1842, however, the celebrated pathologist, Rokitansky, made what must be considered a most valuable addition to our knowledge of this subject. His name will always be closely associated with
with the history of this degeneration. For, it was he who first marked it off as a special form of degeneration which usually affects several organs simultaneously; and whereas previous writers had contented themselves with a naked eye description of an isolated case or so, which had come under their notice, Rokitansky in his Handbook of Pathological Anatomy (Iyd. Soc. Ed. Vol. II. p. 121) gathered together the main outlines of the pathological appearances which this degeneration presents in the liver, spleen, and kidneys. He traced its connection with various so-called cachexias induced by syphilis, aague, advanced stages of rickets, tuberculous and other exhausting diseases. The degeneration he named "lardaceous or bacony disease", and he was of opinion that it consisted in the infiltration of the tissues of the affected organs by a "crude, albuminous blastema"; "crude"—because of its persisting in the condition of crudity; probably "albuminous"—because to the naked eye it resembled a translucent coagulated albumen" (Vol. I. p. 327).

Here, then, we have a great advance in regard to this question. We
have the post mortem appearances of the affected organs carefully recorded, the simultaneous occurrence of the change in various organs, and what is of very great importance, the diseased conditions in the train of which the waxy change is liable to make its appearance, clearly and definitely set forth; thereby rendering its detection by subsequent observers comparatively easy. To Rokitansky, therefore, we are indebted, not merely for an extension of our knowledge regarding this subject, but also for the reduction of that extended knowledge to a scientific basis, by means of which all future investigation was very much simplified.

In this country, Dr. Budd described this degeneration in the liver as "scrofulous enlargement of the liver" ("Diseases of the Liver", 1845, p. 246 et seq.) Budd applied the term "waxy" to a condition of the liver which he regarded as a modification of "fatty liver" (p. 246). The true waxy degeneration of the liver, however, he described under the designation given above. He quotes cases from Portal.
(Mal du Foie) and Abercrombie (Diseases of the Stomach) to show that those authors had previously described a similar change. Kokitansky's researches on this question were well known to him, for we find him making special mention of them. The term "scofulous enlargement" was made use of to describe this change in the liver because of the fact that it sometimes occurred in persons much wasted by scofulous disease, especially of the bones. After recording the clinical features of a case of this nature, which had occurred in the practice of his brother, he proceeded to describe, with some minuteness, the post mortem appearance of the enlarged liver. According to him, "the increased size of the liver, and the semi-transparency, probably depended on some peculiar matter deposited in the lobules, in the cells or between them."

In the second edition of his work on "Diseases of the Liver," published in 1852, he states that, at his request, Professor Miller had made a chemical examination of an affected liver and had
had found that the foreign matter to which the organ owed its large size was not fatty, but albuminous. On page 317, he sums up the result of his study of this affection of the liver in a series of propositions, the chief of which are:

1st. The liver becomes enormously enlarged, and much thickened, and its lower edge much rounded.

2nd. The liver contains after death but a small quantity of blood, and is consequently pale.

3rd. When the disease is far advanced, the lobules can scarcely be distinguished; the hepatic substance is uniform and compact, somewhat glistening or semi-transparent so that the cut surface looks very much like that of compact bacon.

4th. The foreign matter to which the liver owes its large size is albuminous.

5th. The foreign matter is situated within the lobules, and it would seem that it is deposited in the central portions of the lobules. In the parts of the liver which are most diseased the secreting cells are few in number, and they
they are not enlarged. The foreign matter is not within the cells, but between them, and in advanced stages of the disease, seems, in some parts of the liver, completely to take their place, filling up the interstices of the capillary vessels that form the lobular network.

In 1844 Christensen of Copenhagen described the waxy "sago-spleen", and compared the appearance which the enlarged Malpighian bodies of the spleen presented on section of the organ, to "grains of boiled sago swimming in sago soup." (Copenhagen: Ugeskrift. 1844. 268. Oppenheim's Zeitschrift, 1845. Bd. 30. S. 137.)

Dr. Handfield Jones, of London, gave a minute description of the naked eye appearances, as well as the microscopic characters of the waxy "sago-spleen" at a meeting of the Pathological Society which was held on Jan. 2nd 1852. This paper is published in the Transactions of the Society. Vol. III, p. 333; and in the same volume (p. 259) is recorded a case, by Dr. Hamilton Roe of a girl aged nine years who died from empyema and whose spleen is described as being "bacon-like"; the new homogeneous material occupying...
"occupying the site of the Malpighian bodies."

About this time (1851-2), the workers on this degeneration were both numerous and distinguished. In this country and in Germany the names of Bennet, Gairdner, Sanders, Jones, Virchow and Meckel are all associated with the investigation, and the conclusions at which they arrived, though in certain cases contradictory to each other, yet served to advance to an extraordinary degree the Pathology of the degeneration in question.

In the "Edinburgh Medical Journal" for March, 1868, p. 841 et seq., a most interesting sketch is given of the history of the waxy degeneration from 1851 to 1868.

It would appear that the term "waxy" was in use in Edinburgh during the time of Home; and was by him made use of to express a pale and indurated state of the liver, which caused it to appear somewhat like bees-wax. By degrees, it came to be applied, in a rather loose manner, as descriptive of similar appearances in other organs; no exact
exact pathological signification being attached to the term.

That distinguished physiologist, Professor Bennett, in 1845, made a minute microscopic examination of an enlarged waxy liver. This investigation was not published till 1853 when the results appeared in his "Clinical Lectures." At that time, he was of opinion that the waxy change was an advanced form of fatty degeneration; the fat being absorbed leaving the empty shrunk liver cells aggregated together without a nucleus.

Professor Gairdner, in 1848, recognised a waxy kidney as a distinct form of Bright's disease. He then considered the waxy degeneration of the kidney to be due to the "spontaneous obliteration" of the capillaries of the kidney, with "subsequent thickening and varicose dilatation of tubuli throughout the organ."

About this time (1851-2) Dr Gairdner acted as pathologist to the Edinburgh Royal Infirmary. In the summer of 1852, Dr Gairdner being absent on the Continent on account of his health, Dr Sanders, the late respected Professor of Pathology
of Pathology in this University undertook the duties of pathologist in his stead. Whilst acting in this capacity Dr. Sanders had an opportunity of examining the liver and spleen of a patient who had died of phthisis. The spleen was found to be waxy, as well as the liver. When Dr. Gairdner returned, Dr. Sanders showed him sections of the waxy organs, and he at once recognised the appearance presented by the translucent material as similar to a change which he himself had previously observed in the liver and kidney, and which he had described as "horny" in his notes of the post-mortems. Hereupon, it was resolved to investigate the matter more carefully. Dr. Sanders turned his attention more particularly to the degeneration in the spleen, whilst Dr. Gairdner, assisted by Drs. Drummond and Kirk, took up the kidney and liver changes.

Dr. Kirk, afterwards better known from his association with Dr. Livingstone in his famous expedition on the Zambezi, and as British Consul at Zanzibar, appears to have been amongst
amongst the first, if not the first, to demonstrate the fact that, in the kidney the primary seat of the waxy change was to be found in the arterioles and capillaries. This he pointed out to the Physiological Society in June, 1853, and published in the Edinburgh Medical Journal. Sep. 1853 p. 277.

At a meeting of the Physiological Society, held on the 17th Dec. of the same year (1853) Drs. Gairdner and Sanders contributed the results of their investigations of the waxy degeneration of the liver and spleen, and published in the "Edinburgh Medical Journal" for February 1854 (p. 135 et seq.) The President, Dr Bennett showed a specimen of waxy spleen, and at the same time took occasion to announce that, though formerly he supposed this degeneration to have been "an ultimate form of fatty degeneration," he was now satisfied, from numerous observations, that it was "a primary alteration of the cells, and, though frequently associated with fatty degeneration, was not essentially connected with it." Dr Gairdner, after touching lightly
lightlingly on the waxy kidney and spleen gave a detailed account of the naked eye appearances of the waxy liver, and stated that, under the microscope, the chief change was to be found in the "glandular epithelium, which were compressed, irregular in form, and had atrophied nuclei, and presented a peculiar 'honey' refraction." He was inclined to regard the waxy change as "a peculiar modification of the protein compounds, in virtue of which they approached the character and possibly the chemical constitution of keratin, and presented a much greater resistance than in the normal state to acid and alkaline solvents." Dr. Sanders, with great clearness and fulness, described the waxy "sago" spleen, both in its naked eye and microscopical features. Apparently, he made use of certain staining agents in his investigation; for we find him stating that "this translucent substance is very little acted on by the usual reagents; it does not lose its transparency when treated with acids, or alkalies or alcohol: chromic acid and iodine render it yellow and brown, but
but do not alter its homogeneous aspect." In his opinion, however, the degeneration presented such permanent and well-marked characteristics as to render its detection by the microscope a matter of little difficulty. And he evidently relied more on its physical properties for its recognition than on the application of chemical reagents. He considered it "highly probable that this change is produced by a peculiar transformation of the normal corpuscles into some imperfect protein compound; for the normal elements are seen apparently in stages of transformation, becoming pale and altered in shape, and aggregating together into homogeneous masses."

"These important researches have not received the attention which they undoubtedly merit; and this is more especially the case as regards German writers on this subject, who, naturally consider the researches of Virchow as of great interest and importance. Even in our own country they do not appear to have attracted very great attention outside the influence of Edinburgh."
Edinburgh medical circles; for it is seldom we find them referred to. Hyber and Scheutte, whilst professing to give a satisfactory account of the history of the amyloid change, omit to mention the names of these Edinburgh investigators. Parkes, however, in the "British and Foreign Medico-Chirurgical Review", Vol. XIV p. 147 et seq., gives a review of the work done in Edinburgh along with an account of Neckel's researches on the same subject.

As I shall have occasion to state further on, the views of the Edinburgh observers with reference to the participation of the liver cells in the degenerative process, differed from those of Dr. Budd, cited above, in that the former emphasized the occurrence of the waxy change in the liver cells, whereas the latter, even as far back as 1845, was in doubt as to the deposition of the waxy material in the cells, and in 1852 positively affirmed that the foreign matter did not occur in the cells, but between them.
investigations, but independently of them, the study of this degeneration was carried on by pathologists in Germany, and the results of these researches have become widely known.

Meckel, in "Annalen des Charité Krankenhauses zu Berlin", Heft II, S. 264, (1853) published an account of the "Lardaceous or Cholesterine Disease", embodying the results of an extensive chemical investigation of the lardaceous material, along with a microscopical examination of the lardaceous liver, spleen, and kidneys, intestinal canal, thyroid gland, and brain. He pointed out its occurrence in the arterioles and capillaries in these organs; and, chiefly from his chemical observations, considered the morbid change to be due to a deposit of cholesterine in the tissues. Therefore he adopted the term "cholesterine" as descriptive of the affection. He likewise tested the reaction with iodine and sulphuric acid. As regards the liver he was of opinion that the change probably began in the liver cells.

It would seem that up to 1853 Virchow was in doubt as to the existence
ence of any special tardaceous or waxy degeneration. (Virchow's Archiv. Bd I, S. 116; II., 296; I., 292; II., 268 and 416). At one time he spoke of a "colloid" degeneration, and afterwards of an "albuminous" change, but not, apparently, with any precise acquaintance therewith. In 1855 he discovered the blue reaction with iodine and sulphuric acid, first of all in the "corpora amylacea" of the brain and spinal cord (Virchow, Archiv. VIII, 2, 3, 1854). This reaction led him to consider the waxy substance as of the nature of cellulose, seeing that cellulose is stained blue on the addition of iodine and sulphuric acid. Starch also was found to give an ultramarine tint with iodine alone. Virchow, accordingly, named the degeneration "Amyloid," and this term is now in general use in Germany, although the theory, according to which it first came to be applied, has since been completely refuted. The discovery on the part of Virchow of this chemical reaction, applicable to all cases of waxy degeneration, undoubtedly facilitated the study of the
the subject. By means of it Virchow soon covered the ground which had been traversed by the British observers and added still further to our knowledge regarding its occurrence in various parts of the body. In this country the iodine test alone is mainly relied on for the naked-eye demonstration of this affection, without having recourse to the addition of sulphuric acid.

Since these researches of Virchow and Miechel, and those of the London and Edinburgh pathologists were published, numerous additions have been made to the literature of this degeneration. In tracing the subsequent history of this subject, however, I shall not attempt to give a detailed account of all the communications which have appeared in connection with the waxy degeneration, but shall confine myself to a consideration of a few of the more important.

In 1856 Dr. Wilks published a series of "Cases of Lardaceous Disease, and some Allied Affections," in Guy's Hospital Reports, illustrating more particularly
particularly the causes of the disease, and containing the results of an independent study of its pathology. Dr Wilks disputes the iodine and sulphuric acid reaction. He regarded the hardaceous disease as analogous to the cancerous or tuberculous.

Friedreich and Keule, in 1859, published an important contribution to our knowledge of the chemical composition of the waxy substance (Virch. Archiv. Bd XVI, s. 50 et seq.). They gave the following as its percentage composition:

\[
\begin{align*}
C &= 53.58 \\
H &= 7.00 \\
N &= 15.04
\end{align*}
\]

The substance was not, therefore, of the nature of cellulose, as Virchow had supposed; but its chemical composition showed it to be albuminous in its nature. And this was subsequently confirmed by Carl Schmidt in Ann. d. chem. u. Pharm. Bd CX, p. 250; and in 1865, by Kühne and Rudneff (Virch. Archiv. Bd. XXXIII, s. 66). Frerichs (Diseases of the Liver, Sgd. Soc. Vol II, p. 107 et seq.) treats of this
this degeneration as it occurs in the liver, giving an account of its history (omitting to mention the Edinburgh investigations), anatomical appearances, etiology, clinical history, duration & progress, diagnosis, prognosis, and treatment. According to him, the "waxy degeneration of the liver commences in the glandular cells, similar changes being observed in the more delicate vessels, the walls of which become thickened, rigid, homogeneous, and lustrous, while their channel is narrow and not unfrequently entire by obliteration." (p. 171).

C. Wagner (Arch. d. Heilk. 5481 [1861]) contributed an important paper on this subject, in which it is interesting to note, the opinion he advocated with regard to the waxy liver was at variance with the commonly accepted ideas of the time. Along with Budd, he maintained that in the lobules of the liver, the degeneration was restricted to the arteries and capillaries, the liver cells merely becoming atrophied from pressure or containing droplets of fat or granules.
The capillaries of the lobule, swelling up by reception of amyloid material, in his opinion, exerted a pressure on the liver cells, thereby causing them to atrophy and disappear, those still remaining being turbid and filled with fat drops, more especially near the margin of the lobule.

Professor Grainger Stewart, during the years 1861-68, published in the "Edinburgh Medical Journal" and the "British and Foreign Medico-Chirurgical Review" some very valuable papers on the "waxy or amyloid form of Bright's disease." In a paper read before the Medico-Chirurgical Society of Edinburgh, January 9th, 1861 (Edinburgh Med. Journal, 1860-61, p. 710 et seq.) after a brief historical account of the waxy degeneration, he proceeded to give a detailed description of the macroscopic and microscopical appearances of the waxy or amyloid kidney, together with the symptoms presented by the disease, and a series of illustrative cases. He considered that the enlargement and induration of the organ present in almost every case of this degeneration could not
not be explained by the mere change in the arteries and Malpighian bodies; but that, in addition, "an infiltration of the whole organ with some dense pale matter, evidently not amyloid in its character, because presenting no special reaction with iodine and sulphuric acid" took place "the transmission of this exudation through the walls of the vessels being favoured by their degenerated condition" (page 414). As regards the clinical history of cases of this disease, we find in the same paper by Professor Stewart what must be considered a very complete account. Indeed, it is mainly owing to his investigations that the clinical aspect of this form of Bright's disease was at first established. But, as I do not purpose entering on the symptomatology of this degeneration, it will be sufficient for my present purpose, merely to point out this fact, without going into further details. The views as to the symptoms which accompany waxy degeneration of the kidney, recorded by Professor Grainger Stewart in this paper, were further confirmed by him in an article published in the "Edinburgh Medical Journal for August
August 1864 p. 97 et seq. in which he completed the history of three of the cases mentioned in his former communication, and gave a summary of several other cases in which post-mortems had been made. Another communication on "Haemorrhage from Waxy or Amyloid Degeneration," he contributed to the British and Foreign Medico-Chirurgical Review," 1868, Vol. XII page 201 et seq. in which he narrated a few cases illustrating the occurrence of haemorrhage from the stomach and intestines in this disease.

Dr. Dickinson (Pathology and Treatment of Albuminurea 1868) and (Trans. Path. Soc., Vol. XXX) advocated views with regard to this degeneration which have met with much opposition. In his opinion, the waxy or lardaceous disease consists in "a general deposition" of the fibrin or albumen of the blood "modified by loss of alkali or gain of acid." The following are the chief grounds he puts forward in support of this statement:—

1st. Chemical analysis has shown, on an average, that waxy livers contain about one quarter less alkaline salts.
salts than normal livers.

2nd. Alkalies, such as potash or soda, even in very dilute solution, cause the red coloration with iodine, which characterises the waxy material, to disappear from the tissues before there has resulted any material injury even to the microscopic structure of the tissue. Fibrin dissolved in very dilute hydrochloric acid (6 parts of acid to 10,000 parts of water), and recovered by evaporation, is transformed into a gelatinous material, which furnishes a similar coloration with iodine.

3rd. As one of the most frequent causes of this degeneration is prolonged suppuration (pus being an albuminous material containing abundant alkaline matter), the free discharge of pus renders the blood poorer in albumen and alkalies. The dealkalized fibrin, being in excess, is, according to Dickinson, deposited as an infiltration in the affected tissues.

Hyber (Inaug. Dissert. Dorpat: 1871; and Virchow's Archiv: Vol. 34) makes some further additions to our knowledge concerning the wide-spread occurrence of
of the waxy material in the tissues of the body; but his researches do not throw much light on the nature or ultimate cause or causes leading to the origin of this material in the tissues. The coloured drawings with which he illustrates his dissertations are very faithful and excellent representations of the waxy change as it occurs in various organs.

