NORMAL AND MORBID CONDITIONS OF THE TESTES FROM BIRTH TO OLD AGE IN ONE HUNDRED ASYLUM AND HOSPITAL CASES.

BY
SIR FREDERICK W. MOTT, K.B.E., M.D., LL.D.,
F.R.S., F.R.C.P.,

DIRECTOR OF THE PATHOLOGICAL LABORATORY OF THE
LONDON COUNTY COUNCIL ASYLUMS.

[With Special Plate.]

THE material dealt with in this article was collected from 100 cases of deaths, occurring at all ages from birth to 86, in London asylums and various civil and military hospitals.*

In a majority of the asylum cases, especially those dying at Claybury and upon which I made the *post-mortem* examination, the contents of the vesiculæ seminales were examined. In a small number of cases the thyroid, adrenals, and pituitary glands were also examined. In all the hundred cases the testes were weighed and subsequently examined by the histological methods to be described.

MACROSCOPIC APPEARANCES OF THE TESTES AFTER PUBERTY.

It was found that sections of fresh or formol-hardened testes, when examined with a hand lens, revealed naked-eye pathological changes in a majority of the asylum cases; the converse was noticeable in the adult hospital cases.

In the normal testes occurring in cases of death from injury or disease without mental symptoms, the weight of each of the organs, as a rule, was normal. Upon section the tubuli seminiferi appear white, plump, and closely packed together, without appreciable intervening fibrous tissue.

In the asylum cases the most marked deviation from the normal condition was found in two groups of cases—namely, (1) general paralysis, (2) dementia praecox.

(1) The weight of the testes in general paralysis varied considerably. It was not infrequent to find one testis considerably smaller than the other, and the tunica albuginea adherent. The weight is not always an index of the functional efficiency or otherwise. There was no correlation between the naked-eye cortical changes in the brain in general paralysis and the morbid changes in the testes.

In a relatively small proportion of the cases of general paralysis examination with a hand lens of a sectioned testis showed no abnormal naked-eye appearance. In the majority of the cases, however, strands and localized patches of fibrous tissue of variable extent and degree separated the white seminiferous tubules and some of the tubules might appear smaller than normal.

(2) In the regressive atrophic condition met with in the great majority of cases of dementia praecox the tubules appeared attenuated and less plump than the normal, and were either of a greyish colour or did not present the uniform milky white appearance of the normal tubules. There may or may not be an increase of interstitial tissue. As a general rule, the degree of morbid naked-eye change of the testes in dementia praecox conforms to the duration of the mental disease and the clinical signs and symptoms of the mental decadence rather than to any obvious naked-eye changes or defects in the brain. In general paralysis the dementia corresponds in great measure to the degree of cortical destruction; nevertheless, there is no correlation in this disease between the brain atrophy and the testicular atrophy.

With the exception of cases of senile dementia and congenital imbecility with epilepsy, the testes in other cases dying in the asylum did not, as a rule, show any marked departure from the normal—for example, cases of epileptic insanity, Korsakoff psychosis, paranoia, and manic depressive insanity.

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Table of Classification of the One Hundred Cases from which the Material for Investigation was Obtained.

Asylum Cases.		Hospital Cases.	
1. Dementia praecox ...	23	1. Born dead or dying before puberty ...	8
2. General paralysis ...	23	2. Dying after puberty of various diseases ...	8
3. Juvenile general paralysis ...	4	3. Under puberty death from injury shock ...	1
4. Psychoses—for example, manic depressive insanity, paranoia ...	7	4. Over puberty death from injury shock ...	1
5. Epilepsy ...	3	5. Military cases—injury of brain or spinal cord, with sepsis of variable duration ...	8
6. Congenital epilepsy, with idiocy or imbecility ...	4		
7. Organic brain disease ...	5		
8. Imbecility ...	2		
9. Senile dementia (octogenarians) ...	3		
	74		25

HISTOLOGY.

The following methods of histological investigation were employed:

HISTOLOGICAL METHODS.

1. Examination of the contents of the vesiculæ seminales by dark-ground illumination and an oil-immersion lens.

2. An emulsion of the testis was prepared by rubbing up a small portion of the organ in a mortar with Ringer's fluid. The emulsion was examined with an oil-immersion lens and dark-ground illumination. The same method was employed in examining the brain for spirochaetes.

3. Smears of the seminal contents of the vesiculæ were stained by Delafield's haematoxylin and eosin, by Heidenhain's haematoxylin and eosin, and with Giemsa or polychrome aniline dye stains.

4. The organs were hardened in 10 per cent. formol solution, and portions of them were cut into sections with the freezing microtome. These sections were stained with scarlet* or Sudan III and some were counterstained with haematoxylin; subsequently the sections were mounted in Farrant's solution. This method was employed to demonstrate the amount and distribution of the lipid substance. In some cases the sections were placed in Marchi fluid.

