the prestige gained for them in 1889. Of the nasal douche and gargle advocated in the Local Government Board memorandum I cannot speak more confidently than of drugs and lozenges. The trouble about all these local measures is that the very people who are most liable to infection are much too busy and too preoccupied to carry out a mucous membrane drill with any regularity.

CONCLUSION.

In conclusion, we must, I fear, confess to a very unsatisfactory position at present in regard to preventive measures in the treatment of influenza. But to know how little we know is an essential step in progress. The great need is organized research and organized hospitalization, and now is the time for these things to be carried out. Let us not cease to urge upon those responsible for the public health the importance of the problem and the great uncertainty of our present knowledge, reminding them that economy here is of the falsest, and that the country possesses no asset to be compared in value with the health of its citizens.

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

BY

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CORRELATION OF BIOCHEMICAL AND MORPHOLOGICAL CONDITIONS OF SPERMATOGENESIS.

It has been shown that sections of the testis of a newborn child exhibit lipid granules in the interstitial cells, also lipochrome granules similar in appearance to lutein. Fine lipid granules are also seen in and between the embryonic epithelial cells of the seminiferous tubules. Sections of the testis of a four months infant show that the seminiferous tubes are about twice the size of those at birth; no lipid granules are seen in the interstitial tissue. The appearances of sections of the testis of a boy aged 11 show almost similar appearances to those at four months; the tubes are not much larger. A few of the tubules show cells with mitotic figures and cells of Sertoli can be seen, but they contain no lipid granules.

Not until puberty and active spermatogenesis has commenced are lipid granules found in the interstitial tissue. Usually large droplets of ruby-red-stained fat are seen aggregated together in this tissue. Fine orange-stained granules can be seen in abundance in the interstitial cells of Leydig, in the spermatogonia, and especially filling the cells of Sertoli. The large droplets are probably lipid, with a greater proportion of unsaturated fatty acid.

The fact that the lipid ceased to appear in the interstitial cells as soon as, and as long as, spermatogenic cell growth ceased and reappeared with active spermatogenic proliferation, may be regarded as very suggestive evidence of the phosphorized lipid being connected with nuclear proliferation.

This conclusion, moreover, is supported by the fact that in advanced regressive atrophy the fine orange-stained lipid granules have almost entirely disappeared from the interstitial tissue.

The cells of Sertoli may in some cases of advanced atrophy still contain lipid. Only large ruby-red droplets of varying size are usually seen in the very atrophied tubules, which may be explained by a fatty degeneration of the cells.

THE CORRELATION OF BIOCHEMICAL PROCESSES WITH THE HISTOLOGICAL APPEARANCES.

1. In films of seminal fluid from the vesiculæ seminales and sections of the testis stained with a basic and acid dye, such as haematoxylin and eosin, Giemsa or Leishman stains, the following microchemical reactions are observed. The head of the normal spermatozoon, consisting of nucleinate, is stained blue by the basic dye. The tail, except the axial thread, stains pink—that is, the lipid which forms the main constituent of the tail is stained pink.

2. In frozen sections of formalin-hardened testes stained with scarlet dye and haematoxylin, and mounted in Farrant's solution to show the distribution of the lipid granules, the following appearances can be observed. The spermatids in the process of development into spermatozoa are stained posteriorly by the scarlet dye and anteriorly by the basic dye. The fine orange lipid granules are seen in the spermatogonia, spermatocytes, and especially in the cells of Sertoli. The lance-shaped heads of the spermatozoa stained blue are seen diving into the cells of Sertoli, where it may be presumed they behave like living organisms and feed upon the store of lipid in these "nurse" cells. In situations where sheaves of spermatozoa have attained further development and projected their tails into the lumen of the tube prior to escape as free organisms there is a paucity of fine orange granules observable in the Sertoli cells. Chemical investigations by Miescher and Kossel have shown that the tails consist almost entirely of lecithin and cholesterol with a small amount of protein. Lecithin represented by the formula—

may be looked upon as glycerophosphoric acid combined with choline, a base with the constitution of a tertiary amine, and with two molecules of fatty acids (Koch, 1902).