The discovery by Cornil (Arch. de Physiol. 1875, Ser. II, Tom. II, p. 679) of a new test for the detection of the waxy substance formed another step in advance in the study of this subject. This was the "methyl aniline violet" test, which is now in such common use in pathology. Cornil found that this reagent stained the waxy portions of the organs red, whilst the unaffected parts were stained blue. The addition of a weak acid caused the blue colour of the healthy tissues to become paler in appearance, whilst the red coloration of the waxy parts retained its intensity or even turned a brighter red. For microscopical purposes it possesses many advantages over the iodine stain, but this latter is of greater service
service in ordinary naked eye examination.

About the same time as Cornil, Jürgens (Virchow’s Archiv. 1875 Bd. 65, S. 189) studied the methyl-aniline reaction, and published a paper giving a beautifully coloured illustration, showing the characteristic appearance presented by the waxy, as contrasted with the healthy parts, when stained by this reagent.

The relation which syphilis bears to lardaceous disease constituted the substance of an address delivered by Dr Hilton Fagge in the course of a discussion on “Syphilis” before the Pathological Society of London in 1876 (Path. Soc. Trans. Vol. XXVII. p. 381).

And at a subsequent meeting of the same Society he brought forward detailed evidence in support of the view that lardaceous degeneration owes its production to one of two causes:—either chronic suppuration or syphilis (Path. Soc. Trans. Vol. XXVII. p. 324 et seq.).


At a meeting of the Pathological Society of London held on the 15th April, 1879, the report of which is published in Vol. XXX of the Transactions of the Society, an interesting discussion took place on the lardaceous degeneration. The discussion was opened by an address from Dr. Dickinson, in which he anew gave expression to views similar to those to which reference has previously been made. In the liver, according to him, "it involves the terminal branches of the hepatic artery, and infiltrates the cells of the middle zone of the lobule." (page 515). Suppurative and syphilis
syphilis are the only two conditions which, in his opinion, are "beyond question" causes of this degeneration. He had not been able to satisfy himself that it ever ensues from tuberculosis or bone disease in the absence both of suppuration and syphilis. (Page 515.) Dr. Turner took up the statistical aspect of the subject, and laid before the Society statistics with reference to the cases which had occurred in the London Hospital from the year 1875 up to the date of meetings. These figures I shall have occasion to refer to further on, and therefore I do not now touch upon them.

Professor Greenfield exhibited microscopic specimens of lardaceous liver, spleen and kidney stained with methylanilin violet. The iodine reaction appeared to him "a very rough and uncertain one, because it sometimes fails, neither does it lend itself well to microscopical examination, nor is it permanent; and it stains other degenerated or altered albuminous bodies in a way which is indistinguishable from lardaceous material."
material. He had used with success the methylamin stain, introduced by Xornil, and preferred it for microscopic work rather than iodine. Having stated several points of difficulty in the way of accepting the theory of "infiltration" advanced by Dr. Dickinson he preferred to adhere to the view that the lardaceous change was a true degeneration. He reminded the Society that, though the durability of the lardaceous material was great, it often underwent "fatty degeneration, molecular disintegration, and even calcification." Dr. R. Smith was also opposed to the theory of infiltration. In his opinion the artificially produced lardaceous material resulting from the action of dilute hydrochloric acid was nothing else than the well known substance syntonin. Dr. Goodhart offered the suggestion that the length of time necessary for the production of lardaceous disease in cases of suppuration depended in great measure upon the "duration and intensity of the fever. The greater the intensity..."
sity of the fever, or perhaps if it be prolonged without much intensity, other things being not adverse, the more rapid will the faradaceous change be produced. This view might throw light on the fact that this affection is very common in hot climates, and would likewise connect this change with those by saline changes in the vessels which occur in various febrile conditions. Dr Stephen Mackenzie thought an examination into the nature of the hyaline change in the vessels which he described, might throw some light on faradaceous disease. Dr Ralfe drew attention to the circumstance that iodine not only gives with fibrin treated with dilute hydrochloric acid the deep brownish-red stain, which is held to be characteristic of the faradaceous material, but also with ordinary fibrin, and with alkali albumen or casein. This re-action merely denoted the presence of an albumen other than ordinary albumen, and the equally ready development of the reaction with alkali
alkali, as well as with acid albumen.
showed that it is not caused by the
removal of alkali." With reference
to the hyaline change, it might be
that it is "the first step in the"
"lardaceous degeneration."

Quite recently Dr Kühling
of Strasburg (Pirchow's Archiv Bd. 103,
S. 1) has contributed a valuable
paper on this subject in which he
demonstrates the close connection sub-
sisting between the hyaline and waxy
degenerations in the spleen.

Having thus, in a somewhat
fragmentary manner, endeavoured to
trace the history of the waxy degener-
ation from the time of Malpighi down
to the present date, I shall now pro-
ceed to discuss

The Etiology of this Degeneration.

Ever since Rokitansky (loc. cit.)
published his researches on this sub-
ject, waxy degeneration has been re-
cognised as having a connection with
certain so-called constitutional or
euchistic conditions dependent upon
phthisis
phthisis, syphilis, malarial fever, scrofula, rickets and other wasting diseases. Certain tumours, it would appear, may be associated during their course with the development of the waxy change. Thus, Schueppel (Kiemsen's Cyclopaedia, English Edit. Vol. IX) records a case in which an enormous fibro-myxoma had developed in the region of the left kidney in a man forty years of age, whose liver was the seat of waxy disease.

According to the same authority, cancerous and sarcomatous tumours may likewise be accompanied by this degeneration: the slower the growth of the tumour and the more gradual the approach of symptoms of constitutional affection, the more apt is the degeneration in question to be met with. Schueppel states that it is by no means necessary that any retrograde metamorphosis, breaking down, or ulceration should take place in the tumour, in order that waxy degeneration may be set up. Leuco-cytemia, and the haemorrhagic diathesis, as well as acute rheumatism followed
followed by cardiac disease have also been known to be associated with the waxy change.

In rare instances waxy degeneration may be found, and none of the above conditions may be present to account for its occurrence. Wilks (loc. cit.) instanced some cases of this kind and named them "simple lardaceous disease"; and Dr Hilton Faggie (loc. cit.) cites two cases in which death occurred from acute mischief, altogether unconnected with the presence of the lardaceous disease: in one, death was caused by pyaemia after amputation of the thigh for a diffused poplitel aneurism; in the other from acute pneumonia and pericarditis. And Hrerichs (Diseases of the Liver. Syd. Soc. Vol. II pp. 627, 718) likewise records two cases where no evident predisposing cause existed. In the statistics which I have collected several such cases likewise occur.

Statistics have been brought forward in order to show the comparative frequency with which each of the above-named diseases is to be regarded.
regarded as having a causal connection with waxy degeneration. Hennings (Inaug. Dissert. Hiel. 1880) makes out that chronic phthisis and chronic suppuration of bone, are to be regarded as the most frequent predisposing causes.

1st Chronic Suppuration of Bone.

Hoffmann (Inaug. Dissert. Berlin 1868) found only six out of eighty cases associated with chronic suppuration of bone, while C. Weber refers not less than fourteen out of thirty-seven (38%) and E. Wagner eleven out of forty-eight cases, (23%) to this affection of bone. Hilton Pagge (loc. cit.) found fifty-two out of his two hundred and forty-four cases (21.3%) associated with supplicative disease of bone. Turner (Path. Soc. Trans. Vol. XXX pp. 519, 520) out of fifty-eight cases observed in the London Hospital, noticed thirteen (22.4%) cases of bone disease with prolonged suppuration. Taking an average of all these, we find, that out of four hundred and sixty-seven cases of waxy disease, ninety-six (20.5%) suffered from chronic suppuration.
2nd As regards Chronic Phthisis which has long been considered as the most frequent of all the diseases in whose train the amyloid or lardaceous degeneration makes its appearance, statistics show that it is much more frequently associated with this degeneration than is chronic suppuration of bone. Hoffmann numbered fifty-four cases of phthisis among his eighty (67.5%); C. Weber, fifteen in his thirty-seven (40.5%); C. Wagner, twenty-seven in his forty-eight (56.25%); Hilton Fagge, sixty-seven out of his two hundred and forty-four (27.4%); and Turner twenty among his fifty-eight cases (34.4%). In four hundred and sixty-seven cases of amyloid or lardaceous degeneration, therefore, we find one hundred and eighty-three, which showed well-marked evidence of phthisis—equal to 39.18 per cent.

3rd Syphilis, both congenital and acquired, stands in very close relation to waxy degeneration. Indeed, if one is to judge from the statistics of Dr. Fagge, its connection with the degeneration is even closer than that of phthisis, be-
cause in seventy-six of his two hundred and forty-four cases of lardaceous disease of the viscera, there was satisfactory proof (either from other post mortem appearances, or history, or both) of the existence of syphilis. This is equal to 31.2 per cent. — or 3.8 per cent more than his cases of phthisis. On the other hand Dr. Turner among his fifty-eight cases of lardaceous disease found only eight in which evidence of syphilis existed (13.8%). Unfortunately, I have no record of the occurrence of syphilis from the statistics of Hoffmann, Weber and Wagner's cases. But if those of Dr. Pagge and Dr. Turner be added together and an average taken, we shall find that, out of a total of three hundred and two cases of lardaceous degeneration, eighty-four showed satisfactory proof of the presence of syphilis in conjunction with the lardaceous change, which is equivalent to 27.8 per cent. For purposes of comparison as to the relative frequency with which waxy degeneration is associated with syphilis on the one hand and phthisis on the other it may
may be well to test the averages as these are contained in the figures of Dr. Turner and Dr. Tagge.

We have shown that syphilis has an average of 27.8 per cent. of the cases; and, further, as regards phthisis, we find that, from the same three hundred and two cases, eighty-seven presented well marked phthisical change, equal to 28.8 per cent., or 1 per cent. more than that of syphilis; whilst as regards chronic suppurative disease of bone, these three hundred and two cases contained sixty-five, or 21.5 per cent.

To sum up, we may state that from the statistics of Drs. Tagge and Turner the three great pathological associates of waxy degeneration are found to be phthisis, syphilis, and these diseases of bones, which are attended or followed by prolonged suppuration. These alone constitute over 78 per cent. of the cases of waxy degeneration recorded by the above authors. Throwing these statistics into tabular form, the results will appear thus:
<table>
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<th>Waxy Degeneration</th>
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<tr>
<td></td>
<td>with Suppuration</td>
<td>with Chronic</td>
<td>with Syphilis</td>
</tr>
<tr>
<td></td>
<td>of Bone</td>
<td>Phthisis</td>
<td></td>
</tr>
<tr>
<td>Hoffmann</td>
<td>6 out of 80 cases</td>
<td>34 out of 80 cases</td>
<td></td>
</tr>
<tr>
<td>Weber</td>
<td>14 &quot; 37 &quot;</td>
<td>15 &quot; 37 &quot;</td>
<td></td>
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<tr>
<td>Wagner</td>
<td>11 &quot; 48 &quot;</td>
<td>27 &quot; 48 &quot;</td>
<td></td>
</tr>
<tr>
<td>Fagge</td>
<td>52 &quot; 244 &quot;</td>
<td>6 7 &quot; 244 &quot;</td>
<td>76 out of 244.</td>
</tr>
<tr>
<td>Turner</td>
<td>13 &quot; 58 &quot;</td>
<td>20 &quot; 58 &quot;</td>
<td>8 &quot; 58.</td>
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**Total**

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<tr>
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<th>96 &quot; 467 &quot;</th>
<th>183 &quot; 467 &quot;</th>
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<tr>
<td></td>
<td>or 20.5 per cent</td>
<td>or 39.18 per cent</td>
<td>or 27.8 per cent</td>
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For purposes of comparison I shall give the statistics of Fagge and Turner by themselves, so as to make a thoroughly fair statement:

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<td></td>
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Of late years, certain authorities, notably Dr. Dickinson and Dr. Hilton Fagge, have been disposed to reduce the conditions under which waxy degeneration may originate to the two following, viz:—
syphilis and chronic suppuration. Dr. Dickinson, in his address to the Pathological Society of London (loc. cit.) declares syphilis and suppuration to be the only two causes which are “beyond question”; and he had not been able to satisfy himself that tubercle or bone disease, in the absence, both of suppuration and syphilis, ever acted as causes. Dr. Hilton Fagge’s statistics (loc. cit.) confirming as they tend to do, the views of Dr. Dickinson in regard to the causation of waxy degeneration are so remarkable as to warrant their entire insertion. The statistics were collected from the post mortem records of Guy’s Hospital during the twenty-one years from 1855 to 1875 inclusive, by Mr. Lancaster. During that time, the number of cases of lardaceous degeneration amounted to 294. Of these 154 were cases in which chronic suppuration had existed for a considerable length of time but in which there was no evidence of
of syphilis. These 154 cases contain:

67 cases of Phthisis

29 " " Joint disease (generally either hip or knee-joint).

12 " " Disease of Vertebrae (in most psoas abscess existed).

10 " " Caries or necrosis of other bones

6 " " Pelvic abscess (cellulitis).

3 " " Empyema, discharging externally.

4 " " Scrofulous disease of kidney.

3 " " Dysentery.

3 " " Tubercular ulceration of intestine.

2 " " Bedsores, following fracture of spine.

1 case " Abcess of Liver, discharging externally.

1 " " Suppurating ovarian cyst.

1 " " Carbuncle of 8 months' duration

1 " " Empyema; pneumothorax; scrofulous kidney.

1 " " Compound fracture of leg (3½ months).

1 " " Old running abscesses and fistula.

1 " " Stricture, and old cystitis.

1 " " Chronic pyæmia & abscess in areolar tissue.

1 " " Ulcerating cancer of the uterus.
1 Case of Ulcerating sarcoma of abdominal wall.
1 " " Ulceration of leg.
1 " " Iliac abscess (caecal in origin)
1 " " Dilatation of bronchi and suppuration.
1 " " Discharging sore in neck.
1 " " Caseous disease of glands.
1 " " Calculous pyelitis.

154 Total.

In addition there were 5 cases in which some suppurative had been present, but doubtful whether this had been sufficiently profuse, and long-standing enough to cause tuberculous degeneration, viz:-

1 Case of Stricture with suppurating kidneys.
1 " " Abscess of liver, not discharging externally.
1 " " Tubercular peritonitis and chronic caseous disease of mesenteric glands.
1 " " Inflammation and abscess of testis from blow, of 2½ months' duration, but only opened two weeks before death.
1 " " Chronic Deafness, with discharge from one ear; and of "stoppage of nose", which had lasted for some time
time, and had been attended with discharge.

5 Total.

There were also:

76 cases in which there was satisfactory proof, (either from other post mortem appearances or history or both) of the existence of Syphilis. In about 34 of these there was evidence of former or present bone disease or suppuration leaving about 42 in which the affection seemed attributable to the syphilis per se.

3 cases were also found in which there was at any rate a suspicion of syphilis:

1 a case of gout with large red kidneys and fibroid testes.

1 case of cirrhosis of liver (patient had had a chancre six years before and was said not to have been intemperate.)

1 case of Cachexia with enlargement of ulna with apparent gummata in the spleen.

The total number of cases, therefore
in which there was evidence either of syphilis or of suppuration, amounted to 238 and there remain only six out of the 244 in which no such evidence was made out. Of these six:

1. was a case of lardaceous disease in liver, kidney and spleen. (In this case the testes seem not to have been examined.)

2. cases of cirrhosis of liver with lardaceous change. (Testes seem not to have been examined in one of these; the other was a female.)

1. case of small ulcer of stomach. (In this case it is noticed that the two last ribs on one side were considerably enlarged as well as their cartilages probably from syphilitic periostitis.)

1. case of Pyaemia after amputation of the thigh for a diffused proptotic aneurism.

1. case of acute Pneumonia and pericarditis.

6

Influence of Age

In regards to the occurrence of Waxy Degeneration:

This degeneration may occur at any age.

According
According to Rakitansky and others, (Schweppel - Kiemien's Cyclopædia Vol.11) waxy liver may occur even as a congenital condition; and it may be met with very late in life - as late as seventy years. Statistics bearing on this point are not very numerous. The following are given by Frerichs and Wagner, and refer to the waxy liver:

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<thead>
<tr>
<th>Frerichs found among 68 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10 years of age......... 3</td>
</tr>
<tr>
<td>Between 10 and 20.............. 19</td>
</tr>
<tr>
<td>&quot; 20 &quot;, 30 ................ 19</td>
</tr>
<tr>
<td>&quot; 30 &quot;, 50 ................ 18</td>
</tr>
<tr>
<td>&quot; 50 &quot;, 70 ............... 9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Wagner found among 48 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10 years of age........ 5</td>
</tr>
<tr>
<td>Between 10 and 20............. 5</td>
</tr>
<tr>
<td>&quot; 20 &quot;, 30 .......... 18</td>
</tr>
<tr>
<td>&quot; 30 &quot;, 50 ........ 13</td>
</tr>
<tr>
<td>&quot; 50 &quot;, 70 .......... 7</td>
</tr>
</tbody>
</table>

**Influence of Sex:**
Males appear to be much more frequently the subject of this degeneration than
than are females. Of Frerich's 68 cases 53 were males and 15 females; whilst 33 of Wagner's 48 cases were males and 15 females.

**Influence of Climate.**

This affection is said to be common in hot climates, but I am not in possession of any precise data on this point. In those localities which are the most favourable for the development of Phthisis, which is the most common associated condition, we should naturally expect to find this degeneration more common than in dry bracing localities. The presence of Syphilis, unfortunately, is not limited by any mere climatic conditions, and so far as its connection with this degeneration is concerned, may exert its baneful influence at all seasons and in various climates.