5. Portions of the gland were cut out into sections of uniform thickness, after embedding in paraffin or treating with the celloidin method. Some pieces were stained in bulk with haematoxylin and eosin, treated first by celloidin method, and after placing in chloroform subsequently embedded in paraffin. This method is very useful, as thin serial sections can be obtained without any shrinking of the tissue. Giemsa, polychrome or the Heidenhain, eosin and van Gieson stains were used for staining the sections. The films and sections were mounted in neutral Canada balsam.

THE DEVELOPMENT OF THE TESTES FROM BIRTH TO PUBERTY.

The development under normal conditions, and under abnormal and diseased conditions, other than congenital syphilis, will now be considered.

At Birth, and in Infancy and Early Childhood.

1. The testes of full term identical twins, born dead but in a healthy bodily condition, also of a healthy full term child, born dead, were examined.

The histological appearances of sections were as follows:

The seminiferous tubes, seen in longitudinal, oblique, and transverse section, are filled with embryonic cells, lying upon a thin membrana propria; there is no sign of differentiation. The cells have round or oval nuclei, with a delicate reticulum of chromatin and a dense membrane. The cells with round nuclei are the spermatogonia; those with oval nuclei are the cells of Sertoli. The amount of cytoplasm is relatively small, it is faintly stained with eosin and presents a homogeneous appearance. The interstitial tissue is relatively more abundant than the tubules at this stage; it is like ordinary connective tissue, except that there are groups of fairly large polygonal epithelioid cells scattered through the organ—the cells of Leydig; these cells may be seen occasionally in double rows, with an interval between like a tubular gland (Fig. 1). These special interstitial cells are very numerous in all the sections. The cytoplasm is three times as abundant as the nucleus; it is stained deeply by eosin. A lipochrome substance may be observed in many of the cells, exactly like the lutein found in the cells of the ovary, in the form of fine light-yellow granules, distributed throughout the cytoplasm. These cells are not unlike liver cells; they stain red with scarlet (see Fig. 1).

2. Sections of a testis of a child, aged 4 months, dead of pneumonia, with a syphilitic rash on the legs, back and head, showed the following appearances: The seminiferous

* Schiariach.

tubes have developed considerably by a proliferation of the embryonic cells, so that they appear nearly double the size of the tubes at birth; the interstitial tissue appears relatively less (Fig. II). A few fine lipid granules, stained yellowish-orange, are seen scattered in the seminiferous tubules, and abundant scarlet-stained granules are seen in the interstitial tissue. *Only a few interstitial cells are now seen; they are smaller than in the testis of the infant at birth.* They can, however, be recognized by the clear outline of the cell—the round, comparatively deeply-stained basophil nucleus, which is easily discerned in the eosin-stained cytoplasm. The lipochrome in the interstitial cells is less obvious than at birth. The appearance of lipid granules in the seminiferous tubules and in the interstitial tissue may be explained by supposing that it has been, and is still being, utilized by the embryonic sperm cells in their formative activity and proliferation; the interstitial cells now disappear or assume a resting stage, in which they will remain until puberty, when they again appear and become active in the spermatogenic function for reproduction (Fig. V).

3. The testis of a child aged $3\frac{1}{2}$, dead of bronchopneumonia (Fig. III), exhibits smaller tubules than in Fig. II; there is more interstitial tissue, and these two facts suggest that there is some arrest of development.

It is possible that when the interstitial cells of the infant are no longer active the internal secretion has already performed its office of impressing on the body the male characters and upon the nervous system the special instincts and affective characters of the male sex. We do not find any evidence of maturation of the male germ cell; it is otherwise in the female, for sections of the ovary of a female infant aged 18 months showed complete Graafian follicles, with a perfect ovum, zona pellucida, discus proligerus and zona granulosa. It is a reasonable hypothesis to suppose that the cells of the zona granulosa and discus proligerus of these Graafian follicles of the infant produce an internal secretion which impresses on the central nervous system the instincts of the female and the psychic characters peculiar to the sex. Moreover, the continual formation of follicles which do not undergo dehiscence till menstruation occurs may, through a bio-chemical influence on the somatic cells, impress female characters, not only on the mind, but on the growth of the body. If the male characters are dominant in the somatic cells this internal secretion would play an important part in determining the female characters.

EARLY STAGE OF ACTIVITY OF THE GLAND.

4. The testes of a boy aged 9, who died of shock from injury, exhibited appearances very similar to the following, though less advanced.

5. The testes of a boy aged 11, who died of fracture of the base of the skull, were examined, with the following results:

The basement membrane of the tubules is more distinctly seen; the tubes are larger, generally speaking filled still with only cells such as are seen in the infant, but here and there are observable early stages of formative activity recognizable by karyokinetic figures in the nuclei of some of the spermatogonia and spermatocytes; the sustentacular cells of Sertoli may now occasionally be clearly differentiated, but these syncytial cells contain but few lipid granules (Fig. IV). There is no evidence of spermatids. *There is some slight fine granule lipid staining in the tubules, but no interstitial lipid, so that the interstitial cells are still practically in the resting stage, appearing as flattened nucleated cells or round nucleated cells, with a small amount of cytoplasm, which when examined with an oil immersion is seen to be stained faintly pink.*

AFTER PUBERTY.