From the following considerations it appears probable that the phosphorus of the glycerophosphoric acid enters into the formation of the nuclein, a fatty acid being formed which combines with the lecithin continually taken up from the blood and lymph. The presence of the unsaturated fatty acid with the lecithin favours the oxidation processes necessary for the active metabolic processes connected with the cell proliferation (Thunberg, 1909, 1913; Warburg, 1913; and Warburg Myerhof, 1913).

The "iodine value" indicating the degree of desaturation of fatty acids of lecithins obtained from various organs shows a high figure for lecithin from testicles—117—as compared with 73 for lecithin from ox heart, 81 from liver, and 69 from thyroid (Cruickshank, 1914).

Miescher's experiments show that the tails of the spermatozoa consist largely of a phosphorized fat and some cholesterol, therefore I examined frozen sections of the testicles for cholesterol by Liebermann's test.

The sections were taken out of water, floated on to a slide, a covering glass placed over the section and glacial acetic acid was attracted under the covering glass by the application of filter paper to the edge; a drop of sulphuric acid was next drawn under the covering glass.

The granules in the interstitial substance and in the circumference of the tubules became pink, and finally turned to green when examined with a magnification of 100. When the magnification was increased to 500 or 600 the fine granules in the spermatogenic cells, especially the Sertoli cells, were seen to be stained green, also the spermatids and heads of the spermatozoa, which leads me to believe that these active developing cellular organisms have a thin covering membrane containing cholesterol. Seeing that cholesterol is insoluble in cold alcohol, and yet this reagent dissolves out nearly all the substances stainable by the scarlet dye, it follows that the cholesterol, although it has exactly the same distribution as the lipid which is stained by this dye, must only represent a fraction of the lipid in which it is in combination.

We know that cholesterol with lecithin enters into the formation of cell membranes. There is good reason, therefore, to suppose that the abundance of lipid found in the

cells of Sertoli during active spermatogenesis may be utilized for forming the tails and covering membrane of the head of the spermatozoa, but the question arises, Is this lipid substance a phosphorized lipid and can its phosphorus be utilized in the manufacture of nucleic acid, the principal constituent of the heads? Wherever there is active cell proliferation there is abundance of peroxidase granules—that is, peroxidase ferments may be contained in these fine lipid granules found especially in the syncytial cells.

THE BIOCHEMISTRY OF THE SEXUAL ORGANS.

A full account of our knowledge of the biochemistry of the sexual organs is given in the admirable work of Marshall, *The Physiology of the Reproductive Organs*, and I shall only briefly summarize the subject in so far as it helps in the arguments relating to the results of my own researches upon spermatogenesis in health and disease.

"According to Slowtsoff, human semen consists roughly of 90 per cent. of water and 10 per cent. solids, which upon incineration yield 1 per cent. of ash." The solids contain 2.3 per cent. proteins. "In the ash K, Na, Ca, Mg, P, Fe, and S have been found. The quantitative analysis of the ash reveals a remarkably large amount of calcium and phosphoric acid—namely, about 20 per cent. Ca and 30 per cent. P_2O_5 ."

The chemistry of spermatogenesis was first investigated by Miescher, who correlated histological examination of the milts of Rhine salmon with chemical analysis. His histological observations enabled him to separate in bulk the portion of the milt containing the heads from that of the tails. He showed that the chemical composition of the former differed essentially from the latter. Miescher found that the heads consisted chemically of two substances—a highly nitrogenized substance which he termed "salmin," and a highly phosphorized substance, nucleic acid. The two are in chemical combination and form a nucleinate.

Kossel continued the researches of Miescher, and showed that the heads of the spermatozoa of other species of fish consisted of a combination of these two substances—namely, a protamine which is specific for each fish and nucleic acid which is common to all vertebrates. It was also shown by these investigators that the tails of the spermatozoa consisted of protein, a large amount of phosphorized lipid, and cholesterol in smaller amount.

During the breeding season the salmon takes no food, but feeds on its muscles. The protamine comes from the muscle. It was shown that the blood of the fish during the breeding season contained a large amount of phosphorized lipid, which therefore, in all probability, is utilized in spermatogenesis. This lipid must have come from the muscle or from metabolic processes incidental to the wasting of the muscles.