Having given statistics from various sources bearing on the predisposing causes of waxy degeneration, I may be permitted to give the general results of some statistics, which, through the courtesy of the Pathologists, I have been
allowed to extract from the post-mortem records of the Edinburgh Royal Infirmary. I have noted all the cases of waxy degeneration from the summer of 1852 to the summer of 1862; and from 1870 to September 1886, the records for the intervening years not having been available for inspection at the time I examined the other volumes. The statistics, therefore, extend over a period of about twenty-six years. During that time the number of cases of waxy change observed was 430. Of these, 275 were males, equal to nearly 64 per cent.; and 155 were females, equal to about 36 per cent.

In 372 of the cases the age was ascertained (the ages of the rest not being given) and the following is the result:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 10 years</td>
<td>3 cases</td>
</tr>
<tr>
<td>Between 10 and 20</td>
<td>50</td>
</tr>
<tr>
<td>20 to 30</td>
<td>121</td>
</tr>
<tr>
<td>30 to 40</td>
<td>108</td>
</tr>
<tr>
<td>40 to 50</td>
<td>57</td>
</tr>
<tr>
<td>50 to 60</td>
<td>26</td>
</tr>
<tr>
<td>Over 60</td>
<td>1</td>
</tr>
</tbody>
</table>

These cases were distributed through
The various ages as follows:

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>16</td>
<td>10</td>
</tr>
<tr>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>19</td>
<td>1</td>
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<tr>
<td>20</td>
<td>10</td>
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<tr>
<td>21</td>
<td>12</td>
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<td>22</td>
<td>11</td>
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<tr>
<td>23</td>
<td>20</td>
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<td>24</td>
<td>16</td>
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<tr>
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<td>9</td>
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<tr>
<td>30</td>
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<tr>
<td>31</td>
<td>11</td>
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<tr>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>217</td>
</tr>
<tr>
<td>Year</td>
<td>Cases</td>
</tr>
<tr>
<td>------</td>
<td>-------</td>
</tr>
<tr>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>34</td>
<td>6</td>
</tr>
<tr>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>36</td>
<td>12</td>
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<tr>
<td>37</td>
<td>10</td>
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<td>38</td>
<td>7</td>
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<tr>
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<td>5</td>
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<td>40</td>
<td>11</td>
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<td>41</td>
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<td>8</td>
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<td>43</td>
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<td>45</td>
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<td>47</td>
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<td>48</td>
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<tr>
<td>49</td>
<td>7</td>
</tr>
<tr>
<td>50</td>
<td>6</td>
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<tr>
<td>51</td>
<td>3</td>
</tr>
<tr>
<td>52</td>
<td>1</td>
</tr>
<tr>
<td>53</td>
<td>1</td>
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<tr>
<td>54</td>
<td>5</td>
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<tr>
<td>55</td>
<td>4</td>
</tr>
<tr>
<td>56</td>
<td>3</td>
</tr>
<tr>
<td>57</td>
<td>1</td>
</tr>
<tr>
<td>58</td>
<td>2</td>
</tr>
<tr>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>365</td>
</tr>
</tbody>
</table>
13y & 1rd. 365 cases
60 years 3
61  1
62  1
63  1
68  1
70  1
Total 372

From the above we find that the greatest number of cases was observed to fall under the 23rd year and the next greatest number during the 30th year: then follow in succession the 24th, 28th, 35th and 32nd years.

By far the greatest number was found between the ages of 20 and 40 years—229 out of the 372; or 61.5 per cent.

Associated Pathological Conditions
Out of the 430 cases, 301 showed evidence of chronic suppuration, but no trace of Syphilis. These consisted of 193 cases of Chronic Phthisis.
46 cases of Suppuration connected with disease of bones and joints.
142 "  " Abscesses in other parts.
2  "  " Tubercular ulceration of intestines.
1. Case of large bedsore, following fracture of spine (lasting less than 3 months).
2. Chronic Pneumonia lasting six months.
3. Large ulcer of left thigh.
4. Ulcerating carcinoma of uterus and vagina.
5. Carcinoma of left supra-renal capsule and mesenteric glands (latter ulcerating).
6. Ulcerating Scirrhus of posterior wall of bladder.
7. Carcinoma of shaft of femur and humerus with suppurating malignant emental cyst.
8. Chronic Bronchiectasis.

There were 4 cases in which suppuration was present but apparently of such short duration or too small amount to cause waxy disease. These were:

2. Cases of Erysipelas followed by extensive suppuration.

1. Case of Intense Pleuro-pneumonia, lung filled with purulent material, metastatic deposit in kidney.
1 Case of Chronic gastric ulcer.

Five cases were noted in which malignant disease, without any evidence either of suppuration or of Syphilis appeared to be associated with this degeneration as a predisposing cause:

1. Case of Large carcinoma of kidney.
1. " Lung (31. Nov.)
1. " Carcinoma of Pancreas and peritoneum.
1. " Multiple Sarcoma.

There were, in addition 20 cases in which the associated condition was an affection of the Heart—hypertrophy or valvular disease, following acute rheumatism; no trace of suppuration or evidence of syphilis. The cases of undoubted syphilis numbered 75.

The remaining cases, partly because of limitation, on the part of the friends, of the regions to be examined post-mortem, and partly because of insufficient history showed no evident predisposing cause. In some of these the pathologist made note of the apparent absence of any sufficient cause of the degeneration.
Organs Affected.

The Liver, Spleen and Kidneys combined were affected in 172 cases.
Liver and Spleen (combined) 35 "
Kidneys and Spleen 71 "
Liver and Kidneys 32 "
Kidneys alone, affected in 40 "
Spleen 31 "
Liver 18 "

In the remaining case, the intestines alone were affected.

As regards the organs affected, I limited myself to the kidneys, spleen and liver, because in a number of the earlier cases, the intestines and other organs seem not to have been tested for the waxy change. Therefore, in subsequent cases, where the kidneys and intestines, or spleen and intestines or liver and intestines were together affected, I merely noted the kidneys, spleen or liver, and took no note of the intestines, as I wished the statistics of the former organs only.

Judging from these figures, the kidneys appear to be the most frequent seat of the waxy change, for they
they were affected in 70 cases in which neither the liver nor spleen showed any change, whilst the spleen was so, only in 31, and the liver in 18. If we enumerate the cases in which these three organs, either alone or in combination, were found to be involved, the kidneys still show a majority.

Kidneys, alone or in combination 345 cases
Spleen, 309
Liver, 257

These results, as will be shown further on, are not in conformity with other statistics on this point.

In some respects the above statistics confirm those previously mentioned. These, as regards the age and sex of those affected, they tend to support the figures of Frerichs and Wagner. As regards the associated pathological conditions, whilst confirming to a certain extent, the statistics given above, they bring out with much greater emphasis the notable frequency with which waxy degeneration is associated with chronic...
phthisis. Out of the 430 cases, 19.3 or almost 45 per cent suffered from phthisis; 75, or 17.4 per cent showed evidence of syphilis; and 46 had bone disease associated with suppuration, equal to 10.7 per cent.

Whilst the most careful scrutiny failed to elicit evidence of the presence either of suppuration or of syphilis in many of the cases, an overwhelming majority exhibited signs of one or other of these. Still, sufficient material has been furnished to cause one to look in some other direction for the predisposing cause. Holding the opinion, as I do, that syphilis and suppuration are the chief factors predisposing to the development of waxy degeneration, I yet maintain that these are by no means sufficient to account for all the cases; and I shall have occasion again to take up this question of causation when referring to the causation of hyaline degeneration.

These conditions I have designated predisposing causes of waxy degeneration; for all that can at present
present be affirmed in regard to their action, is that, in some way or other, during their existence, the degeneration in question may make its appearance. The manner in which the change is brought about, and the precise agency at work in its production have not as yet been definitely determined, the various theories which have been pro-
pounded regarding it, not having in my opinion, gone to the root of the matter.

Theories regarding the Waxy Change.

The older writers held different views regarding it. Thus Bonetus (loc. cit.) believed the change which he described to be due to "obstruction of the viscera." Abraham Vater regarded the affection as a "Scirrhus," for he treats it under that designation. Morgagni (Tom II, Liber III, Epist. XXXVI, p. 68) regarded the enlargement of the spleen, consequent on this change as due to obstruction of the vessels and his description
description of the manner in which the enlargement is brought about is interesting as an illustration of the pathological views of his time. "For the sluggish movement of the blood," he writes, "being increased, whilst, like muddy water outside its channel, it is diverted into the cells of the spleen in which it deposits whatever corpuscles it may hold heavier than it can naturally bear, and thus, partly by obstructing its own return, it distends them (cells) more and more. The more the whole spleen is distended by the swelling of these cells the weaker will it become, and, on that account, more prone to retain in great part that which afterwards flows into it. Therefore it sometimes increases in an incredible manner." Matthew Baillie (loc. cit. Vol II p. 201) regarded the change he described in the liver as "the first step towards the formation of the tuberculated liver." The change in the spleen he gives no opinion upon, whilst to that occurring in the kidney he gives the name of scirrhous as it "exactly resembles scirrhous in other parts.
parts of the body." Budd regarded 
this degeneration in the liver as a 
"serofulose" affection, consisting in an 
albuminous change in the capillaries 
of the lobules. Virchow, as was pre-
viously pointed out, at one time be-
lieved the waxy material to consist 
of a material akin to starch and 
hence named it "amyloid," regarding 
it due to an infiltration. Meckel 
(loc. cit) considered the morbid change 
to be due to a deposit of cholesterin 
and so named it "cholesterin disease." 
Handfield Jones (Brit. & For. Med. 
Arch. Review. Vol. XIV p. 347) regarded 
the degeneration as "a form of unhealthy 
aplastic fibrinous matter, which exudes 
from the bloodvessels instead of the 
"normal plasma, and, solidifying in 
"the interstices of the tissues, causes their 
"atrophy, while itself goes on accumulating 
"causing great apparent increase in the 
"size of the organ." As previously 
stated, Rekitansky ascribed this change 
to an infiltration of the tissues of the 
affected organs by a "crude albuminous 
Blastema." Professor Bennett at one 
time supposed that it was "an ultim- 
ate
ate form of fatty alteration." Dr. Gardner and Dr. Sanders were of the opinion that it probably was the result of a transformation of the protein elements of the tissues. So far as I have been able to ascertain, it would appear that Professor Miller of London, was the first to determine the nature of the waxy substance by means of chemical analysis. Dr. Budd (Diseases of Liver) considered that, from the "waxy" appearance of the enlarged livers due to this degeneration, they probably contained some solid form of fatty matter, and he requested Professor Miller to analyse a portion of one of the affected livers. He (Professor Miller) found that a small proportion of yellow oily fat could be extracted by digesting thin slices of the liver in ether; but that the foreign matter to which the liver owed its large size was not fatty but albuminous. This was confirmed in 1859 by Friedrich and Kekulé (Virchow's Archiv. B. XIV. p. 50 et seq.) who gave the percentage composition of the waxy material as follows:
follows:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>55.58</td>
</tr>
<tr>
<td>H</td>
<td>7.00</td>
</tr>
<tr>
<td>N</td>
<td>15.04</td>
</tr>
</tbody>
</table>

Carl Schmidt (Ann. d. chem. w. Pharm. Bd. CX. s. 250) and Kühne and Rudneff (Virchow Arch. Bd. XXXIII s. 66, 1865) further confirmed the albumenoid nature of this material, having succeeded in isolating it by the ingenious process of artificial digestion, so that now, its chemical nature has passed from the region of theory into the realm of demonstrated fact, and the former views as to its fatty and amyloid nature have of necessity been abandoned. The theory propounded by Dr. Dickinson, viz—that the waxy substance is nothing else than fibrin deprived of a proportion of its alkalies or modified by the gain of acid, seems to my mind to have been sufficiently disproved by the statements of Dr. Pye Smith and Dr. Ralfe (Trans. Path. Soc. Vol. XXX) previously alluded to.
Distribution of the Degeneration.

Hennings (Inaug. Diss. Kiel 1880) makes out that the spleen is most frequently diseased, after which follow in order the kidneys, liver, intestines, stomach, supra-renal capsules, pancreas, lymphatic glands, thyroid gland, aorta, lungs, ovaries, uterus. In Turner's statistics (loc. cit.) out of 58 cases the spleen was affected 48 times, the liver 30 times, the kidneys 15 times, and the intestines 10 times. The spleen alone was affected in 23 cases. The results of the Edinburgh statistics differ somewhat from these, in that the kidneys were found most frequently affected, after which followed the spleen and liver.

Duration:—
The commencement of the disease being of a very insidious nature it is extremely difficult to arrive at a satisfactory solution of the question of its duration. All agree that its usual course is a very chronic one, lasting as it often does for several months or even
even years, and, when once thoroughly established, tending as a rule, along with the original disease, to gradually weaken and ultimately cut off the patient. Commonly, the predisposing cause is believed to remain in operation for a considerable time, possibly even years, before the degeneration in question makes its appearance. But, whilst this very commonly is the case, it would seem, from the evidence of a few recorded cases, that a shorter period may suffice for its production.

Cohnheim (Viechow’s Archiv. LIV. p 271) records the case of a soldier, wounded on the 16th August, 1870, by a shot in the thigh, who died on the 28th of January 1871. At the autopsy a sinus cavity was found in the affected limb which communicated with the hip and knee joints: and it was found that the spleen was the seat of amyloid change.

An amyloid spleen was also found at the autopsy of a soldier who had received a complicated fracture of the right leg from being run over on the 18th of August 1870, and died on the 21st.
21st December of the same year. And in one of the cases recorded in the Edinburgh statistics, the patient sustained a fracture of the two first lumbar vertebrae, the result of a fall on August 18th, 1870. On August 21st complete paraplegia set in, and there speedily followed an extensive bed sore on the back, reaching from the shoulders to the nates. Patient died on the 19th Nov. of the same year, three months after the injury; and at the post mortem the kidneys and intestines were found to be waxy.

In these cases the suspicion naturally arises that there might have been, in addition a syphilitic taint. But in those about to be quoted from Dr Fagge’s list, this suspicion may be set aside, seeing that special care was taken to search for evidences of syphilis, and none were found. In certain of Dr Fagge’s cases, the origin of the predisposing cause consisted in suppuration springing from some local disease, “having a definite starting point, so as to allow of one’s forming an opinion as to the length of
of time required for the development of the lardaceous change in the viscera. One case had pelvic cellulitis lasting eight months; a second had been the subject of a carbuncle for the same period of time. A third suffered from an ulcerating sarcoma of the abdominal wall, which had discharged for four months only. In a fourth, a bedsore had existed for seven months, the result of a fracture of the spine received a fortnight previous to its occurrence.

“Lastly, a fifth case was one in which amputation of the leg had been performed three and a half months before death on account of a compound fracture with abscess. The patient died of diphtheria and it is particularly noted that the lardaceous change was just commencing in both the liver and the spleen.”

(Trans. Path. Soc. Vol. xxvii. p. 335.)

We may, therefore, conclude that in certain cases of suppuration connected with bone disease, waxy degeneration may apparently become developed in the course of three and a half or four months.

Chemical
Chemical Characters of the Waxy Substance

Charles in his "Phys. and Path. Chemistry" p. 122 et seq., describes the chemical characters of the waxy material as follows:— "It occurs in the form of an amorphous, friable, white substance, whose percentage composition is:

<table>
<thead>
<tr>
<th>Element</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>53.6</td>
</tr>
<tr>
<td>H</td>
<td>7.0</td>
</tr>
<tr>
<td>N</td>
<td>15.5</td>
</tr>
<tr>
<td>O</td>
<td>22.5</td>
</tr>
<tr>
<td>S</td>
<td>1.5</td>
</tr>
</tbody>
</table>

"It is insoluble in water, alcohol, ether, dilute acids, and the alkaline carbonates. Saline solutions do not cause it to swell up; neither is it digested by pepsin at the ordinary temperature of the body. It is soluble in strong hydrochloric acid, the solution, when dilute with water, precipitating sytonin, and when boiled with dilute sulphuric acid (1:6) it dissolves with a violet colour; and with strong sulphuric acid furnishing leucin and tyrosin. The alkalies dissolve
"dissolve it, transforming it into a" "substance analogous to albuminose." "Organs in which this change occurs" "are said to be extremely slow to" "decompose." Charles gives the following as

Chemical Tests.

(1.) Iodine gives a reddish or mahogany brown colour to the waxy substance. With iodised chloride of zinc a more marked red coloration is produced. If a little iodine solution is first added to it, and then a little dilute sulphuric acid, a violet or bluish colour sometimes results.

(2.) Methyl aniline violet, in a watery solution, stains this substance a rosy red, or reddish violet colour.

(3.) eosin stains it a bright red.

(4.) A solution of the substance in strong sulphuric acid gives a purple violet colour with sugar or acetic acid. Purified lardacein also dissolves readily in dilute ammonia, and when excess of ammonia is driven off, the neutral solution gives precipitates with dilute acids.
(5) It also gives the xanthoproteic or yellow coloration got by the action of strong boiling nitric acid, which is changed to an orange or amber red colour by the addition of ammonia when the liquid is cold.

(6) Milloni's re-agent (1 part of mercury treated with 2 parts of nitric acid, sp. gr. 1.4, in the cold, and then over a water-bath till completely dissolved. This is to be diluted with 2 parts of water, and the clear liquid decanted after three or four hours) causes a rose or red coloration on the addition of heat, and this is changed to an orange by caustic potash. Unless a very dilute solution is used a red precipitate is apt to appear.

Process for Separating the Waxy Substance from an Organ in which it appears.

This ingenious process is based on the circumstance that the waxy material (lardacein) is insoluble in gastric juice, or in pepsin and dilute hydrochloric acid at the ordinary temperature.
(5) It also gives the xanthoproteic or yellow coloration got by the action of strong boiling nitric acid, which is changed to an orange or amber red colour by the addition of ammonia when the liquid is cold.

(6) Millon's re-agent (1 part of mercury treated with 2 parts of nitric acid, sp. gr. 1.4, in the cold, and then over a water-bath till completely dissolved. This is to be diluted with 2 parts of water, and the clear liquid decanted after three or four hours) causes a rose or red coloration on the addition of heat, and this is changed to an orange by caustic potash. Unless a very dilute solution is used a red precipitate is apt to appear.