Adolescent.

The vesiculæ seminales and testes of a healthy boy aged 15 (Case 6), who died twenty-four hours after a motor accident which crushed the chest, showed the following histological appearances:

Seminal Fluid.—The spermatozoa, observed by dark-ground illumination and in stained films, of the semen from the vesiculæ seminales are not so numerous, and appear to be smaller than those in the semen of the normal adult. Spermatozoa were found also in an emulsion of the testis, but they did not appear to be as large as those found in the emulsion of the testis of the adult.

Sections of the Testis.—The tubules are now fully developed, closely approximated, and twice the diameter of those seen in the boy of 11. Nearly all the tubes now show abundance of

spermatozoa, and active spermatogenesis in all stages (Fig. V). Numerous groups of interstitial cells are seen, and coarse granules of scarlet-stained lipid within and around these cells are observable. The interstitial cells appear to lie outside the lymph space surrounding the basement membrane of the seminiferous tubules. *The fine orange-stained granules of lipid within the sustentacular cells are not nearly so abundant as in corresponding cells of the testis in the adult (Fig. VI).*

It is obvious, therefore, that with the dawn and development of the sexual desire there occur two histological changes—namely, the reappearance of the interstitial cells in an active state, and the accumulation in and around them of these orange-stained granules; and this may be regarded as an indication of the presence of a phosphorized lipid, which may serve as the raw material from which can be built up the nuclein necessary for the active formative cell processes connected with spermatogenesis. I have purposely said *may* because the other view is that the nucleic acid is formed from protein and circulating inorganic phosphates (see below), but physiological chemistry has not yet settled the synthetic processes underlying the formation of nucleic acid, which is the main chemical substance in the constitution of the head of the spermatozoon. A further discussion of this subject will appear in another monograph when the results of chemical analysis of the testes in health and disease which are now being undertaken are completed.

Adult.

The following cases afforded an opportunity of examining the testes in healthy adults.

CASE 7.

W. L., an engine driver, fell off his engine and was killed. He was brought into Charing Cross Hospital. Sections of the testes showed normal spermatogenesis in all stages; the number of the spermatozoa in the tubules was not so great as in most normal cases. The interstitial cells of Leydig were extraordinarily well seen forming large groups in the loose connective tissue between the tubules (Fig. VII). The basement membrane of the tubules was not thickened. Frozen sections stained with scarlet dye and haematoxylin showed most clearly the cells of Leydig filled with the orange-stained granules of lipid. The cells of Sertoli are likewise filled with these fine orange-stained granules.

Among the cases dying of injury and in which spermatogenesis is normal, it is remarkable how variable is the readiness with which the cells of Leydig can be discerned. In some, as W. L., they are seen in every low power field in every section; in others they can only be found by searching.

Among asylum cases it has struck me that the testes of general paralytics show these cells in greater numbers than the testes of other forms of insanity. Too much importance must not, however, be attached to this statement, for unless serial sections of both testes were made and examined, a definite conclusion that the hormone cells were in greater numbers in the testes of persons suffering with general paralysis than other persons dying in the asylums is unwarranted.

CASE 8.—Normal Spermatogenesis in the Adult.

F. H. C., aged 24, was admitted to Charing Cross Hospital suffering with multiple injuries of the pelvis, and died the same day from shock.

Sections of the testis from this case stained for lipid showed abundant granules in the syncytial cells—so abundant as to form a ring around the tubule within the basement membrane (Fig. VIII). Comparatively little lipid was seen in the interstitial tissue. Frozen sections stained with haematoxylin and scarlet and mounted in Farrant solution showed interstitial cells containing lipid granules, but there was considerable congestive stasis in the blood vessels and capillary haemorrhage (doubtless the result of the injury), and this would account for the relatively small amount of lipid in the interstitial tissue. The tubules show active spermatogenesis in all stages (Fig. IX). This case will therefore serve for the description of normal spermatogenesis.

NORMAL SPERMATOGENESIS IN THE ADULT.

A section of the normal seminiferous tubule shows a well defined membrana propria, with flattened nuclei, supporting several layers of cells. The layer of cells lying on the basement membrane consists of spermatogonia, and between the spermatogonia are the syncytial cells of Sertoli, which are larger, have oval nuclei, and project inwards between the various layers of cells which are undergoing successive stages of active mitosis, incidental to spermatogenesis. The cells of Sertoli, or sustentacular

FIG. I.—*Testis of Twin Fetus.*
(Mag. 105.)
To the right between the tubules in the interstitial tissue are seen numbers of polygonal cells. These are the cells of Leydig.

FIG. II.—*Testis of Infant aged 4 Month.*
(Mag. 105.)
The tubules have increased to nearly double the size; the interstitial tissue was correspondingly diminished. The cells of Leydig are not visible.

FIG. III.—*Testis of Child aged 3 Years.*
(Mag. 105.)
The tubules are smaller than in Fig. II. The cells of Leydig are not seen. There is much more interstitial tissue than in Fig. II.