The researches of Loeb show that the iron of the nucleus of a cell acts as a catalyser, in the presence of oxidase, converting molecular into atomic oxygen—not only may complex substances be split up into simpler substances, but simple substances may be synthesized into complex substances thereby.

The first step in all proliferation is the taking up of the raw material for growth by the living cell; it is brought to the gland by the blood and lymph channels.

Our previous remarks show that certain elements are especially required—namely, Ca, N, P, Fe. In all active proliferating cells there is oxidase ferment in the form of fine granules, and these, under the influence of the iron catalase in the nucleus, are able to convert the molecular oxygen into atomic oxygen, and the chemical processes which are set in action enable the cell, including its nucleus, to build up substances like unto itself from the raw material brought by the blood and lymph. The first morphological change is visible in the chromatin of the nucleus, karyokinetic figures appear heralding the division of the nucleus and the cell. It is highly probable either that the oxidase granules are lipid substances with a certain amount of unsaturated fatty acid, or they have a lipid film on the surface, the phosphorous having an affinity for the oxygen with which it is in unstable combination, consequently O_2 is readily converted into free atomic oxygen, O , by the catalyser iron of the nucleus.

Some experiments of Marshall carried out in 1908 suggest that these phosphorized fats may act as oxygen

carriers, and that they may thus fulfil an important function in all respiration.

That phosphorized fats are in all probability the source of nucleic acid is supported by the following facts. Neither nucleic acid nor pentoses are present in the fresh egg, and purin bases are only present in very small amounts. During development of the egg these substances rapidly increase in amount, indicating a synthesis of nucleic acids from the reserve material of the egg—namely, proteins and phosphorized fats.

Wolfgang Ostwald has determined the amounts of oxidizing ferments present in the testes of toads, frogs, and newts. The watery extracts of these organs had the power of decomposing hydrogen peroxide with the formation of water and oxygen, and of oxidizing guaiaconic acid to guaiacum blue, so that a blue colour appeared when these extracts were added to an emulsion of guaiac resin. These reactions indicate the presence of a catalase and of a peroxidase in the extracts of the sexual glands. Such ferments are present in many, if not all, organs and tissue fluids, but a special significance is attributed by Ostwald to their presence in the ova and spermatozoa.

MICROCHEMICAL TESTS REGARDING THE NATURE OF THESE LIPID GRANULES.

A phosphorized lipid—for example, lecithin—is stained an orange colour, fat or a fatty acid a deep ruby-red, by scarlet. Sections of the medulla oblongata from three cases of death by shock caused by gunshot wounds with compound comminuted fractures of the femur, with fat embolism, showed this remarkably well.

Degenerated nervous tissue, in which there is free fatty acid the result of decomposition of the phosphorized fat (myelin), is stained black by Marchi fluid (1 per cent. osmic acid in 5 per cent. potassium bichromate solution), whereas the myelin of normal nerve is stained an ash-grey. Both these microchemical reactions have been employed in this investigation. I have found that in sections of normal testicle there is invariably within the spermatogonia, cells of Sertoli, and to a much less degree the spermatocytes, an accumulation of fine granules which are stained orange or ash-grey according to the staining reaction employed. Under a low power these granules form a ring within the basement membrane of the tubes (see Figs. VI and VIII), but the interstitial staining by these methods varies very considerably as to the amount of fatty acid and phosphorized fat present in testes where active spermatogenesis is taking place. We may ask the question, Is this variability in the amount of fatty acid present in the interstitial tissue due to a decomposition of the phosphorized fat in the formation of the nucleic acid? But wherever we have this fatty reaction the cholesterol reaction is also obtained, so that it is not a simple fatty acid but a cholesterol combination. The fine orange granules of phosphorized lipid also give this cholesterol reaction; we must therefore suppose that this substance is present in the granules found in the spermatogenic cells. But cholesterol is present in the tails of the spermatozoa, although in much smaller amount than lecithin; moreover, these two substances form the periplasm constituting the osmotic membrane of the spermatocytes, spermatids, and spermatozoa.