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ture of the body. Advantage is taken of the power of the gastric juice to digest the normal tissues and constituents of the organs affected, which may thus be separated from the lardacein, leaving it comparatively pure behind.

Charles gives the method thus:

"Cut the organ in pieces, remove the vessels as far as possible, wash in cold water, boil, and treat the residue with alcohol and ether. Next boil repeatedly with alcohol acidulated with hydrochloric acid, and then digest with excess of gastric juice at 40°C., so long as the filtrate gives the xanthoproteic or a peptone reaction. Boil the insoluble residue once more in spirit containing hydrochloric acid and then wash thoroughly with water. Waxy substance (lardacein) remains behind."

General Characters common to Organs affected by this Change.

When an organ becomes the seat of well-marked waxy degeneration, it usually undergoes the following changes:
1st. Increase in size. This increase may be comparatively slight, or the enlargement may be most marked, the organ being twice its normal size, or even larger. Occasionally, the organ may be diminished in size.

2nd. Increase in weight. The absolute weight is increased, and also the specific gravity.

3rd. Increase in consistence. The organ feels harder and firmer to the touch than natural.

4th. In colour it is generally paler than normal.

5th. Its surface is generally smooth and the capsule tense.

6th. On section it exhibits a peculiar, glistening, translucent appearance, somewhat resembling beeswax or glue, and also described as bacon-like, from its resemblance to "smoked" ham or bacon. The cut surface is usually considerably paler than natural, and frequently appears somewhat mottled.

7th. A solution of iodine poured over the surface gives the characteristic mahogany red coloration.
Pathologists are almost at one in their opinion with regard to the histological elements involved in this degeneration. All agree that the arterioles and capillaries are the parts primarily and principally affected; but opinions are still at variance as to the changes which the glandular epithelium undergoes in consequence of the waxy degeneration. As this difference of opinion is chiefly limited to the case of the liver, I shall, therefore, proceed to discuss the principal changes found in

The Waxy or Lardaceous Liver.

Naked-eye appearances.—The typical waxy liver is seen to be enlarged uniformly in all its dimensions. This enlargement may be slight or it may be quite well-marked or even excessive. Its weight is also increased;— on an average it weighs about twice the normal amount; but it may, in certain cases, weigh as twelve pounds or more. The capsule remains smooth, tense, and transparent. Instead of being sharply
sharply defined, the anterior border is usually, though not always, rounded and thickened in appearance. The surface of the liver has a peculiar light greyish brown, or yellowish grey, or fawn-coloured appearance, sometimes congested and mottled. In consistence it is firm, elastic, and resistant to the touch, the impression left by the finger disappearing slowly. On section the cut surface is commonly pale and anaemic-looking, with a reddish background, and presents a peculiar glistening glazed or varnished appearance variously described as resembling beeswax, lard, or smoked bacon. On closer inspection, the cut surface may be seen to be not quite homogeneous. It may be possible, even in somewhat advanced cases, to mark out the position of the waxy change in the individual lobules of the liver. In a transverse section of the lobules it may be possible to make out that it occupies the middle zone of each, surrounded by a portion of comparatively healthy liver tissue. The middle zone appears as a shining, translucent, pale grey
grey ring, whilst the centre and circumference may be composed of normal liver tissue. On the addition of a watery solution of iodine, the waxy parts take on the characteristic mahogany red colour, whilst the rest of the organ is stained of a yellowish hue. On making thin sections of a waxy liver, and holding them up to the light, so as to allow the light to pass through, the waxy material is seen to have a transparent, glassy, homogeneous appearance, contrasting strongly with the opaque margins and central portions of the lobules.

It sometimes happens that, instead of a diffuse form of waxy liver such as I have described, the waxy degeneration occurs more or less localized. Rindfleisch and Hilton Tagge record cases of this kind.

Complications:

Not unfrequently other changes are found in combination with the waxy. Thus, we very commonly have a fatty change along with the waxy.
Cirrhosis, syphilitic disease, metastatic abscesses, tumours, tubercle, as well as other complications, may be associated with the waxy degeneration of the liver. And the naked-eye description would be modified in accordance with the particular complication present.

Microscopical Appearances:—
Examined with a low power, about 50 diameters—sections of unstained waxy liver present the following appearance:—The middle zone of the lobules is seen to be in great part composed of a peculiar transparent, glassy or horny substance of high refractive index. In the slighter forms, this substance may be observed apparently occupying the position of the intra-lobular capillaries of the middle zone; but when the degeneration has become advanced, the greater part of the lobule may become affected. This method of examining unstained sections, is, however, a very imperfect one, as it gives but a faint idea of the
the elements of tissue involved. And so, it becomes necessary to have recourse to various staining agents which have the power both to differentiate the waxy material itself, and also to bring into prominence the cellular elements of the organ affected, in order to gain a more thorough knowledge of the relation which the degeneration bears to the surrounding tissues. Various staining agents are now in use for this purpose:—

1st. Watery solutions of iodine have been used ever since Virchow published his remarkable researches on this subject. The iodine solution stains the waxy parts of a brownish colour when viewed by reflected light, the rest of the liver appearing of a yellow hue. By transmitted light similar appearances are seen, but somewhat more indistinctly. The disadvantages of this stain are that the cellular elements of the organ are not well differentiated, so that, in many cases, it is very difficult to determine precisely the structures in-
volved in the degenerative process; that it stains the glycogen normally present in the liver cells; and that it stains the endothelium of vessels containing blood, as well as the coloured blood corpuscles the same colour as it stains the waxy material. It is therefore unsuitable for microscopical purposes.

2nd. Watery solutions of iodine along with the addition of dilute sulphuric acid is a method which commends itself to many German observers in preference to all other methods of staining. Stilling (loc. cit.) recommends a weak watery solution of iodine, consisting of iodine 2.5 parts, iodide of potassium .5 parts, and distilled water 100 parts. The sections are to be moved to and fro in this solution until the dark red colour is distinctly perceived in the waxy part. They are then transferred to a two-per-cent solution of sulphuric acid, and examined from time to time in this liquid, or in glycerine. The blue colouration of the waxy parts which results, does not make its appear-
ance at once, but usually during the following days. This is said to be a very delicate test for waxy degeneration, but it often fails, and does not, in my opinion, present any advantage over some other methods about to be mentioned. The delay caused by its use is often very inconvenient, and whilst it doubtless is good as an additional test, it does not recommend itself to my mind as an exceptionally useful method for ordinary purposes. It also has the disadvantage of not satisfactorily differentiating the tissue elements.

3rd. Methyleneblue: A weak, watery solution gives a rosered coloration to the waxy parts whilst the other parts are stained a bluish colour. For ordinary purposes this stain is undoubtedly the most serviceable of all others for the detection of the waxy change. It brings out the cells and their nuclei with satisfactory distinctness, and possesses most of the advantages of double staining. Cornil, who first introduced this stain for waxy degener-
-ation, after staining the sections in the methyl violet solution, removed the extra stain from the tissue by means of a weak acid, such as formic or acetic acid. In this way, the healthy parts appeared a pale blue, but the waxy retained their distinctive red colour. Weak watery solutions of gentian violet give precisely similar results to those just described.

4th Eosin stains waxy parts a pale pink, if used in weak solution. As this is a very transparent stain, it is advantageous to use along with it some darker contrast stain, such as logwood or methyl blue.

5th Saponin gives a beautiful pink colour to the waxy parts, whilst the non-waxy are stained dark red.

6th Iodine green brings out the affected parts of a pale pinkish appearance, and gives a bluish green colouration to the non-affected parts.

7th Picro carmine usually gives a yellow colour to the waxy parts, but in certain cases of waxy degeneration
eration of the liver. I have seen a distinct pink produced in the peripheral parts of the lobules, where the degeneration appeared to be of a more recent development, whilst towards the central portions the colour was yellow. The pink seemed to merge gradually into the yellow. Likewise in the kidney I have noted, in an early stage of degeneration, some of the capillaries of the Malpighian bodies stained most distinctly pink, whilst in Malpighian bodies in other parts of the section, the affected capillaries were of the usual yellow colour. (See slide 19)

8th Logwood stains waxy tissues commonly a pale blue; but as in the case of picric-carmine I have observed marked differences in the depth of colour produced.

9th Carmine, magenta, and other nuclear stains, as a rule impart their distinctive colours to the waxy substance.

By means of the above staining reagents the arterioles in the portal spaces
spaces, and the capillaries of the middle zone of the lobules are seen to be primarily affected by the waxy change. In the former the degeneration may be observed in favourable cases to begin between the individual muscle fibres of the middle coat; in the latter, so far as my observation has extended, (and I have taken some pains to arrive at a just conclusion on the point) the walls of the capillaries are themselves the primary seat of the change. I am well aware that this opinion is not in accordance with the views of some observers, notably Tisselin, Heschl, Schuette, and Woodhead, who maintain that, so far as the capillaries of the middle zone of the hepatic lobules are concerned, the primary seat of the waxy change is not in the walls of the capillaries themselves but outside them, between them and the hepatic cells. Schuette and Woodhead have published drawings illustrating this condition. I have often, in my investigations with a view to eluci-
date this point, noted what appeared at first sight to confirm this view; but closer observation with higher magnifying powers, served to show, that what at first seemed to me to be a patch of degeneration outside a capillary wall, was merely a waxy change of the wall itself, the seeming capillary wall being found to be atrophied liver cells with their nuclei elongated and fusiform from pressure. I do not, however, mean to affirm that waxy degeneration never begins outside the capillary walls in the hepatic lobules. I only assert that, after careful observation I have failed to note the circumstance. As regards the liver cells, opinions still differ as to the part played by them in this degeneration. It seems strange that, on this point, which can only be settled by the microscope, pathologists still hold such widely different views. I do not intend to enter into any controversy in this connection, nor shall I make any general assertion of opinion. Every observer
observer ought, in these cases, to confine himself to what he has himself noted; and, speaking personally, I can only affirm that in the sections examined by myself, I have never come across a single instance in which a liver cell could really be regarded as undergoing a waxy change. The liver cells, so far as I have seen, become atrophied, and in those near the periphery of the lobules, droplets of fat may very commonly be observed. In certain cases, the portal and hepatic veins are found to be affected; and in them the change commences usually in the middle coat between the muscle fibres. In the larger branches, patches of waxy material may be seen in the middle coat, having a somewhat irregular distribution. Instead of the whole wall being simultaneously changed, only parts show the presence of degeneration.

With reference to the waxy change in other organs, there is now little or no difference of opinion; and as I shall have occasion to refer to this change
change in the spleen and kidneys when discussing the hyaline change in these organs. I shall now proceed to the consideration of

Hyaline Degeneration.

Under this designation has been described a retrograde change occurring in certain tissue elements, in consequence of which they become more or less swollen and assume a peculiar glassy, homogeneous, hyaline appearance, somewhat resembling waxy degeneration, but differing from it in respect that no distinctive waxy reaction is obtained on the application of the recognised tests for that degeneration. On looking into the literature of the subject one meets with certain apparently contradictory statements regarding the change in question which at first sight are calculated to mislead. Thus, one observer describes a hyaline change having its seat in the external adventitia of arteries; another notes its occurrence
occurrence in the middle muscular coat of arteries; whilst a third main-
tains that the intima of arteries, and the walls of capillaries con-
stitute the seat of the disease. Some have affirmed that this is a change which is very common in old persons, and in certain chronic diseases; and others, that it is to be met with in its most typical forms in acute infective diseases, such as pyaemia and septicaemia, and in certain fevers, such as scarlet fever, measles, typhus, and small-pox. These apparent con-
tradictions are the consequence of a fragmentary and imperfect investi-
gation of the change as a whole by the observers in question, and are quite capable of being brought into complete harmony by a more extended study of the subject.

Following the arrangement adopted in the case of the waxy degeneration I shall, first of all briefly refer to the

History of
History of Hyaline Degeneration

The history of hyaline degeneration is a somewhat difficult subject to investigate satisfactorily, not merely on account of the number of papers which have been published bearing directly on the change, but more especially, because of the large number of dissertations which have been produced, having a more or less indirect connection therewith. I shall not attempt, therefore, to give a full or complete account of these, nor shall I enter into any detailed criticism of those papers to which reference is to be made, with the exception of one or two of the more important.

In 1864 Henker published his well-known work on "Alterations des muscles dans la fièvre typhoïde &c" (Leipzig, 1864), in which he described the so-called "hyaline", "vitreous" or "waxy" degeneration of individual muscle fibres occurring in certain muscles in typhus and typhoid fevers and other acute diseases.
By some this form of degeneration is classed along with the true hyaline degeneration of fibrous tissues which I am about to describe. Others however, do not regard it as of this nature; and although presenting some features akin to true hyaline degeneration, the differences between them are such as, in my opinion, suffice to exclude this form from our present description. Apart from this, so far as I have been able to ascertain, the first to describe a change which may be regarded as essentially hyaline were Russmaul and Maier who, in 1866, published a paper in the "Deutches Archiv für klin. Med." Vol. 1 p. 484, describing a hitherto unknown change affecting the external fibrous coat of arteries and consisting in a hyaline swelling of the fibres. This change they named "periarteritis nodosa."

In the same year (1866) Magnan (Thèse de Paris) discussed a change of this nature in his thesis on "General Paralysis." Indeed
-indeed, a great number of the communications on hyaline degeneration have been based on observations of the change as it is found in the vessels of the pia mater in cases of chronic nerve diseases, and more especially in the disease known as "General Paralysis." It will be sufficient merely to name some of the authors who have contributed papers in this connection.

These are:
- Arndt (Virchow's Archiv. Vol. 41, p. 401, 1867);
- Meyer (Medic. Centralblatt, No. 8 (1867) and (Virchow's Archiv. Vol. 58 p. 270, 1873);
- Schüle (Allgem. Zeitschrift für Psychiatrie, p. 449, 1868);
- Obersteiner: (Virchow's Archiv. Vol. 57 p. 10, 1871);
- Lubimoff (Virchow's Archiv. Vol. 57, p. 571, 1873) and (Archiv für Psychiatrie, p. 579, 1874); and
- Adler (Archiv für Psychiatrie, 1874 pp. 77 and 346).

Schüppel, in 1871, described a hyaline change occurring in tubercle
of lymphatic glands (Untersuchungen über Lymphdrüsentuberculose, &c, Tübingen 1871.)

In 1872, the well known paper by Sir William Gull and Dr. Sutton on "Arterio-capillary Fibrosis" was published in the Med. Chirurg. Trans.: Vol. 55 p. 275 et seq. and some of the changes they described correspond very closely with certain forms of the hyaline degeneration of vessels. After describing a "hyaline-fibroid" change of vessels throughout the body, but more particularly those of the pia mater, in cases of "chronic Bright's disease" they give the following general summary of their microscopical observations (p. 283):

1. "The arterioles throughout the body in that condition usually called chronic Bright's disease with contracted kidney, are more or less altered."

2. "This alteration is due to a "hyaline-fibroid" formation in the walls of the minute arteries, and a "hyaline-granular" change in the corresponding capillaries."

3. "This change occurs chiefly out-
side the muscular layer, but also "in the tunica intima of some arteries."

4. The degree in which the affected vessels are altered, and the extent to which the morbid change is diffused over the vascular system of the different organs, varies much in different cases.

5. The muscular layer of the affected vessels is often atrophied in a variable degree.

Again on page 296, we find the following: The changes although allied with senile alterations, are probably due to distinct causes not yet ascertained. It is beyond the purpose of this paper to enter into any statement of opinion with reference to the somewhat sharp discussion which followed the publication of the views regarding "Chronic Bright's Disease," promulgated here by Sir William Gull and Dr. Sutton. Sufficient is it for me to note the description of the occurrence of the hyaline change of the vessels in these chronic affections and the fact that
that these observers expressed no opinion as to the cause of the affection which they described.

Nielsen gave a detailed account of this degeneration as it occurs in the vessels of the pia-mater (Archiv der Heilkunde, 1870 p. 119). He noticed in various cerebral diseases, as well as in many acute affections (typhus, measles, scarlatina, variola, syphilis, phthisis, pneumonitis, dysentery and rheumatism) the walls of the capillaries of the pia mater to be thickened and highly refractive. Generally, he found only small portions of the capillary wall thus affected, and not the whole length thereof. The affected parts were commonly found at the points of division of the capillaries into two or more branchlets.

Klein in the "Report on the minute anatomy of Scarlatina" - Local Government Board New Series. No. 8, 1876 p. 241; and in the Trans. Path. Soc. 1877 p. 430 gives a description of the hyaline degeneration of the intima of arterioles, and
and of the walls of capillaries in the spleen, liver, kidneys and lymphatic glands in scarlatina of man. He regarded the hyaline substance as of the nature of elastic tissue.

In 1879 the Committee of the Pathological Society of London published the report of their investigations into the nature of Pyaemia Septicaemia, and purulent Infection (Trans. Path. Society Vol. XXX). In addition to many other most valuable contributions to the pathology of these septic diseases, a careful and accurate account was given of hyaline degeneration of the bloodvessels throughout the body, generally, and more particularly of the bloodvessels of the spleen, liver and kidneys.

So far as I have been able to learn, Recklinghausen seems to have been the first to have applied the distinctive term—"hyaline"—to this degeneration. This opinion is founded on statements made by pupils of his, who have studied in his laboratory, and contributed papers on this subject, notably Wieger, Peters.
and Stilling. Recklinghausen himself has not directly published very much on this degeneration, yet valuable work in connection therewith has been done in his laboratory under his superintendence. Wieger, Peters, Meyer and Stilling have each made important additions to our knowledge of the subject from his laboratory. In his "Handbuch der Allgemeinen Pathologie," Recklinghausen alludes to the hyaline degeneration and notes the close relationship which may sometimes be observed to subsist between the hyaline and the waxy degenerations. He regarded the former, not as a distinct degeneration, but as a stage in the development of the latter (p. 417).