FIG. IV.—*Testis of Boy aged 11 Years.*
(Mag. 105.)
The tubules are larger than in Fig. II. The tubules are approximated. There is a small amount of interstitial tissue. The cells of Leydig are not visible.

FIG. V.—*Testis of Boy aged 15 Years ; died of Injury.* (Mag. 105.)
The tubules show active spermatogenesis. The fine black dots are the heads of spermatozoa.

FIG. VI.—*Testis of Boy aged 15 Years ; died of Injury.* (Mag. 70.)
Scarlet-stained preparation to show lipid. The interstitial lipid (black) is very well shown. Compare the staining of the tubule with the adult, Fig. VIII.

FIG. VII.—*Testis of Adult aged 24 Years ; died of Injury.* (Mag. 385.)
Portion of spermatic tubule, with four heads of spermatozoa seen. To the right is a large collection of cells of Leydig, polygonal in form and with a large round nucleus.

FIG. VIII.—*Testis of Adult ; died of Injury.* (Mag. 70.)
Scarlet preparation showing abundant interstitial lipid which appears black. Observe also the black zone beneath the basement membrane. This is due to the spermatogonia and cells of Sertoli being filled with lipid.

FIG. IX.—*Testis of Adult; died of Injury.* (Mag. 376.)
Transection of spermatic tubule, showing active spermatogenesis.

FIG. X.—*Diagram to illustrate Spermatogenesis.*
I shows the various stages in the development of spermatozoa from spermatogenesis—spermatocytes—spermatids; II, the heads of the spermatozoa dipping into the cells of Sertoli; III, the further stage of development of spermatozoa; IV, mature spermatozoa with tails free in lumen prior to escape. Beneath are two interstitial cells.

FIG. XI.—*Film of Fluid from Vesicula Seminalis of Case of Dementia Praecox Early Second Stage; died of Acute Lobar Pneumonia after three days' illness.* (Mag. 875.)
The film was stained with haematoxylin and eosin. Only a few spermatozoa seen, and these take the acid dye and are degenerated. Compare with Fig. XII.

FIG. XII.—*Film of Fluid from Vesicula Seminalis of Case of Manic Depressive Insanity.* (Mag. 875.)
The film was stained in a similar manner to Fig. XI. Observe that the spermatozoa are stained by the haematoxylin, and have a normal morphological appearance.

FIG. XIII.—*Testis from a Soldier dead from Sepsis caused by Bullet Wound of Lower End of Spinal Cord.* (Mag. 162.)
Spermatic tubules show no spermatozoa; most of the cells have undergone coagulation necrosis.

FIG. XIV.—*Testis from a Boy aged 7; dead of Chronic Tuberculosis.* (Mag. 105.)
The tubules are the same in size as at birth. Round-celled infiltration of interstitial tissue. No cells of Leydig seen. Compare with Fig. I

FIG. XV.—*Testis from a Case of General Paralysis.* (Mag. 96.)
To the left are normal seminiferous tubules. To the right are completely atrophied tubules. Below is a part of a nodule of interstitial cells.

cells, are particularly rich in lipid granules. Within the above mentioned outer layer of cells are larger cells (the spermatocytes), the large nuclei of which show all forms of karyokinesis. The spermatocytes are products of division of the spermatogonia, each of which, on dividing into two, gives rise to one cell like itself, and another which grows larger, and passes into the second layer to form a spermatocyte.

The spermatocytes undergo a division. A product of the division of the spermatocyte again divides, giving rise to spermatids, the number of chromosomes becoming reduced to half the number during this process. The spermatids are small cells with spherical nuclei; they elongate, and the nucleus becomes shifted to one end. The young spermatozoa thus formed collect into irregular groups, and appear deep in the sustentacular cells of Sertoli, which serve as a support and source of nourishment to the young spermatozoa. As they grow and acquire their tails at this stage of spermatogenesis the heads appear to be nearer the lumen of the tubule, and the tails of the spermatozoa project freely into the lumen of the tubule; a little later in the process of development the spermatozoa grow in size and are pushed further towards the lumen, and eventually become completely liberated (Fig. IX).

Examination of the spermatids in haematoxylin eosin stained sections with an oil immersion shows a nucleus stained deeply with the basic dye surrounded by a thin layer of eosin stained cytoplasm. These develop into spermatozoa in the following way: The nucleus becomes shifted to one end, and assumes an oval and then a lance-head shape, and behind this is seen the eosin stained cytoplasm which later, in the Sertoli cells, grows to form the main part of the tail.

The process is continually going on in the seminiferous tubules of the testis, successive crops of spermatozoa being continually produced. The various stages of development may be observed in the normal testis, or even within the limits of a single tubule (Fig. X).

The reduction in the number of chromosomes, which takes place in the formation of the spermatids, is analogous to the casting out of the polar bodies of the ovum; both processes constituting a preparation for the conjugation of the male and female gamete which takes place in the fertilized ovum.

THE LIVING SPERMATOZOON.