Again in 1879 at the fifty-second meeting of German naturalists and doctors held at Baden Baden (Protocoll der 52 Versammlung deutsch. Naturforscher und Aertze, Sect. XIV, p. 259) he gave a brief account of this degeneration along with the colloid.

Wieger, at the suggestion of Recklinghausen
Linghaisen undertook an extensive investigation of this degeneration as it is found in lymphatic glands, and his results were published in Virchow's Archiv. Vol. 78, p. 25 et seq. He examined various lymphatic glands (axillary, inguinal, lumbar) taken from cases suffering from, or that died of various forms of disease. Axillary glands removed along with carcinoma of the breast were found to be the seat of hyaline change. Glands from cases of chronic pleurisy, phthisis, cystadenoma, and other subacute or chronic diseases were likewise affected by this form of degeneration. Thirteen cases were thus examined only one of which was under fifty years of age, whilst six were between seventy and ninety-three years. The lymph cells and small blood vessels were the parts which showed the hyaline change. Weiger concludes his paper with the admission that, either as to the essential nature of the change, or as to the ultimate cause or causes of its production, nothing very definite was known.
Professor Weigert, of Leipzig, classes this change under pathological coagulations and discusses it along with the so-called "coagulation necroses" in a paper published in Virchow's Archiv Vol. 79, p. 87 et seq.

In 1880 P. Meyer contributed an elaborate article on the "Formation and Role of the Hyaline Material in Aneurisms and in Vessels" to the Archives de Physiologie, Tom. VIII p. 598 et seq.

Peters (Virchow's Archiv. 1882, Vol. 87, p. 477) studied hyaline degeneration in blood vessels and in the false membrane in various cases of diphtheria in man. In the same volume (p. 114) Professor Arnold treats of the anatomy of miliary tubercles of lymphatic glands and spleen and gives a description of a hyaline change occurring in these miliary tubercles. Professor Rachmann, of Dorpat, also in the same volume (p. 325) contributes a paper on a case in which the hyaline and waxy degenerations were both found in disease of the human conjunctiva.
In 1882, Vallat (Virch. Archiv. Vol. 89, p. 193) described a "fibrinous or hyaline" degeneration in tubercle and in syphilitic gummata.

Quite recently Stilling of Strasbourg (Virchow's Archiv. Vol. 103, p. 21, et seq.) has published an important paper on "The Connection between Hyaline and Amyloid Degeneration of the Spleen." For the detection of the amyloid change he used iodine alone, and iodine along with sulphuric acid. He also used iodine-green in the form of a weak watery solution (5 to 150 ag. dest.). This he found very serviceable. The sections were allowed to remain in the iodine-green solution for twenty-four hours, and then washed in distilled water and mounted in glycerine, when the amyloid material appeared a reddish violet, whereas the hyaline parts of the arteries came out blue, and the hyaline clumps within the follicles remained uncoloured. Stilling regarded iodine-green as a much better staining agent than either methyl-violet, methyl-green or safranine. He entirely discarded...
discarded the use of methyl-violet which he characterizes as "extremely unsatisfactory" in its action. His reason for so sweeping a condemnation of this stain for the detection of waxy degeneration appears to have been founded mainly on certain statements regarding its action which Hyber (Virch. Arch. Vol. 81. p. 3) had previously published, and does not seem to have been the result of his own unbiased investigation of the matter. Because, immediately after his condemnation of the stain he proceeds to quote in support of his statement, remarks made by Hyber, to the effect that it stained the ordinary colloid masses in the thyroid and casts in the tubules of the kidneys which were not amyloid, of a distinct reddish hue, and that it only gave a slight waxy reaction in a case in which the subsequent application of the iodine-sulphuric-acid test revealed the presence of a well marked amyloid change. He gives no reasons, founded on his own experience of the use of the stain, in support
support of his wholesale condemnation thereof; and, therefore, we may conclude that he accepted, without sufficient examination the statements of Hyber quoted above. Used in the manner first recommended by Cornil, in my opinion, the methyl-anilin-violet stain is one of the most useful which we at present possess for the detection of the waxy degeneration. As additional staining agents Stilling made use of Alum carmine and an orange stain. His researches were exclusively confined to the changes occurring in the spleen in the cases which came under his observation. He gives a short clinical account of the cases in which he examined the spleen. These were nine in number. One was that of a young woman who died of Phthisis Pulmonalis and chronic dysentery, and whose spleen was found, post mortem, considerably enlarged, pale, and somewhat flabby, but yet of considerable consistence. The follicles were very indistinct. On the application of iodine solution, red spots and streaks were here and there observed.
observed, but not very marked. Microscopic examination revealed a more marked degree of amyloid degeneration than was apparent to the naked eye. The medium sized arteries, and the capillaries of the Malpighian bodies were seen to be affected by the amyloid change. In the former the middle coat was, as usual, the part degenerated, and it was observed that the capillaries situated towards the more peripheral portions of the Malpighian Bodies were most commonly affected. The larger veins, the trabecula and fibrous reticulum were unchanged. In addition to this, in many parts of the spleen, shining masses were seen imbedded in the walls of the medium sized arteries of the splenic pulp which did not exhibit the amyloid reactions. These took on only the ordinary yellow tint of the normal tissues after the iodine and sulphuric acid staining. Often in these masses the innermost parts of the degeneration gave the amyloid reaction, whilst the outermost gave the hyaline. Within the follicles the arteries were in some cases hyaline
hyaline, in others amyloid; and hyaline and amyloid arteries frequently were found near to each other in the sections.

This case is extremely interesting, as it serves to demonstrate the very close relation subsisting between these two degenerations, but it does not, in my opinion, suffice to prove, as some have maintained it does, that the one degeneration is merely a stage in the progress of the other, or that the one really passes into the other.

The remaining cases examined by Stilling showed the hyaline change only. The first was a case of scrofulous disease of the hip-joint for which excision of the head of the femur and removal of diseased portions of the acetabulum was performed. Death resulted in a few days from acute peritonitis. Another suffered from an inflammatory affection of the knee joint, for which resection of the joint was performed, and subsequently amputation of the leg was had recourse to. This latter operation was followed by the death of the patient.
patient the same evening from secondary haemorrhage. A third was a case of pleurisy followed by empyema, the disease lasting two months. A fourth had diabetes. Death was sudden, and a small gangrenous patch in the right lung with commencing pleurisy of the same side were found, post mortem. The next was a case of phthisis pulmonalis. A sixth had disease of left hip joint along with disease of the lower dorsal vertebrae. The seventh suffered from osteomyelitis. And the last had pyopneumothorax.

Stillin states that, in the cases examined by him, the hyaline degeneration affected the middle coat of the smaller arteries; and the external adventitious coat of the same was likewise not unfrequently found thickened and hyaline. But he asserts that the elastic intima as well as the endothelial lining of the vessels were in every case observed to be unaffected. A hyaline change of the cells of the Malpighian bodies was
was also described (Fig. 1). No opinion is given as to the probable nature of the hyaline degeneration, nor does he enter into any discussion as to the etiology of the diseased condition.

Lastly, as regards the history of this degeneration, Professor Greenfield, in his class lectures, 1886-87, entered into a somewhat detailed description of the hyaline change, and as a result of his researches, gave it as his opinion that, in all probability, it is in some way dependent upon the presence and action of micro-organisms. To Professor Greenfield, therefore, belongs the honour of having first pointed out one of the most active agencies at work in the production of this form of degeneration.

Having, on the advice of Professor Greenfield, decided to devote my attention to this subject, with a view more particularly to the elucidation of the causation of this change, the material for the investigation was obtained from the Pathological Laboratory during the time I had the honour...
honour of working under Professor Greenfield. At the outset I limited myself chiefly to the observations of the hyaline degeneration as it affects the vessels of the spleen and kidneys, but later on, other instances of its occurrence were studied. It was, first of all, necessary to obtain specimens of organs which were likely to exhibit the degeneration in an early stage and in an acute form, so as to afford a satisfactory basis for its examination. Because, it was thought that it was just as reasonable to expect to arrive at a correct conception of hyaline degeneration from a study of the more chronic forms which it assumes as to hope that a satisfactory knowledge of the inflammatory process might best be acquired by the investigation of some form of chronic inflammation. The process ought, indeed, as far as possible, to be studied as a whole; but an accurate acquaintance with the phenomena of the acute stage is indispensable in order to arrive at
at a sound conclusion as to the essential features of the subacute or chronic stages. This appears self-evident; yet it seems necessary to draw special attention to the fact, as many of the apparently contradictory statements which have been published regarding the hyaline change may be traced to the non-recognition of the necessity for this method of investigating it. Accordingly, organs from various acute diseases, which had run a more or less rapid course, were at first selected for investigation; and the acute diseases in connection with which the change was observed were the following:

Pyemia, Septicaemia, infective periostitis or acute necrosis, infective endocarditis, or ulcerative endocarditis, acute yellow atrophy, acute military tuberculosis, tubercular meningitis, simple acute meningitis, diphtheria, croupous pneumonia, acute inflammatory Bright's disease, scarlatina, typhoid or enteric fever, and phosphorous poisoning.

In further treating of this sub-
ject. I shall now proceed to describe

Hyaline Degeneration
of the Spleen.

Hyaline degeneration is frequently met with in the spleen. It affects both the vessels and certain of the cellular elements of the organ. Unlike the waxy change, it does not present any marked features distinguishable by the naked eye. Nevertheless its presence may with some degree of certainty be predicted, especially in the acute stages, after a careful naked eye inspection of the organ.

Naked-eye-appearances of the Organ:— These vary considerably in different cases, and, of course, in each case, present the essential post-mortem features characteristic of the disease which is associated with the hyaline change. Generally, however, when the hyaline degeneration is present in an acute stage, the organ is found to be enlarged, sometimes
sometimes considerably so, and the capsule is somewhat stretched. The surface of the spleen is dark red or purpure, and mottled, and its consistency is usually softer than natural. On section, the cut surface is at first dark red in colour, afterwards becoming of a brighter red. In certain cases the cut surface is pale, and somewhat greasy-looking, as in some forms of septicaemia. The splenic substance bulges out on section, and appears more or less diffusent. The Malpighian bodies are frequently indistinguishable, at other times they are faint and indistinct; but in scarlet fever, diphtheria and typhoid fever, they are commonly more or less prominent. In short, the spleen presents the appearances which characterize the organ when it is the seat of acute congestion. In the more chronic forms of hyaline degeneration, little or no deviation from the normal may be observed even on a very careful naked-eye examination of the organ the change being only ascertained by means of a microscopical
Microscopical investigation.

Microscopical Examination of The Spleen.

Owing to the diffusent condition of the spleen in many of the more acute cases, it was a matter of no little difficulty to get a series of fairly good sections for purposes of investigation even after portions of the organ had been thoroughly hardened in absolute alcohol. When cut in the ordinary way by means of the freezing microtome, the sections almost invariably went to pieces before they could be removed from the basin of water. Should this difficulty be overcome and the sections placed on the slide and stained, very often the pressure of the cover-glass, in its descent, alone sufficed to separate them into several fragments, thus showing their extreme friability. As a rule, pieces of the organ were chosen which had been hardened in absolute alcohol, but parts
parts hardened in Miller's fluid were also frequently selected. In the spleen the hyaline degeneration is seen to affect the smaller arteries and capillaries, and certain of the cellular elements of the Malpighian bodies.

Hyaline Degeneration of the small arteries of the Spleen.

Three forms of this degeneration are met with in the small arteries of the spleen. One form, which is very characteristic, affects the intima primarily and chiefly; the second involves the middle muscular coat; and the third has its seat principally in the external fibrous coat. These three forms may occur independently of each other; but more commonly we find two of them associated in the same section of the affected vessel. More rarely do the three occur side by side in the same vessel.

1. "Hyaline degeneration of the intima of small arteries of the spleen:--
This form of hyaline change assumes quite a typical appearance in the spleen, and in its more advanced stages, presents a well marked and easily recognised pathological condition. The process commences by a slight thickening of the intima here and there along the course of the vessels. This thickening is at first confined to the intima, and usually extends only a comparatively short distance in the direction of the longitudinal axis of the vessel. The intima is not universally thickened in this manner: here and there in the long axis of the artery is the change seen, the intervening portions being quite normal. Neither is the intima around the entire circumference of the vessel wall commonly involved. On the contrary, a transverse section of a portion of artery thus degenerated may exhibit the swollen hyaline intima occupying only part of the circumference, very frequently one half, when it gives rise to a semilunar or crescentic swell-
...ing of that half, the opposite half being unchanged. The degeneration may, however, extend all round the vessel, in which case a more or less uniform swelling of the intima is seen on transverse section. Longitudinal section shows the intima of the affected vessels thickened from place to place, as formerly stated, and this may be on one side only, or on both sides, equally or alternately. In acute cases the homogeneous hyaline material advances both in a longitudinal and in a transverse direction. As it proceeds outwards towards the periphery of the vessel-wall it partly pushes before it, and partly invades the middle muscular coat, which gradually becomes thinner and thinner and may ultimately completely disappear, at the parts where the change is advanced, its place being taken by the hyaline material (Figs. 1-2). In these cases the nuclei of the muscular fibres are the last to disappear. Even in comparatively high grades...
of the degeneration, a narrow row of shrivelled muscle-nuclei may be seen to intervene between the hyaline mass and the external fibrous coat (Figs. 12-2). In some cases little extension of the change appears to take place between the individual muscular fibres of the middle coat, the attack on these being chiefly directed from within outwards; and in these cases the external margin of the hyaline mass is seen to be more or less sharply defined and regular in outline. In other cases, delicate processes of the degeneration may be observed to pass between the muscular fibres of the middle coat, giving an irregular, somewhat serrated appearance to the outer margin of the mass. Most commonly, however, the pushing outwards of the middle coat by the advancing degeneration is a much more marked phenomenon than is the process of invasion between the individual muscular fibres. Whilst the muscular coat is thus being
being pushed outwards and atrophied, the endothelial lining of the artery is likewise frequently pushed inwards, but not to the same extent, probably partly on account of the counter-action of the blood-pressure within the vessels, and partly owing to special circumstances in connection with the mode of operation of the agency at work in the production of the process. The endothelium is commonly more or less thinned and atrophied; but, in the typical form of the degeneration I am now describing, it does not, as a rule, otherwise participate in the change. The external coat is often thickened, and the fibres composing it swollen and hyaline. Opposite the affected parts of the vessel, in the higher grades of the degeneration, the outer coat is encroached upon to a considerable extent by the outward growth of the hyaline material (Fig. 1). In addition to extension in a direction transverse to the vessel wall, there is progress of the disease in a longitudinal direction.
direction also, and this is often greater than the other. It follows the course of the intima for short distances in the long axis of the vessel. In cases where one gets a complete longitudinal section of a hyaline mass in an advanced stage, and is able with certainty to distinguish the proximal from the distal extremity (proximal as regards the heart) it may be observed that the former is sometimes more or less obtuse, whilst the latter has a somewhat acute angle, the degeneration apparently passing gradually into the healthy intima beyond. Or, the mass may appear fusiform or crescentic in shape with a central bulging, and more or less acute extremities. Or both ends may be obtuse. In shape, therefore, the higher grades of the hyaline mass vary considerably on longitudinal section. On transverse section, they present, in an exaggerated degree, the appearances described above as characterizing the earlier stages. Looked at with a low power (50 diameters) the
the advanced forms are seen, on longitudinal section, as clear, highly refractive, glassy swellings or bulgings of the affected parts of the vessels. Under a high power, these swellings appear quite homogeneous, or perhaps very faintly granular. Occasionally, round corpuscular bodies are seen in their substance, which look like (and very probably are) transversely divided muscle nuclei, not yet degenerated.

As previously stated, the vessel wall is not affected in this manner in its whole course. Only at intervals along their course, is the change met with, even in advanced cases, in the smaller arteries of the spleen, the intervening portions remaining unaffected. It is noteworthy, that whilst, as a rule, there is abundant evidence of inflammatory changes in the tissues in the immediate neighbourhood of the vessels thus degenerated, little or no trace of abnormal division of the nuclei of the muscular fibres of their middle coat, or of marked cellular infiltration
tion of their outer coat can be noticed. The lumen of the arteries is frequently diminished at the parts affected. Sometimes it appears almost entirely obliterated. At other times it may be normal or even slightly dilated. "With reference to the relative dimensions of the more advanced forms great variations were noted. It will, however, be sufficient for me to give the relative measurements of a longitudinal section of the largest hyaline mass observed which chiefly occupied one half of the vessel wall. In length it was found to measure a little more than three times the transverse diameter of both sides of the unaffected portion of the vessel in whose course it occurred, the measurement being taken as near to the hyaline mass as possible, in order to obtain a fairly accurate result. The width of its broadest part (on one side of the vessel wall) almost equalled that of the transverse diameter of both sides of the unchanged part.
of the longitudinal section of the
artery in close proximity to the mass.
So that, in its advanced stages,
this form of hyaline degeneration
may assume comparatively large
dimensions.

A special feature of this form
is, that it not unfrequently is met
with, at or near points of division
of the vessels. See Figs. I & II.

Slight variations from the above
description were met with in a case
of phosphorus poisoning and in a
case of acute yellow atrophy of
the liver. A case of phosphorus
poisoning came under Professor
Greenfield's care last winter, in
which the patient—a female, aged
48, married—swallowed, for a sui-
cidal purpose, an infusion of the
heads of a couple of boxes of lucifer
matches. Extreme cardiac debility
set in, and death followed within
48 hours after swallowing the in-
fusion. Along with other well-
marked changes in the various or-
gans characteristic of this form of
chemical poisoning, there was found
on
on post mortem examination, a distinct hyaline degeneration of the small arteries of the spleen and other organs. In the spleen, the vessels showed the change here and there throughout their course; just as in the form I have described above; but usually at the parts affected the change was not so translucent as ordinary hyaline but somewhat of a yellowish hue extended pretty equally all round the vessel wall and involved the endothelial cells lining the interior, the elastic intima, and the middle coat. It appeared as if these structures had undergone degeneration in the order indicated; because in many places, the endothelium had passed into a state of molecular disintegration whilst the elastic intima and muscular coat showed well-marked recent hyaline change. This came out well on staining with micro-carmine, when the inner portions of the degeneration stained yellow and the outer took on a pink tinge. Logwood gave in some
some cases, a dirty brownish yellow colour to the hyaline parts.