The spermatozoon is a living organism produced in incalculable numbers by the testis during the greater part of a healthy man's life, and it may be regarded as the most remarkable organism in Nature, for concealed in its minute structure and bio-chemical organization is the specific energy of the highest vital dynamics of evolution. In a normal emission of man, Lode calculated that there are about 226,000,000 spermatozoa, and that 339,385,500,000 must be produced in man between the ages of 25 and 55.

The semen is the mechanical medium in which the spermatozoa move, and when ejected it is mixed with the secretion of the prostate and Cowper's glands.

Examination of the Contents of the Vesiculæ Seminales Post Mortem.

The seminal secretion of the testes is stored in the vesiculæ seminales. There may be a biological advantage in this, for I have found that examination of the semen in the vesiculæ seminales of people dying of various diseases show spermatozoa in various stages of degeneration. Moreover, in two of the cases the contents of the vesiculæ, examined by dark-ground illumination, showed that some of the spermatozoa were still alive and active eight hours after the patient's death. Now the specific energy of these active spermatozoa must have been greater than the inactive dead organisms. Consequently, in a person suffering with disease it is probable that only those with a normal specific energy survive; thus only the fittest are left for fertilization. As will be shown, there is reason to believe that this degenerative process of the spermatozoa may commence in the early stages of normal spermatogenesis.

In many cases of disease, especially dementia praecox, the appearances of the spermatozoa proved that for some time past no living spermatozoa had existed; they all showed appearances of marked degeneration (Fig. XI), the staining reaction was not normal, the heads showed obvious bio-chemical and morphological changes; the tails

were broken off from many; the heads gave an oxy-chromatin reaction, staining with the eosin instead of the haematoxylin. Many showed only fine granules of chromatin stained by the basic dye.

I have placed seminal fluid from the vesiculæ in a sterilized sealed-up tube and kept it for more than four months, and the same forms could be seen as were observed in the films made at the time the seminal fluid was first collected. This fact is of importance, for it shows that spermatozoa may be found in the vesiculæ when active spermatogenesis has for a long time ceased.

SUMMARY OF NOTES OF SPECIAL CASES OF INTEREST.

In the vesiculæ seminales of a demented man, aged 81, who died of pneumonia, abundant spermatozoa were found; some in various stages of degeneration, but quite a number of the heads took the basic dye as if they were still capable of fertilization. Examination of sections of the testes showed that the majority of the tubules exhibited all stages of active spermatogenesis.

In a case of juvenile general paralysis of the insane, fluid from the vesiculæ seminales, examined by dark-ground illumination in pericardial fluid, was found crowded with spermatozoa, a few very active. The majority stained normally with the basic dye.

In a case of typical dementia paralytica, aged 69 at death, in which there was advanced brain degeneration, arterio-sclerosis and cirrhosis of liver, death occurring from bronchopneumonia, the fluid from the vesiculæ showed abundance of spermatozoa, mostly degenerated. Still, active spermatogenesis must have been going on while he was in a state of profound dementia.

In another case of paralytic dementia the patient was in good general health till he had seizures which continued for a fortnight, when he died of exhaustion. My notes state that there is little active spermatogenesis in the testes. It is probable that since the patient began to have seizures with prolonged asphyxial conditions spermatogenesis had been arrested. Prolonged venosity of the blood may have interfered with the oxidation process necessary for biochemical decomposition and recombination processes of nuclear formation. It may be concluded that the vesiculæ seminales, which were filled with spermatozoa, had them stored there before he had the seizures, and, as the patient was in an unconscious or semi-conscious state the whole time, they were never evacuated.

THE SEMINAL FLUID IN DISEASE.

THE EXAMINATION OF THE FLUID IN THE VESICULÆ SEMINALES OF CASES OF GENERAL PARALYSIS OF THE INSANE.

Among twelve successive cases of general paralysis of the insane, of all ages and in all stages of the disease, as regards cortical decay and destruction, spermatozoa were found in the vesiculæ seminales of eleven, and in such a condition as to support the view that they had, just prior to or not long before death, been possessed of vitality, and were capable of fertilizing. The one case in which no spermatozoa were found in the vesicula seminalis might have shown spermatozoa in the other vesicula had it been examined.

The evidence of recent spermatogenesis afforded by examination of the contents of the vesiculæ in these 12 cases of general paralysis of the insane, accords with the evidence afforded by histological examination of a much larger number of testes, including these 12 and other cases; for I did not find one young or old (excepting a case of juvenile general paralysis of the insane, which began at 8 years of age) in which there was not evidence of active spermatogenesis in some of the seminiferous tubules, although usually scattered through the organ was partial or complete destruction of the sperm cells of some of the tubes, leaving only the basement membrane and sustentacular framework (Fig. XV).

Now, one of the common characteristics of general paralysis of the insane is excessive sexual desire, and masturbation is frequent in both the early and demented stage. Yet, although this is so frequent and may extend over years, it has not been sufficient in any one of the large number of cases I have examined completely to arrest spermatogenesis or produce a similar regressive

atrophy of the seminal tubules to that met with in the great majority of cases of dementia praecox.