In the case of acute yellow atrophy, the vessels of the spleen showed similar changes; but, in addition, the external coat was thickened and hyaline, whereas in the phosphorus poisoning case, it was only encroached upon by the degeneration, not swollen. Logwood gave the same reaction as in ordinary hyaline degeneration.

Staining Reactions.

It will be convenient to give here the general staining reactions applicable to hyaline degeneration as a whole, because, for all practical purposes, these are the same in most of the forms which it assumes. In those cases in which slight modifications are met with, as regards any of the more common staining agents, the same will be noted along with the description of the change.

1. Picro-carmine:— This stains the
the hyaline material pink if the degenerative process has been more or less acute, and the change a recent one. If the course has been more chronic, or if very acute and about to pass on to molecular disintegration or fatty degeneration (which is comparatively rare in the spleen, so far as I have been able to observe) a yellow colour is produced. Sometimes an intermediate brownish colour may be observed. These reactions may be seen in perfectly fresh sections, and often each may be noted in the same section.

The micro-carmine used was that of Ranvier.

2. Alum-carmine leaves the degenerated parts unstained, or gives them a very faint, yellowish-pink hue.

3. Logwood stains the material a reddish blue, or purple colour in the early stages in some forms, and later it gives a pale blue tint. Usually, the latter is the more commonly seen.

4. Methyl-anilin-violet colours the
the affected parts blue; but in certain cases a distinct pinkish tinge is imparted, reminding one of the waxy change. Not uncommonly a well-marked rosy-red colour is seen on mounting some sections, which slowly fades until, in about a week, a faint pinkish hue is assumed, which may persist. This appearance takes place when the sections are mounted in Farrant's solution. When mounted in acidulated glycerine, according to Cornil's method, the red colour fades much more rapidly, and may entirely disappear leaving only a pale blue behind. Gentian Violet gives similar reactions.

5. Magenta causes a rose-red colouration of the affected parts which varies in intensity according to the strength of the solution and the time during which the sections are allowed to remain in the stain.

6. Carmine gives its colour to this material in a manner somewhat
what similar to that of the waxy but, as a rule, more intensely.
7. Safranine, in the form of a weak, watery solution stains the affected parts a beautiful pink colour, almost identical with that of the waxy.
8. Iodine gives a yellow stain to the hyaline material.
9. Iodine-green, in a weak watery solution, stains the early hyaline masses a greenish-blue. When the degeneration is somewhat advanced it produces a reddish purple colour in the hyaline parts similar to that which it gives to the waxy degeneration.

Chemical Characters:

The hyaline material is insoluble in dilute acids and alkalis as well as in chloroform, ether, and absolute alcohol. Strong nitric acid stains it yellow, but does not cause any shrinking or solution of the mass.
2. The second form of Hyaline Degeneration occurring in the small arteries of the Spleen is that chiefly affecting the middle muscular coat:—In this the middle coat becomes more or less swollen and homogeneous, the outlines of the individual muscle fibres being lost and their nuclei indistinct or entirely absent in parts. In the earlier stages, an apparent increase in the number of muscle nuclei may be observed; but in the later stages a marked decrease is evident, the whole middle coat being converted into a hyaline cylinder with here and there an isolated nucleus. Sometimes there is evidence of the degeneration having extended from the interior of the vessel; at others the change appears to have originated in the outer coat and spread inwards to the middle coat. As in the previous form the nuclei of the muscular fibres are the last to become changed and disappear. The intima is not un-
frequently somewhat swollen, and the endothelial cells lining the interior of the vessel are also commonly enlarged and their nuclei swollen. As a rule, there is no diminution of the lumen of the affected vessels. On the contrary, it frequently is increased, probably from paralysis of the muscular fibres consequent on the hyaline change. The external coat, where it exists, is also liable to be thickened and its fibres swollen and hyaline. Unlike the previous form, this is not so liable to occur in detached parts, here and there, in the course of the affected vessels, and is not commonly confined to a portion only of the circumference of the vessel wall. Sections, both transverse and longitudinal, exhibit the change as involving the entire middle coat more or less equally all round and extending throughout entire longitudinal sections. See Figs. 34, 19.
3. "Hyaline Degeneration of the External coat of small Arteries of the Spleen:--

As has been previously mentioned, the external coat may frequently participate in this change along with the middle and inner coats; not unfrequently, however, it may be found thickened and hyaline when these show comparatively little change. The individual fibres composing it swell up and assume a hyaline appearance. At first a slight proliferation of the connective tissue nuclei appears to take place, but afterwards they become partly atrophied from compression and partly undergo hyaline degeneration. As to the extent of the increase in thickness which occurs in the external coat, it is very difficult to determine with any degree of accuracy. Speaking generally, I should say that, from some of the sections which I have examined, the external coat may swell up to twice or three times its normal size or even more.

The
The above changes in the three coats of the small arteries of the spleen may very commonly be met with, side by side in the same section, in cases of diphtheria.

II. Hyaline Change of the Maltighian Corpuscles of the Spleen.

As the change in the capillaries and cells of the Maltighian corpuscles appears to take place simultaneously, and, as in consequence, these corpuscles come to assume a peculiar appearance requiring description, it will be convenient to describe the appearances as a whole so as to avoid unnecessary repetition. Taking, as a basis for description, Maltighian corpuscles which have been transversely divided and which are more or less circular in form, we shall find that they appear somewhat swollen and more prominent than normal, and, consequently, more conspicuous, both to the naked eye and under the microscope.
microscope. Looked at with a magnifying power of about 50 diameters the central portions of some appear considerably denser than natural and stain deeply with logwood, and alum carmine and other dyes. In others, the centre presents a paler appearance, which takes on stains very feebly, whilst the parts outside show increased opacity and are deeply stained, and towards the periphery of the corpuscles a zone of comparatively healthy follicular tissue may be observed. Here, then, we evidently have a process, commencing in some part, most commonly the centre, of the Malpighian corpuscles, and having a hyaline change in the part primarily affected. Examined more carefully by means of higher magnifying powers, the dense deeply-stained portions are seen to consist at first of numerous small round cells closely crowded together, which come to form a fettled mass, embedded in which are the lymph cells in close aggregation but in-

-distinct
distinct, and looking as if seen through a film of glue. There appears to occur a swelling of the delicate connective tissue fibrils supporting the capillaries in this situation, along with enlargement of the connective tissue cells lying on this reticulum accompanied by swelling and proliferation of their nuclei. In addition, the endothelial cells lining the capillaries, with their nuclei, seem to swell up. These, together with the lymph cells in the meshes of the reticulum, and probably also leucocytes which have emigrated from the vessels, all become fused together, constituting the dense felted mass above described. The part which each plays in the process is difficult to determine, and probably is different in different diseases. In some cases the cells, in others the delicate reticulum appear to play the chief part. As the process extends outwards towards the periphery of the follicles the part first
first affected becomes less dense and assumes a pale, hyaline appearance, forming a marked contrast to the surrounding deeply stained part. The centre now is clear and only a few cells and nuclei are seen, which are sometimes very large and swollen, lying on or within the meshes of what appears to be a greatly thickened hyaline reticulum. Very frequently, some of the cells fall out in the process of cutting and mounting, and empty spaces are thus left in some parts. As previously stated, the process may extend so as to involve a considerable portion of the interior of the follicles. Sometimes the central pale portions of the Malpighian corpuscles take on a distinct pinkish tinge on addition of iodine green and methyl violet, the dense parts remaining of the same colour as the unaffected structures of the organ, but staining more deeply. See Fig. 473.
In addition to the changes described above, the fibrous trabecula and the delicate reticular network of connective tissue throughout the substance of the spleen may show more or less hyaline degeneration. Many of the isolated capillaries scattered through the splenic pulp may likewise exhibit a hyaline change.

**Hyaline Degeneration of the Kidney.**

The kidney is likewise a very common seat of the hyaline change. As in the case of the spleen, the naked eye appearances of the organ may vary considerably, and it will be sufficient to note that the general features are those of "cloudy swelling." The kidney is usually, in acute cases, somewhat enlarged and on section, the cortex is increased in thickness, and the cut surface may be pale or mottled.
Of course, in each case, the post-mortem appearances which characterize the disease associated with this hyaline degeneration will be found. The history of the case will naturally aid in coming to a conclusion; but in acute cases the microscope alone can enable us to determine with accuracy the presence or absence of this degeneration.

The afferent arterioles and the capillaries of the Malpighian bodies are the parts most frequently and most markedly affected. The capsule of Bowman also participates in the change along with the capillaries of the glomerulus.

As regards the small arteries of the kidney, including the afferent arterioles, these do not, as a rule, in acute cases, exhibit the well-marked hyaline changes which are found in the small arteries of the spleen. Their walls are frequently somewhat thickened but usually this does not involve one coat more highly than another.
The characteristic features of the hyaline degeneration, as it occurs in the kidney are to be met with in the Malphighian bodies. In these the change assumes various forms.

1. The afferent arteriole may have its lumen filled with a hyaline looking material which stains deeply with logwood and which on examination with high powers may show quite a homogeneous appearance, or it may be finely granular. This hyaline looking material may extend into and occlude some of the capillaries of the glomerulus as in Fig. 5, which, however, does not show the very minute granular condition of the material as seen under a high power, nor does it bring out the gradual shading off of certain portions into the surrounding capillaries which may be well seen in slide 14, from which the drawing was taken. Portions of the affected capillaries are, in this form, filled with
with a mass which stains deeply with logwood, and which apparently distends their lumen considerably. At parts the wall of the capillary may be thinned in consequence of the distension and the material in its interior may become diffused through the thin wall into the tissues immediately surrounding. In this condition, the remaining capillaries of the tuft are more closely aggregated together than normal and there is an apparent increase in the number of nuclei in the glomerulus. The capillary tuft may not, even in an early stage, completely fill up the interior, a space being frequently found between them and Bowman's capsule. In a case of so-called "surgical kidney" in which these deeply stained plugs in the capillaries of the glomeruli showed under a high power distinct traces of minute granules, a small area of tissue was seen in the immediate neighbourhood of some of the masses
masses which was more or less homogeneous and hyaline, staining a pale blue with Logwood, and, under a low magnifying power, forming a marked contrast between the deeply stained mass and the rest of the glomerulus. Figure 6 shows this fairly well as seen under a power of about 75 diameters.

Tracing this form onwards a further stage is noted in which the deeply stained portion has formed a dark ring within the Malpighian body, extending more or less completely around the margin of the tuft as in slide 5, & Fig. 7 which shows it as magnified about 75 diameters. The breadth of this dark ring may be pretty uniform throughout, or it may be considerably wider at one part. Outside, between it and Bowman's capsule, may be seen, in some sections, traces of degenerated capillaries with only a few remaining of nuclei, whilst within the dark ring the capillaries have become converted into a paler, somewhat
somewhat homogeneous or faintly granular mass, with very indistinct nuclei. Occasionally there is evidence of the presence of more than one dark ring, which, of course, considerably modifies the above description. Ultimately, the Malpighian body may come to contain a deeply stained, homogeneous mass which is usually considerably smaller than the cavity in which it is found, and frequently presents a sort of laminated appearance.

Even in this stage some degree of difference may be observed in the density of the logwood stain in the mass, pointing to its mode of origin in the manner indicated above. See Slide 6 and Fig. 10. Fig. 8 (a) shows a modification of this form, constituting an intermediate condition in which the deeply stained portion is more diffused throughout the capillary tuft, obscuring the nuclei and matting together the contents. The drawing does not bring out exactly the appearances seen in the specimen (slide 7), but it shows the diffused
diffused staining of the Malpighian body. In some cases the homogeneous material within the Malpighian bodies is, in the later stages, stained of a yellowish-brown colour, from the presence of blood pigment. Not unfrequently, in very acute cases, the hyaline mass undergoes molecular disintegration and fatty degeneration.

II. In this form the individual capillaries of the glomeruli undergo a different change at first from that just described, although the termination of both may frequently be very similar. There is no very evident trace of plugging of any of the capillaries; but at first there is a marked increase in the number of nuclei within the Malpighian body, and the capillaries completely fill up the cavity, so as to be in close contact with Bowman's capsule. The walls of some of the capillaries become swollen and hyaline, and their lumen, in consequence, becomes encroached upon and may be completely obliterated. This usually takes
takes place, in the first instance, in some portion of the outer margin of the tuft close to the capsule; and, indeed, the contiguous parts of the capsule may likewise be involved. The thickened walls of adjacent capillaries coalesce, as the degeneration proceeds, and their nuclei become flattened and atrophic, as well as partly undergoing the hyaline change. The degeneration extends so as to involve the entire glomerulus, which comes to have an appearance such as that represented in Fig. 9, and Fig. 8 (b), in which a more or less concentric arrangement of the degenerated capillaries is seen along with a few compressed, atrophied nuclei. This form, in all its stages, stains feebly with logwood. Ultimately, the glomerulus may be changed into quite a homogeneous mass, with no appearance of capillary structure and showing an entire absence of nuclei. The hyaline mass, when formed, tends to undergo similar changes to those which were described as occurring.
in the previous form. Picrocarmine and the other common staining agents stain this form in the usual way in which they stain hyaline degeneration.

III. The degeneration may be mainly confined to the capsule of Bowman, the capillaries taking little part in it. The capsule, in part of its circumference, or in its entire extent, appears thickened and hyaline. The delicate connective tissue fibrils which support the membrana propria externally may also show considerable thickening, in which case the capsule not infrequently is very considerably increased in breadth, it may be five or six times. The membrana propria may alone be swollen, but when the supporting connective tissue fibrils also participate, there occurs, as a primary condition, usually a certain amount of proliferation of the connective tissue nuclei. As the fibrils swell up and become hyaline, many of the nuclei disappear and the remainder are
are seen compressed and atrophied between the thickened connective tissue fibrils. Logwood stains this a pale blue, as in the previous form; the other staining agents give their usual reaction.

Fig. 11 and slide 10 illustrate this condition. Slide 10 shows Malpighian bodies, in various stages and forms of degeneration.

These three varieties may be seen in the same section and not unfrequently modifications and combinations of them are met with.

The number of degenerated Malpighian bodies which may be observed in an ordinary microscopic section varies very considerably, and no definite statement can be made with reference to the point. In some sections, several may be counted, whilst in others taken from the same organ, only one or two may be seen in sections similar in size. Moreover, in many sections it frequently happens that numer-
ous Malpighian bodies fall out during the processes of cutting and mounting, which further prevents any accurate estimate of the number of those showing degeneration. Speaking generally, however, I have found the degenerated Malpighian bodies less numerous in very acute cases of septic disease than in certain cases of subacute or chronic Bright's disease, in which the second and third forms above described were present in a typical form.

As regards situation, the degeneration may affect any part of the cortex in which these Malpighian bodies exist; but it is much more commonly seen in those situated near the outer margin of the cortex.

In some cases of advanced cloudy swelling and fatty degeneration of the epithelium of the convoluted tubules of the kidney, such as may be seen in cases of phosphorus poisoning, in acute yellow atrophy of
of the liver, and in acute pyaemia and septicaemia, sections stained in logwood, and cleared up in oil of cloves, and mounted in Canada Balsam show what appears to be well-marked hyaline degeneration of the renal epithelium of these tubules, whilst sections mounted in Farrant's solution, exhibit the ordinary appearances of advanced cloudy swelling, with fatty degeneration of the cells. Such being the case, it is necessary to be on one's guard as to the results obtained in these cases, when the sections have been cleared up in oil of cloves. The cloves-oil dissolves out the fatty globules from the cells, leaving a hyaline appearance behind, which may very readily be mistaken for the true hyaline degeneration.

As regards the so-called "hyaline" casts which are often met with in the renal tubules little need be said, as they are so very well-known.
Hyaline Degeneration in the Liver.

In the liver this degeneration is not so commonly met with as in the spleen and kidney, judging from my own observations. It may sometimes be seen in the small branches of the hepatic artery in the minute portal spaces. It affects chiefly the muscular coat; but the external fibrous coat may also be swollen, and the individual fibres more or less hyaline-looking. I have not been able to observe the typical swelling of the intima of these vessels, which forms such a marked feature of the degeneration as it occurs in the spleen. In typhoid and other fevers, and in acute septic inflammations, plugs are, not unfrequently, found in the branches of the portal vein, within the substance of the liver, which are perfectly homogeneous and hyaline-looking, and sometimes stain a deep purple colour with logwood; at other times giving only
only a pale bluish or greyish tint. In addition, in some cases of advanced waxy degeneration of the capillaries of the liver lobules, those capillaries which were primarily affected stain yellow on the application of micro-carmine, whilst those which have recently undergone degeneration take on a distinct punkish tinge with the same stain, pointing to a gradual transformation from a change corresponding, in some respects, to hyaline, on to the waxy degeneration proper. In a case of tuberele of the liver with advanced waxy change in the capillaries of the hepatic lobules, micro-carmine stained the degenerated capillaries of the outer zone pink, and those in the middle and inner zones yellow, thus marking out the lobules with some degree of distinctness.

Hyaline Degeneration in Lymphatic Glands.

Lymphatic glands, having a some-
what similar structure, histologically, to that of the spleen, hyaline degeneration in them assumes very much the characters which it presents when seen in the spleen. The lymph follicles may undergo similar changes to those which have been described as occurring in the Malpighian follicles of the spleen.

In some cases of advanced waxy degeneration in other organs the fibrous stroma of certain of the lymphatic glands become greatly swollen and hyaline-looking. On using the ordinary staining reagents for waxy degeneration no definite waxy reaction is obtained, but an intermediate stain becomes developed between the waxy and hyaline. Thus, with methyl-violet, a faint pink is seen in the swollen fibres.

Hyaline changes in Tubercle

These changes vary according to the stage of the tubercular process, and the organ in which the tubercle
tubercle follicles are present.
In acute miliary tubercle, the small round cells which at first constitute the chief part of the tubercle follicles may, in good specimens, be observed to lose their outlines and become fused together towards the central portions of the tubercle follicles, giving rise to a more or less homogeneous appearance which stains brownish-pink with picric carmine, and dark blue with logwood. At the periphery of the follicles, at this stage, the small round cells are crowded together, but their outlines may be quite distinct. Stained with picric carmine, and mounted in Farrant's solution, this central mass almost always has a somewhat granular appearance, and is never, so far as I have been able to observe, quite homogeneous. If, however, the sections exhibiting this change be stained in logwood, or alum carmine, cleared up in oil of cloves, and mounted in Balsam, a distinct homogeneous, hyaline appearance may
may very commonly be seen in the central degenerating parts of the tubercle follicles even before very marked caseation has set in. It thus appears that a granular condition results in the case of micro-carmine staining, and that a hyaline condition is manifest after staining with log-wood or alum carmine when the sections are cleared up in oil of cloves. Unstained sections likewise show a more or less granular condition of the central parts of the tubercle follicles at this stage. So that it is necessary to receive the statements regarding hyaline degeneration of the cells of tubercle follicles founded on examination of sections mounted in Balsam with some degree of caution, unless some additional evidence is given, other than that commonly afforded. Because, just as in the case of the change in the epithelial cells of the renal tubules mentioned on a previous page, the oil of cloves may dissolve out
out any fatty or oily particles which may be present, even in an early stage, in the degenerating parts of the follicles, and thus give them the appearance of being homogeneous and hyaline, whereas sections of the same follicles, examined unstained and stained, and mounted in Farrant's solution, have a more or less granular look.

Apart from these changes in the cells, which I consider to be of a doubtful hyaline nature, a true hyaline degeneration may sometimes be observed in tubercle follicles. Thus, there may occur a true hyaline change in those vessels which are in close connection with these follicles in cases where the infective material has been carried to the part by the bloodvessels; as, for example, in the kidney, where I have found, in certain cases of acute miliary tubercle, true hyaline degeneration of Malpigian bodies, situated in the tubercle...
tubercle follicles, in which tubercle bacilli were found in the capillaries of certain of the glomeruli in the parts affected, and in the convoluted tubules in immediate relation to these Malpighian bodies, pointing to the fact of these bacilli having been carried by the bloodvessels to the capillaries of these glomeruli, some of which found a lodgment there, whilst others passed into the proximal portion of the corresponding convoluted tubules.

Again, in cases of tubercle of glands, and of the spleen, true hyaline degeneration of the connective tissue fibrils in the midst of the tubercle follicles, may be seen, if the course of the disease has not been very acute. There occurs, therefore, a true hyaline degeneration in certain cases of acute tubercle, irrespective of the so called hyaline change, which takes place in the cellular elements of the tubercle follicles, and which is said to precede in
in them, the subsequent caseation which is so frequently seen in these cases.

In cases of tubercle, which are more chronic in their course, or which show further advanced changes, interesting conditions may sometimes be met with. Thus, in a case of general tuberculosis involving the lungs, kidneys, liver, spleen, intestines and lymphatic glands, tubercles were found in the spleen, undergoing changes which I shall presently describe. In the lungs, there were present several chronic fibroid tubercles, small—almost microscopic—in size, scattered here and there throughout the substance of the organs; but, in addition to these, there was well-marked recent acute tubercular bronchopneumonia, with numerous tubercle bacilli in the pulmonary arterioles, in the broncho-pneumonic patches, as well as in the bronchi-oles and air-cells of the affected areas. The kidneys contained several chronic tubercle nodules varying considerably
considerably in size, some being fibroid, others partly caseous. But in certain Malpighian bodies, usually only in one in a medium-sized section, masses of tubercle bacilli could be seen after the usual double staining process, forming plugs in some of the capillary loops, as well as extending around others. A very small area of kidney structure immediately surrounding these Malpighian bodies showed some slight degree of irritative reaction whilst the nuclei of the Malpighian bodies themselves in some cases appeared more numerous, in others almost normal. Such an early condition of tubercle follicle formation in the kidney, along with the presence of chronic tubercles throughout the organ is evidently not very commonly met with. Koch (Micro-parasites in Disease, Syd. Soc. p. 103) records a case of tubercle of the kidney in which he found many of the glomeruli and adjoining convoluted
'vuluted tubules filled with masses of bacilli; from which it may be concluded that bacilli can pass from the blood into the tubules and thence into the urine.' A precisely similar condition to the above was observed by myself in a case of tuberculosis of the kidney; but in these cases the change was much further advanced than in those Malpighian bodies in the case under consideration, in which, as previously stated, bacilli were confined to certain capillaries in the glomeruli. The surrounding irritative change being very slight indeed. The liver showed the presence of numerous tubercle follicles of various sizes, and in various stages of development. These were chiefly confined to the portal spaces. Typical tubercular ulcers were found in the intestines. In these ulcers, tubercle bacilli were found, not, however, in such numbers on the floor of the ulcerated patch as in the subjacent tubercle follicles, and in the corresponding lymphatics. Plugs of rounded
rounded, or slightly elongated micrococci-like bodies filled some of the veins or lymphatics (it was difficult to decide which of the two) proceeding from the ulcerated part. These stained brown after double staining in the usual way with gentian violet and resorcin or Bismarck brown, but in many cases they retained the blue colour of the gentian violet, even after passing through the nitric acid solution, when eosin was used as a contrast stain. Some of the mesenteric glands were undergoing the tubercular change, and in them various stages of the tubercular process were observed. The glands were somewhat enlarged, and tubercle bacilli, varying considerably in length, from about half the usual size, or less, up to the fully formed bacilli, were found in them in large numbers. The spleen contained very many tubercle nodules, both on its surface and throughout its substance. These were of different sizes, from points almost microscopical
copical, to nodules having a diameter of a large pin head. The larger and medium-sized nodules were, for the most part caseous in the centre. In the centre of some of the smaller nodules, thick, swollen, hyaline-looking bands were seen, which stained a deep red with picric-carmine, and formed a sort of irregular, reticular structure enclosing compressed spaces in which were contained cells in various stages of atrophy and degeneration. Each nodule was surrounded by a zone of fibrous tissue which took on a very faint pinkish stain with picric-carmine. This zone was of considerable thickness and the individual fibres composing it were, in some instances, enormously swollen and homogeneous, presenting an extreme degree of hyaline degeneration. Vessels were frequently found in it, with greatly thickened walls, having undergone extensive hyaline change. Their endothelial lining was swollen, but, apparently, their
their lumen was not much diminished in size. In the larger nodules the centre was, for the most part, caseous and stained yellow with micro-carmine. Proceeding from the periphery of the caseous part, thick hyaline bands, similar to those in the smaller nodules, and staining similarly with micro-carmine, passed outwards to the fibrous zone surrounding the nodules. As in the smaller tubercles, this zone consisted of greatly swollen, homogeneous, hyaline fibres, staining feebly with micro-carmine and other stains, and occasionally containing bloodvessels with very thick hyaline walls, just as in the other nodules. Between the thickened, hyaline fibres, nuclei, compressed and atrophied, were seen. On staining sections of the spleen for tubercle bacilli, only an isolated one in some of the nodules could be found; but in many of the sections masses of round, micro-cocci-like bodies, each having a diameter closely approximate to that of tubercule
icle bacilli, and retaining their blue colour after having been stained with gentian violet and anilin oil water for about twelve hours, then decolourized in nitric acid solution and stained with eosin as a contrast stain, were observed in the cells between the hyalin reticulum, in the interior of some of the nodules, and formed plugs in the vessels in the external fibrous zone of others. Plugs of the same bodies were, in a few cases, found in the lymph sheath of some of the arteries in close contact with caseous nodules, and also in some of the lymphatics or veins (it was difficult to decide which) throughout the splenic pulp. On very careful examination, some of these micro-organisms appeared slightly elongated, as if they were developing into bacilli. Indeed, a few had attained the length of nearly half a tubercle bacillus. It seems natural, therefore to regard them as in all probability the spores of tubercle bacilli. That these, like many other bacilli, do
form spores, is a matter of common observation. The question then arises: What becomes of these spores after they have been formed? Koch has declared that no one has succeeded in demonstrating them in the tissues. In his paper on tubercle (Syd. Soc. Micro-parasites in Disease, p. 105) he records an interesting case, in which plugs of micro-cocci were found in the capillaries in various organs, and in close proximity to tubercle bacilli, and Watson Cheyne published a similar case, in which there was found a similar combination of micro-cocci, and bacilli in miliary tubercle of the lungs. These micro-cocci, in the double staining process with gentian violet and Bismarck brown or resorcin, took on the brown stain of the latter whilst the tubercle bacilli, of course, remained blue. From this circumstance Koch regarded the combination of these organisms with the tubercle bacilli, as due to a "mixed infection," which he supposed would
would be found to be not a very rare thing. Indeed, he succeeded in some experiments on animals, in producing an artificial combination of anthrax and septicaemia, and of tuberculosis and splenic fever, thus proving the possibility of the existence of a true "mixed infection" in animals. That a "mixed infection" may likewise be present, in certain cases, in the human subject, both clinical experience and pathological observation seem equally to establish. But may not Koch, in regarding the presence of these micro-organisms in combination with tubercle bacilli as undoubted evidence of a "mixed infection," have allowed himself to attach too much importance to the fact of these organisms taking up the brown colour in the double staining process, in place of retaining the blue colour of the gentian violet (behaving, thus, like ordinary micrococci)? Evidently, he imagined that these micro-organisms ought to
to have exhibited the same staining reactions as the tubercle bacilli themselves, if they were to be regarded as their spores; and because they did not have the same staining reactions, he set them down as evidence of a "mixed infection." That this is so, in many cases, I do not wish to deny; but it appears to me that it need not necessarily be the case on every occasion. Because, as regards the spores of the tubercle bacilli, one might very naturally suppose that, having a more delicate and more permeable sheath than the fully formed bacilli, they might, on that account, the more readily part with the blue stain of the gentian violet in presence of such a powerfully penetrating staining agent as vesuvin. (Are not young offspring always more tender than their parents; and why not, also, those of the tubercle bacilli?) Moreover, the tubercle bacilli themselves, in some cases after the lapse of
of only a few hours, give up their blue colour in presence of vesuvin; so that, it is not so surprising that their spores should do so sooner. It being practically impossible to distinguish between newly escaped spores and micrococci of the same size, except by observing their growth and development, masses of these spores might very easily be taken for micrococci; and as regards tubercle bacilli, which, as is well known, grow and develop very slowly, the spores, having gained entrance into the neighbouring veins or lymphatics, would allow of being carried by these, either into the general circulation and so to various organs or to the nearest lymphatic glands, before much advance in their growth could take place. One would, however, expect to find, on minute examination, some trace of increase of growth in some of the spores; and such was indeed the case as regards a few of these bodies in
in the sections under consideration. One or two at the margin of some of the plugs were observed to have elongated so as to approach almost half the length of an ordinary tubercle bacillus. In some of the mesenteric glands, as previously stated, these spores could almost be traced developing into fully formed tubercle bacilli. At all events, very minute bacilli, showing only slight elongation, were seen in the lymph paths of these glands alongside of other tubercle bacilli which were longer, and others which were fully formed. In this case, from some primary source of infection, a general miliary tuberculosis, of a somewhat chronic course, and involving the lungs, kidneys, liver, spleen, intestines, and lymphatic glands, was set up. The tubercle bacilli, being few in number in each tubercle follicle, or being possessed of low vital power (a condition not unfrequently met with in artificial cultures of most forms of micro-organisms)
the individual follicles developed slowly. After forming spores, the bacilli would degenerate and die. Some of the spores thus formed would probably remain in the tubercle follicles and develop into bacilli, others would be seized upon by leucocytes in their vicinity and be carried into neighbouring veins or lymphatics. If into the former, they might be brought to the right side of the heart and thence to the lungs (in cases such as this, where organs other than the lungs were involved), where traversing the pulmonary capillaries, they would be liable, if present in sufficient numbers, to cause embolus in some of these capillaries and, finding a suitable soil, become developed into fully formed tubercle bacilli, endowed with their irritative and destructive properties. It is not improbable that a few might pass through the pulmonary circulation, returning to the left side of the heart.
heart, and thence be carried to different parts of the body. The presence of plugs of bacilli in the capillaries of some of the glomeruli in the kidneys of this and other cases, would appear to lend some countenance to this view. And additional evidence is, in this case, afforded by the presence of plugs of what I consider to be spores in the arterioles and capillaries of the spleen. If into the latter, they would probably be carried to the nearest lymphatic gland, where they would develop in the usual manner. In addition to this method of spore carriage the tubercle bacilli themselves might have been carried about in some of the ways mentioned by Koch. But I am convinced that, in the case under consideration, the spores of the tubercle bacilli also took part in the dissemination of the tubercular process; because in the spleen, leucocytes in the immediate neighbourhood of some of
the caseous nodules were seen to contain large numbers of these bodies, which were likewise found in some of the neighbouring veins or lymphatics. Within some of the nodules, similar organisms were found, and it is difficult to avoid coming to the conclusion that these organisms gained access to the veins or lymphatics through the agency of leucocytes. From each chronic tubercle nodule in the various organs affected, some of the spores after their escape from the parent bacilli would thus get into the lymphatics, and so into the lymphatic glands; others would be carried into the general circulation and the greatest number of these would probably be arrested in the lungs, causing in them, or by their development, aided by those already existing in the lungs, the well-marked acute broncho-pneumonia which supervened in this case. Some, after per-forming the circuit (pulmonary) or
or being brought to the heart from the diseased portions of the lungs, would be distributed to the organs in which the tubercular process existed, and in which these spores were found.

"Whether the above be a correct interpretation of the phenomena observed in this case (and I am strongly of opinion, from other observations in this connection that it has something in its favour) is a matter of secondary importance so far as the presence of hyaline degeneration in the tubercle nodules is concerned. I shall, therefore, again emphasize the occurrence of a distinct, typical, hyaline degeneration of the connective tissue fibres in connection with these nodules.

As regards hyaline degeneration in other morbid products, such as syphilitic gummata, my observations have been too limited to enable me to give any very precise description. In certain cases of infarct as in...
in infarct of the kidney in ulcerative endocarditis a hyaline change takes place in the fibrous constituents of the infarct previous to its breaking down. In diphtheritic false membrane a hyaline change is described as occurring at a certain stage, but I have not been able to satisfy myself as to the hyaline nature of the change in question. It may perhaps be accounted for in the same way as was the hyaline change in the epithelial cells of the renal tubules in acute yellow atrophy, and in phosphorus poisoning, in which, as previously stated, the particular method of mounting the sections through oil of cloves served to explain the appearance in question. The hyaline appearance which is so often seen in thrombi is, in all probability, due to the particular grouping and arrangement of the so-called "blood-plates."

Eberth and Schimmelpfeng's experiments on thrombosis satisfactorily determine the manner in which these "blood-plates" behave in relation to artificially produced thrombi, and, doubtless, the hyaline appearance caused by their grouping together in certain positions in thrombi artificially produced, also maintains in thrombi formed in the human subject, and owes its origin to the same cause. There may, however, be other causes at work in certain thrombi, especially in those associated with the presence of micro-organisms, producing a hyaline change distinct from that caused by the aggregation of blood-plates.

Hyaline degeneration has further been described as occurring in the exudation products of acute lobular pneumonia; but I doubt the hyaline nature of the change and am rather inclined to regard it as, in great part, due to the method adopted in staining and...
and mounting the sections.
Lastly, in the fibrous stroma of some tumours, as in certain lympho-sarcomas, I have observed a well-marked homogeneous swelling, presenting all the characters of true hyaline degeneration.

Nature and Causation of Hyaline Degeneration

Hyaline degeneration chiefly affects the fibrous structures in the situations in which it is most frequently found. In discussing its probable nature and causation, it will be convenient for me to consider it in its general aspect as it affects the fibrous structures subject to its influence throughout the various parts of the body, reserving special points for subsequent consideration. The change manifests itself by a swelling of the affected fibres which come to assume a clear, glistening homogeneous
geneous appearance. This swelling may be comparatively slight, or it may be very considerable in amount. In the intima of arterioles, the change may occur in a very typical manner, as was previously mentioned under hyaline degeneration of the spleen. Now it is necessary to make a distinction between hyaline degeneration of the fibres composing white fibrous tissue and the yellow elastic fibres which make up the elastic intima of arteries. Because, it is well known that simple acids or alkalis can cause the former to swell up and assume a homogeneous, hyaline appearance; whereas at the ordinary temperature of the atmosphere these agents do not produce such a result in the latter. Hyaline degeneration of fibres composed of white fibrous tissue may, therefore, be caused by comparatively simple chemical agents such as acids or alkalis, and the presence of either in excess in
in the blood or tissues may cause hyaline degeneration of those fibres. If, however, a dilute solution of hydrochloric acid or caustic potash be injected into arteries of an organ, such as the kidney of a newly killed rabbit, and the organ kept in a flask of sterilized, distilled water, which is prevented from evaporating to dryness, in an incubator, at, or about the body temperature for twenty-four hours, an almost typical hyaline change may be found, involving more or less equally all the coats of the arteries and capillaries through which the acid or alkali has passed.