EXAMINATION OF THE SEMINAL FLUID OF THE VESICULAE SEMINALES IN OTHER DISEASES.

Severe head injuries, even with sepsis, do not, as a rule, arrest spermatogenesis. In one case there was a complete arrest. In two cases of bullet wounds of spinal cord with bedsores and prolonged sepsis there was complete arrest and an appearance of coagulation necrosis of the cytoplasm of the spermatid cells (Fig. XIII). Advanced chronic pulmonary tuberculosis of the most extensive nature may not arrest spermatogenesis. This is of importance, because a large proportion of the asylum cases, including especially dementia praecox, die of tuberculosis. Fourteen out of sixteen successive cases of this disease died of pulmonary tuberculosis.

MASTURBATION DOES NOT CAUSE ARREST OF SPERMATOGENESIS.

A case of mania was of interest in showing that the vesiculae seminales may be crowded with spermatozoa and the testes show normal spermatogenesis, although the notes state that the patient during twenty-five years in the asylum was a pronounced masturbator. It cannot be therefore asserted that masturbation *per se*, even when continued over a great number of years, can produce regressive atrophy of the testes and arrest of spermatogenesis in a male attacked by insanity in adolescence.

CANCER AND SPERMATOGENESIS.

A patient, J. G., aged 67, suffered with dementia and died of carcinoma of the stomach. The testes weighed respectively 17 and 15 grams. There was complete arrest of spermatogenesis, but the vesiculae were crowded with spermatozoa, most of them degenerated. This seems to show that the active cell formation of a rapidly growing carcinoma of the stomach may, by its devitalizing action and utilization of all the materials circulating in the blood for nuclear formation, arrest spermatogenesis.

Another case of chronic alcoholic neuritis, aged 65, with Korsakoff psychosis, cirrhosis of the liver and ascites, was of special interest, for the vesiculae seminales contained abundance of spermatozoa, but the testes showed a complete arrest of spermatogenesis. It may be assumed that the spermatozoa found in the vesiculae were formed during the morbid condition above mentioned. But an active carcinomatosis had taken place in the liver, and it is possible to associate the arrest of spermatogenesis, as in the former case, with the active nuclear formation in the liver. This, however, is merely conjecture; it may be only a coincidence, but it is a suggestive coincidence that makes it desirable to pursue the matter further by an examination of the testes in a number of cases of death from new growths.

EXCESSIVE SUPPURATION AND SPERMATOGENESIS.

A case of very extensive suppurative pericarditis of some weeks' duration showed arrest of spermatogenesis in the testes, although the vesiculae contained abundant spermatozoa, probably formed before the suppurative process occurred. Here, again, an enormous nuclear proliferation and destruction of nuclear matter must have occurred.

NO ARREST OF SPERMATOGENESIS IN CHRONIC MICROBIAL INFECTIONS.

In cerebro-spinal meningitis, in manic depressive insanity, epilepsy, melancholia, and cases of other forms of insanity dying in the asylum spermatogenesis was still active in spite of fatal microbial disease—for example, acute and chronic tuberculosis and dysentery, which are very common causes of death in asylum patients. Again, bronchopneumonia due to inhalation of food (sometimes with gangrene of the lung), influenza, and typhoid fever are frequent causes of death of the insane.

In hospital cases the same applies. This leads one to ask whether the important genetic function is protected from the effects of circulating toxins. The hypothesis I put forward is that the abundant lipoids, consisting of lecithin, cholesterolin, and fatty acids, around and in these seminiferous tubules, serve as a protective barrier against toxins.

SPERMATOGENESIS AND OLD AGE.

Arrest of spermatogenesis due to senility occurs at varying ages in different individuals. The organs of three octogenarians suffering with senile dementia who died at Claybury Asylum were investigated, with the following results. Normal spermatogenesis may occur in a very old man, as the following case shows:

CASE 1.—*Senile Dementia.*

W., aged 81, died of pneumonia, February 22nd, 1916. The organs other than the lungs were fairly healthy considering the age. Testicles each weighed 18 grams, and presented a normal naked-eye appearance; an emulsion of the organ revealed, by dark-ground illumination, spermatozoa.

Spermatozoa.—The vesiculae seminales contained abundance of spermatozoa, many taking the eosin stain only, but a large number showed normal basophil staining spermatozoa. Sections of the organs after hardening in formalin showed, when examined with hand lens, very little excess of interstitial tissue, the seminiferous tubes appeared full, plump, normal in size, and glistening white. Microscopic examination of sections stained by the two usual methods showed normal spermatogenesis in all stages; the basement membrane was not thickened; the interstitial tissue was not increased; the testicles were closely approximated and not atrophied. The cells of Sertoli were filled with orange-stained granules. The interstitial cells of Leydig were present and contained lipid.

In this case the testis was, in fact, as normal histologically as the testis of a much younger man. Indeed, the appearances of virility are far in advance of any case of dementia praecox, and of many other cases dying in the asylums. In contrast with this are the two following cases:

CASE 2.—*Senile Dementia.*

C., aged 85. Wassermann reaction negative in blood and fluid. Testes not weighed. Vesiculae seminales not examined. Scarlet preparations. Coarse lipid in the centre of the tubuli seminiferi. Tubules atrophied, interstitial lipid occasionally seen. Hematoxylin and scarlet: no spermatozoa observed anywhere. The seminiferous tubes were in all stages of degenerative atrophy, from an appearance of thick basement membrane, with a few layers of nucleated cells and coarse granules of lipid, to a condition in which the whole tubule was filled with large vacuolated cells; the only part which took the stain was the nucleus, which was flattened against the wall as in a fat cell. These filled the whole lumen, and were apparently the swollen sustentacular cells, filling the space previously occupied by the spermatogonia and spermatocytes. Here and there groups of interstitial cells containing lipid could be seen; they appeared to be undergoing atrophy. In other places they stood out clearly in groups between the markedly degenerated and atrophied tubules.

CASE 3.—*Senile Dementia, Pleurisy with Effusion, fairly Recent.*

T. S., aged 86. Testes: right 11.5 grams; left (small), 8.5 grams. Sections of the testicles showed microscopic appearances in some ways similar to those of the late stages of dementia praecox, except that the membrana propria was not much thickened, the interstitial tissue was less increased and the epithelium in the tubules showed more nuclear staining. There was a continuous layer of spermatogonia; the cells of Sertoli were not conspicuous. The layer of spermatocytes showed, as a rule, well stained karyokinetic figures of the nuclei but the cytoplasm was vacuolated. This vacuolation was due to lipid contents. Only very occasionally was a tubule found in which there was evidence of heterotypical nuclear division, reduction of nuclear substance, and formation of the spermatids. When spermatids were seen they took the basic dye well. In a few tubules occasional well shaped spermatozoa could be seen. Fairly numerous groups of interstitial cells, smaller than normal, and the majority containing lipochrome pigment, were observable.

Possibly the persistence of the interstitial cells may account for an increased and perverted sexual appetite in old men, due to a stimulation of the desire without the power to perform the sexual act.

ARREST OF SPERMATOGENESIS FROM BIRTH TO ADOLESCENCE.

1. *Complete Arrest before Puberty.*

Examination of the testis of a child, aged 7½, dying from tuberculosis pulmonalis, showed a condition of the tubuli seminiferi like those at birth (Fig. XIV).

There was a pronounced round cell infiltration of the interstitial tissue indicating a chronic inflammatory condition. No interstitial cells of Leydig could be seen. Scarlet stained preparations showed no interstitial lipid granules. A few granules could be seen in the embryonic spermatid cells.

Speculating upon the cause of this arrest, seeing that neither tubercle bacilli nor evidence of tuberculous deposit could be found in the testis, it may be supposed that the child possessed a low vitality and that nature never intended reproduction.

2. Arrest at Puberty.

The following are examples of arrest at or soon after puberty:

Boy, aged 16, died of chronic morbus cordis of long standing. The tubules were atrophic and showed miniature development. As in the testis at birth, the tubules were separated one from another by abundant interstitial tissue. There was no evidence of formation of spermatocytes or spermatozoa; in fact, the epithelium retained to a great extent its embryonic character, and there was little evidence of mitosis of nuclei. The membrana propria was thickened, and chronic passive congestion had given rise to an interstitial fibrosis; no interstitial cells could be discovered.

As a contrast the following acute case of morbus cordis may be cited:

A young man aged 21 died suddenly of cerebral haemorrhage caused by aneurysm due to infective embolism. There was ulcerative endocarditis. The seminiferous tubules are of normal size and are packed together with very little interstitial tissue; normal spermatogenesis with abundant lipid in the interstitial cells, the spermatogonia, and cells of Sertoli.

Chronic disease of long standing before puberty is associated with complete arrest of spermatogenesis at puberty. This fact has been shown by an important research of Kyrle¹ on the disturbances of the development of the male generative organs at all ages from birth to adolescence. He has demonstrated the fact that chronic constitutional diseases, such as tuberculosis, are associated with arrest of development. One hundred cases were examined; among these, seventy-six were highly undeveloped; of the remaining twenty-four by no means all were normal; more than half showed distinct underdevelopment. Only ten were certainly normal.

Kyrle states that at the first glance it would seem that the under-development of the testes in chronic tuberculosis was due to the effect of the toxin. He points out, however, that out of thirty-nine dying in the first year of life, twenty-nine had undeveloped testes, but only one of these died of tuberculosis. He thinks this proves that the undeveloped organ is already undeveloped when the individual is affected by the disease.

He concludes that a considerable number of children are born with undeveloped reproductive organs. The development of the whole organism is directly under the influence of the reproductive organs. Individuals with undeveloped reproductive organs have less vital resistance to disease than those with normal reproductive organs. Among the children dying with undeveloped seminiferous tubes far the greater number were physically undeveloped. The greater number of those dying in early life had undeveloped testes. Kyrle asks the question whether this is a kind of natural selection by which individuals of little genetic worth are cut off in early life.

REFERENCE.