The idea of injecting these chemicals into the vessels of newly killed rabbits having occurred, quite independently to D. R. H. Leith, and myself, we purposed carrying on several experiments together, using various strengths of acids and alkalies along with other chemicals and noting the results. Owing to various causes...
causes, only one set of experiments was performed by us in this connection. Dr. Leith has, however, kindly allowed me to make independent use of the results obtained; and the change found in the vessels were such as noted above, viz.: a homogeneous, hyaline degeneration, almost typical in its appearance — affecting more or less equally the entire vessel wall through which the chemical had passed. We may, therefore, affirm that comparatively simple chemical agents may, when a tissue is kept constantly moist and incubated at the body temperature for some hours, so act on the vascular walls as to produce a change in them closely resembling true hyaline degeneration. But whilst this chemical theory may serve to account for those cases where the coats of vessels show a more or less equal distribution of hyaline change, as, for example, in the degeneration of the middle and outer coats of the vessels, this explanation...
atriation cannot be accepted as suffi-
cient to explain these cases in which
the intima of arterioles becomes af-
fected— not uniformly, nor equally,
but irregularly, in parts, here and
there along the course of the vessels.
If the explanation were to be
found in the presence of some
chemical agent in solution circu-
lating in the blood, we should
naturally expect that the degen-
eration would not be restricted
to certain parts of the intima only,
but would affect it more or less
equally in all directions, as in the
experiment to which reference has
just been made. Such, however,
is not the case, and we must
seek for some other cause. It
might be thought that a localized
exudation of lymph, or an infil-
tration into the affected part would
account for the appearances seen;
but the limited nature of the de-
gen erated intima, its frequent pre-
sence on one side only of the
wall of the arteriole, and not all
round its circumference, appear
to
to set aside this theory as the sole cause of the change. I am inclined to regard it as a true degenerative process originated in the intima by the action of some living agent circulating in the blood stream. The nature of this agent may vary in different cases, but its effects remain the same. A consideration of the diseased conditions coexisting with this degenerative process will serve to throw some light on the mechanism of its production. In *pyæmia* we have, as the chief factor in the diseased process, the presence of multitudes of minute organisms circulating in the blood at some period of the disease. These organisms may be of the nature of micrococci or bacilli or both. *Septicaæmia* is also characterized by the presence of similar organisms. Micrococci are likewise found in diphtheria, and are doubtless active agents in the production of that disease. Ulcerative Endocarditis...
tis and puerperal septicaemia, are each dependent on micro-organisms—chiefly micrococci. Brov- 
pous pneumonia is now, by the investigatons of Friedländer, almost satisfactorily proved to be caused 
by a peculiar micro-organism—named pneumo-coccus. Enteric 
fever, in all probability, owes its 
origin to the so-called typhoid 
bacillus. Tuberculosis has now 
definitely been proved, by the re-
markable researches and experi-
ments of Koch, to be an infective 
disease having its origin in the 
activity of the tubercle bacilli. 
In scarlet fever, and other acute 
fears, micro-organisms have been 
observed in the blood and tissues, 
but their causal relation to these 
fears has not, as yet, been absolutely 
determined. Waldeyer (Virch Arch. 
Vol. 14, p. 533 et seq.) Blebs and 
Eppinger (Prager Vierteljahrschrift 
125, 1875) and Dreschfeld (Lancet 
1884, Vol. 1, p. 607) have described 
micro-organisms in the liver and 
other organs in Acute Yellow Atro-
phy
phy of Liver. Professor Dreschfeld in the case described by him found micro-cocci in large numbers in the liver, "filling the arteries in the portal canals, and in the peripheral part of the lobules between the liver cells, filling up apparent by the capillaries between them." He does not give the approximate measurements of these micro-cocci, but states that, "they were larger than those seen in septic poisoning." In a case of acute yellow atrophy of liver which came under the care of Professor Greenfield, I succeeded in discovering micro-cocci in the arteries of the kidney and in the intertubular capillaries, as well as in the cells lining some of the renal tubules. These micro-cocci were not very numerous in the sections examined. In some longitudinal sections, the larger interlobular arteries showed clusters of them in one or two parts of their course, and in some of the interlobular capillaries a few scattered micro-cocci were found. Those seen
seen in the cells of the renal tubules were smaller than the others, and were more numerous in the cells of some of the looped tubules, and some of the collecting tubules. In fact, they were chiefly confined to these, and usually involved only a comparatively small part and that irregularly. The micrococci varied considerably in size from about .5μ in the epithelial cells of the tubules to 1μ or even as large as 1μ in the arteries and capillaries. In the cells they occurred in the form of numerous minute round points almost filling the individual cells, but usually more abundant towards the periphery. In the vessels they appeared as round or ovoid organisms, singly, or in dumb-bells, or in clusters.

There was no trace of zooglena masses nor of plugging in any of the vessels, the clusters being composed of several organisms, grouped together in an irregular fashion, with intervening spaces between each. In some of the clusters bacilli
bacilli of different lengths but averaging about 4.5 μ and corresponding in width to the round or ovoid bodies which I have described as micrococci, were seen. These were straight or slightly curved, and in some of them distinct evidence of division was observed. Thus, it happened that some were constricted in the centre, and then at the middle of each half another constriction occurred, so that the bacillus was divided into four parts, each of which, before becoming detached, in many cases, showed a central constriction, and when separated appeared as a dumb-bell micrococcus. Others, and these chiefly the longer ones, contained spores in their interior. These bacilli were likewise found quite isolated in some arteries and capillaries. Taking the above facts into consideration it seems reasonable to regard the round or ovoid organisms as the spores of these actively dividing bacilli, and
not independent micrococci. Or, are we to entertain the idea that this is a case of "mixed infection"? Surely not. A further observation as regards the distribution of these Spores remains to be added, and that is, that some of the coloured blood corpuscles were observed to have taken up spores into their interior. May not these facts offer some explanation of the extreme fatality of the disease? It will be observed that no general statement has been made regarding the causal connection between the organisms found in the kidney of this case, and the disease known as Acute Yellow Atrophy of the Liver. Because I am well aware of the dicta of Koch, which must now be followed out in every case before a certain organism can be affirmed to be the cause of any disease. Yet the fact that these organisms were present in the vessels of the kidney in this disease is of some importance as an aid to further investigation.
investigation of the subject.

Granted the presence of micro-organisms in the blood vessels and tissues in the above-mentioned diseased conditions associated with the presence of typical acute hyaline changes in these vessels, the supposition becomes a reasonable one, that these organisms may, in some way, be the active agents at work in the production of these changes.

Further proof is, however, essential before we can arrive at any definite conclusion with regard to this matter. It may be declared that, though these bacteria are circulating in the blood at some period of the disease, yet that no connection need necessarily thereby be proved to exist between their presence and the presence of hyaline degeneration in the blood vessels although the presumption is in favour of that connection. But if these bacteria be found in and around the degenerated parts, having a direct relation thereto,
the presumption is, that they have something to do with the degeneration. As regards the spleen, notwithstanding the fragility of some of the sections, I have been able to trace this close connection between bacteria and the hyaline change, in the intima of the arterioles in cases of pyaemia, and doubtless the same holds good in other cases. The micro-organisms circulating in the blood, obviously tend to impinge on the angles at the points of division of the small arteries; some pass through the endothelium and reach the intima in which they set up the changes already described. The probable manner of their action will be alluded to hereafter. Not only does the passage of these organisms through the endothelium take place at the points of division of arterioles, but direct observation serves to show that this occurs at other places also. Thus accounting for the irregular distribution of the degeneration of the
the intima of the arterioles of the spleen. The changes in the muscular and external coats are probably due to a different cause, viz., to an infection through the lymph sheath of the vessels from the absorption of micrococci, which holds good in some cases; or probably from some chemical agent circulating in the blood or lymph and affecting the coats of the vessels, through which it passes more or less uniformly. The endothelium, being possessed of greater vitality, would withstand this action for a longer time than the other structures of the vessel wall. The alterations in the Malpighian follicles of the spleen in all probability owe their origin to the irritative action of the particular organism found in the vessels in each case, and, in some respects, it may be considered as partly inflammatory in its nature.

But the kidney was the organ in which this close connection was
was most frequently observed. If it be borne in mind that microorganisms are not always to be found in the blood or tissues during the course of disease, that sometimes they may be almost entirely absent, or present only in comparatively small numbers, even in cases in which at other times, they may exist in great abundance, the difficulty and uncertainty connected with the search after them in sections of the various organs may, in some measure, be appreciated. And large numbers of sections may, frequently, be examined before any bacteria are found, and even when found they may exist in such small numbers as to render the search after them both tedious and difficult. After examining very many sections of the kidney in which hyaline degeneration in some of its forms existed, I have come to the following conclusions regarding the mode of production of the three forms which
which I have previously described as occurring in that organ:

I. The first form—that in which there is a plug in some of the afferent arterioles and capillaries of the Malpighian bodies—is caused, in most cases, by plugs of micrococci which are so closely crowded together as to appear almost homogeneous. Occasionally the plugs may consist of inspissated blood serum, as in the branches of the portal vein.

II. This may be caused by the action of both bacilli and micrococci, as in pyaemia and septicpyaemia (See Figures 12, 13, 14, 15, 16, 17).

III. Although bacteria may also account for this form, in all probability chemical agents play an important part in its production.

The fact of the close connection frequently found to exist between bacteria and the hyaline change having been established, it remains to enquire into the probable nature of the action thus originated.
The process may be regarded as akin to what takes place in artificial digestion, in which micro-organisms play a not unimportant part. Indeed, fibrous and elastic tissues, when subjected to artificial digestion undergo a process of swelling closely resembling true hyaline degeneration of the fibrous tissues in the human body. The exact manner in which micro-organisms act in causing hyaline degeneration is a matter for speculation. In all probability their action is a twofold one, partly physical, but chiefly chemical. This latter action may be well seen in Fig. 6, in which a plug of micro-cocci is seen in a Malpighian body, and for a distance round this plug a portion of tissue is paler in colour than the rest, and is more or less homogeneous. Evidently the change is the result of some chemical exudation into the affected part from the plug of
the micro-cocci. But in addition to this chemical action, some organisms—more especially in cases of septic disease—which possess the power of active movement, may, by their physical activity, break up individual fibres and so allow of the imbibition of the surrounding lymph, which, with the chemical products generated by the organisms, increases the swelling and homogeneous thickening of the fibres.

That hyaline degeneration may be caused by the action of bacteria of various kinds is demonstrated by the fact that both bacilli and micro-cocci have been found in the degenerated parts in sufficient numbers to account for the changes produced. But whilst this may be regarded as demonstrated in certain acute, infective diseases dependent upon the presence of micro-organisms, the question naturally arises as to the causation of the hyaline changes found
found in chronic diseases, which, as yet, have not been regarded as having any connection with bacteria. In these latter cases no micro-organisms of any kind may be found; but that is no proof of their entire absence during the whole course of the disease. For, in how many cases of acute infective disease in which bacteria could be discovered at some period of their course, do we find that after a time none may be found? They may have left traces of their presence, however, and these may be of such a nature as that, when once originated, they tend to progress in a steady manner. Science has not yet demonstrated the whole list of diseased conditions in which bacteria, at some time or other may be found. Meanwhile the most feasible hypothesis regarding the occurrence of hyaline degenerations in such cases as general paralysis of the insane and
and other chronic affections is that it is due to some chemical change, the nature of which is unknown, but which may be the result of the previous presence of some form of microorganism.

The fact has already been alluded to, that simple chemical agents, such as acids or alkalies may cause a change in tissues very similar to the hyaline; and phosphorus, as in the case of phosphorus poisoning mentioned above, may also act on the vessel walls in a manner very similar to what is observed in the case of microorganisms. The particles of phosphorus probably impinging on certain portions of the vessel wall during their circulation in the blood, and thus acting locally as destructive agents, as well as producing their general constitutional effects. Such being the case other chemicals may probably act similarly; but this requires to
be proved.

Having traced some of the characters of hyaline degeneration as it is most commonly observed and having noted its relation to micro-organisms and certain chemical agents, I shall now proceed to consider very briefly whether these investigations are calculated to throw any light on the nature and origin of waxy degeneration.

Hyaline

in relation to

Waxy Degeneration

It has recently been stated (Sancet. 1886. Vol. II. p. 877) that Dr. Ralfe considers hyaline degeneration as "the first step in a process which, if acute, leads to fatty degeneration; if chronic, to lardaceous degeneration." This view, must, however, be received with a certain amount of reserve, as though fatty degeneration is not unfrequently a sequel of hyaline degeneration, it
by no means, is the usual or invariable termination of acute hyaline change. And waxy degeneration may exist in an organ in which hyaline changes may subsequently develop from causes independent of the waxy. Thus in a case of chronic phthisis with waxy degeneration of various organs, and advanced waxy change in the liver, an acute tubercular process may occur involving the liver and other organs. The P.W. may reveal the presence of advanced waxy change in some of the vessels of the liver along with well-marked hyaline degeneration in others. Naturally, on finding the two changes side by side in the liver, one would be inclined to regard the one as an early stage of the other. But this need not be the case because the hyaline, in this case, might, and probably would have originated subsequently to the waxy, being the result of the acute process. It may, therefore, be affirmed.
firmed that, any theory, founded solely on the co-existence of these two forms of degeneration in an organ, as to the relation which the one bears to the other, as regards development, must necessarily be imperfect. The actual proof of the one change passing into the other can only be definitely determined by means of exact experimental evidence, derived from experiments on animals. Until this proof is forthcoming, our opinions regarding these points can only be theoretical. But, whilst this is so, there are certain facts available, which may help us in considering the relation subsisting between the two kinds of degeneration:-

Ist. Their physical appearance presents marked similarity. Both the hyaline and the waxy degenerations are characterized by a clear, glassy, homogeneous, translucent appearance; the latter, however, being more pronounced in its physical characters than the former.
Their chemical properties and staining reactions, to a certain extent coincide. Both are insoluble in acids and alkalies, ether, chloroform, and alcohol. Hyaline degeneration in the presence of methyl violet and iodine green, sometimes stains a distinct pinkish colour, reminding one of the waxy change. Safranine, carmine, magenta and other aniline dyes give similar reactions with both degenerations. Picrocarmine stains the early hyaline pink, but later, it stains it yellow just like the waxy. Logwood has a somewhat similar reaction with both degenerations. Iodine sometimes stains hyaline brown, but usually yellow.

3rd. Both degenerations involve similar structures:— Fibrous connective tissue constitutes the chief element of tissue involved in both; and when the blood vessels are involved, the arterioles and corresponding capillaries are
are the parts primarily affected with both changes, and in these situations the fibrous tissue is the principal seat of the degeneration.

1st. The Associated Pathological conditions are, to a certain extent, similar in both cases: - The difference consists, in part, in the degree of intensity of the diseased process. Thus, chronic phthisis is probably the most frequent predisposing cause of waxy degeneration, whilst acute tuberculosis is commonly associated with some degree of hyaline change in many of the arterioles of the spleen, and other organs.

Again, in pyaemia, with multiple acute abscesses, hyaline degeneration is found involving various parts; whereas in cases of empyema with chronic abscesses, waxy degeneration may develop in the neighbourhood of some of the latter, as in a case kindly brought under my notice by
by Dr. Barrett, in which distinct waxy degeneration was found in the lymphatics in the immediate neighbourhood of a small caseous nodule in the lung secondary to chronic empyema. Waxy degeneration of other organs was also present. It is not uncommon to find a hyaline change in the fibrous capsule of the wall of chronic abscesses, which stains partly hyaline, partly waxy. As regards chronic suppurative scrophulous or strumous disease of bones, recent observations seem to prove that this is caused by the presence and action of tubercle bacilli, so that it comes under chronic tuberculosis and has a similar connection with the causation of waxy degeneration. With reference to syphilis and its relation to waxy disease and hyaline degeneration, I am unable to make any observations as my investigations have not been sufficiently extensive to enable me.
me to do so. And as to the somewhat rare cases in which waxy degeneration is present, but in which no history of any evident pre-disposing cause is obtained, may not some mild septic process have existed at some previous period, which, though not very serious in its immediate effects, may nevertheless have set up degenerative processes in some of the vessels which have led on to the waxy change? It will thus be observed that the majority of the diseased conditions, associated with the presence of waxy degeneration have, as their exciting cause, the presence of some form of micro-organism in the blood or tissues. These, circulating in the blood, in comparatively small numbers, or being possessed of low vital activity, probably originate in the vessel walls changes which may, at first, partake of the nature of hyaline, but which, being of a very chronic charac-
ter, may, from the beginning, present the features of waxy degeneration proper.
The relation between these two forms of degeneration may be regarded as analogous to the
relation between the acute and chronic processes of inflammation.
Inflammation, whether acute or chronic, consists of well recognised phenomena, which, though differing according to the stage of the process, are yet regarded as essentially similar all through.
In its course, acute inflammation may pass into chronic; but, on the other hand, inflammation may be chronic from the commencement. The same, probably, holds good as regards the degenerative processes under consideration, in which the hyaline may be designated the acute form, which may, in certain cases, pass into the chronic waxy form: but the latter, like chronic inflammation, may also originate, as an independent process apart from
from the acute hyaline form.

Importance of the Hyaline Change.

Like the waxy, this degeneration derives its chief importance from the disease with which it is associated. Apart, however, from its associated disease, the hyaline change may produce results of considerable importance. Occurring as it does, so constantly in cases of pyaemia, septicaemia, scarlet fever and other fevers, as well as in diseased conditions attended by elevation of temperature, and when involving the coats of arterioles and capillaries, so frequently encroaching on, and sometimes causing total obliteration of their lumen, it is evident that serious interference with the nutrition of the surrounding tissues, in addition to damage of the walls of the vessels themselves, must, as a natural consequence, inevitably result.
result. In its further progress, hyaline degeneration may possibly undergo resolution. Not infrequently, it passes into a condition of granular disintegration and even into fatty degeneration. Probably it may continue hyaline for some time and finally become transformed into true waxy degeneration. At other times it may preserve its hyaline nature all through.

It may become developed in the course of forty-eight hours, as was the case in the woman referred to above, who died from phosphorus poisoning within forty-eight hours after partaking of the fatal dose.

In conclusion, my best thanks are due to Professor Greenfield for much kind encouragement during the time I have had the honour of being associated with him, and also for the very kind manner in which he so freely placed at my disposal the materials contained in his Laboratory.
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