¹ Kyrle, Dr. Josef: Ueber Entwicklungstörungen der menschlichen Keimdrüsen in Jugendalter. *Wien. klin. Woch.*, November 10th, 1910, No. 45. Aus dem pathologisch. Institute in Wien.

(To be continued.)

An Address

ON

CANCER.*

WITH DEMONSTRATION ON THE EPIDIASCOPE.

BY

PROFESSOR J. RUTHERFORD MORISON, F.R.C.S.

A WEEK ago, when I was at the War Hospital, Gosforth, Major Reader, on our round, showed me five cases of malignant disease in soldiers. The first had a cancerous stricture of the oesophagus; the second had cancer of the stomach; the third had intestinal obstruction due to general cancerous peritonitis; the fourth was a man with hopeless inoperable carcinoma of the rectum; and the fifth a man with cancer of the prostate and secondary deposits.

These soldiers, of course, were not old men. The man with cancer of the rectum was only 20 years of age. We used to think of cancer as being associated with old age. So it is; but there is an increasing amount of cancer in the country, and it is increasing more in the younger people than in the older, I think. When I saw the wounded

soldiers and saw those hopeless cancerous soldiers together, I thought what a blessing it was to be wounded instead of to have been caught with cancer.

The fact is this, that tubercle and syphilis and cancer—all of them very closely related—kill more people every year than were killed in any year of the war. We ought to face these facts and make war upon them. We have finished with the Huns, now we ought to make war upon cancer; and how is it to be done?

My brother, the medical officer of health for Cumberland, wrote a paper about a year ago in which he advised that periodical examination of every one in the country should take place at least once a year—he said once in six months, but at least once every year. That is the only way to deal with and to prevent these scourges, or discover them early enough for successful treatment. Sanatoriums for tuberculosis have been proved, almost proved, to be useless except for the individual. The treatment of syphilis in the new venereal centres may be satisfactory enough for the individual, but is of small national benefit.

What we want to do is to have everybody examined once a year and all the syphilitics to be sent to an island and to be kept there until they are cured; nobody to be allowed to enter or leave the island without a doctor's passport, and nobody to enter England without being examined by the Port Authorities. This would eradicate syphilis in two years as hydrophobia was banished. We know that this is true, and, whether popular or not, we ought to have the courage to preach it. That is the only way to prevent, or at all events to recognize, early cases of cancer.

We know about cancer a few things; we do not know the great thing—its exciting cause—but we do know a large number of predisposing causes, so that in many cases it is possible to prevent cancer. Then we know that cancer can be removed by operation, and, if a good operation is done early enough, with a large and steadily increasing percentage of success. I do not say operation is the last word in cancer; it is not. There will eventually be something better, but meantime we are to deal with what we know, and this is that from 75 to 90 per cent. of early cancers can be cured by a satisfactory operation.

PREDISPOSING CAUSES.

The following specimens and photographs, shown by the epidiascope, will impress upon you the predisposing causes of cancer and the importance of early diagnosis.

1. Here is a clay pipe smoker's epithelioma of the lip. It at first appeared as a little scaly, corny patch, which may have existed for three, four, five, six, and even ten years, and then it got a little crack in it. Even the crack could heal with some ointment, and things returned to their normal condition; but there came a day when this crack spread and it developed into an epithelioma of the lip.

2. Here is a chimney-sweep's cancer. This is a very unusual condition, because there are multiple primary foci. Now if you see multiple sores you think it cannot be cancer, but it is so in this case. From irritation of soot in the breeches we may get multiple foci of cancer.

3. This photograph is from an infirmity patient of mine. He was a paraffin worker and he got a paraffin burn, which developed, as you see, into an epithelioma.

4. Here is another example of chronic irritation—chronic superficial glossitis. This tongue spells syphilis, tobacco, alcohol, leucoplakia, and cancer.

5. A case of leucoplakic tongue, one developing carcinoma in the middle. The tongue had been like this for ten years. Some leucoplakic tongues are curable by x-ray or radium treatment—about the only thing as yet which seems to do them any good.

6. A case of leucoplakia, also of long duration—very long duration—but no cancer. Of course you would not advise this man to have his tongue out. You would knock him off his tobacco and alcohol, and give him some antisymphilitic remedies and x-ray treatment, and get him to come up for observation every three months; at the least sign of cancer you would have the tongue out.

7. Here is an instance of leucoplakia of the vulva. Leucoplakia does not develop only in the tongue; it may come on the vulva and on the penis, and wherever it is it is apt to develop an epithelioma.

8. Here is a burn scar. In my own experience of old burns, if the scars do not heal very few of the cases escape cancer. This man had his leg burnt when he was young, and at the age of 30 an epithelioma developed on that burn. The scar never was quite healed. It broke down from time to time and discharged a little and then skinned over, but it never was a sound scar. That scar ought to have been removed and the scar area replaced by skin grafts or flaps from the other or the same leg.

X rays, of course, are another well-known cause of burn giving rise to epithelioma. I have seen quite a number of

* Given before a Scientific Meeting of the North of England Branch.