Now the oxidase reaction (in the few cases in which I have employed this test) corresponds in its distribution, both in the interstitial tissue and in the seminiferous tubes, to the scarlet, osmic, and cholesterol reactions—a fact which seems definitely to show a functional correlation between lipid and oxidases. The following experiment supports the conclusion that these lipid granules are connected with the oxidation processes.

Small portions of the testis of a freshly killed guinea-pig were placed in a solution of vital methylene blue. These fine granules took up the dye. The tissue was placed in saline solution and covered with a covering glass which was surrounded with vaseline. The preparation was put into the warm chamber. After some hours all the blue colour had disappeared. Upon lifting up the covering glass and admitting the air all the coloured granules reappeared. A clear proof that these granules use up and take up oxygen.

It is an interesting fact that the testes of persons dying from the most varied forms of microbial infection in which toxins must have circulated in the blood and lymph for a considerable time nevertheless show active spermatogenesis. The interstitial tissue and the tubuli seminiferi contain abundant lipid in the same situations as in cases of sudden death by injury.

Cortex Adrenalis and the Reproductive Function.

There is evidence to show that one of the functions of the adrenal cortex, the cells of which are filled with lipid substance, is to provide lipid for the building up of the myelin of the developing nervous system. The evidence in favour of this is as follows:

1. A correspondence in size of the adrenal cortex and the brain in the animal series.

2. The great diminution in size of the adrenals in anencephalous monsters.

But it has other functions—namely, the storage of lipid—which, as occasion arises, can pass into the blood and keep constant the supply of lipid to the reproductive organs, where it constitutes the raw material for formative nuclear activity. This functional correspondence of the adrenal cortex and sexual glands is indicated by certain pathological facts—namely:

1. Adenoma of the suprarenal cortex has been found associated with marked sexual precocity.

2. Among my cases an active spermatogenesis in a man aged 69, who died after many years' residence in the asylum suffering with dementia of arrested general paralysis, was associated with a large adrenal cortex.

3. In four male cases of well-marked dementia praecox, with regressive atrophy of the testis, the adrenal cortex was narrow and the cells contained much less lipid than in other cases of mental disease dying in the asylums. I have only paid attention to this matter lately, but it is being followed up to see if there is a correlation.

4. The cortex adrenalis in the teleostei and elasmobranch fishes is a separate gland. The medullary substance, with its chromaffin, is a part of the sympathetic nervous system.

5. Rats fed upon suprarenal gland showed hypertrophy of the testes; other organs did not show hypertrophy (Swale Vincent).

6. The cortex adrenalis is developed close to, or forms part of, the genital ridge, and in one case of dementia praecox, where there was only one testicle, the adrenal gland of one side weighed less than one-half that of the side in which the testis was present, and this difference in weight was mainly due to a diminished cortex.

I have observed in a large number of cases where the patient has died from a disease in which there has been microbial infection and consequent toxæmia a marked diminution of the amount of stainable lipid in the adrenal cortex, and I agree with Elliot that this adrenal lipid probably passes into the circulation to form antitoxins. Now, it is a remarkable fact that however much the lipid may have diminished, on this account, in the adrenal cortex, it does not seem to have diminished in the testis. Possibly this may account for the fact that, in all manner of chronic microbial infections with toxæmia, active spermatogenesis may nevertheless be seen in the seminiferous tubules. This supports the premise that these lipoids form a protective barrier by virtue of the free atomic oxygen liberated upon their surface; thus affording a special provision of nature to protect the germ cells from injury, as well as providing at the same time the oxygen and raw materials necessary for the most fundamentally vital cell activity in the body.

The Oxidase Reaction Applied to the Cortex Adrenalis.—According to Marinesco, the cortex adrenalis does not give the oxidase reaction because the contents of the cells stain uniformly and not as granules, but some cells from which some of the lipid has escaped do show granules of lipid and these stain in a similar manner to the granules in the testicles.

(To be continued.)

SURGICAL TREATMENT OF FACIAL PARALYSIS.

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EVERY large military hospital has had experience of traumatic facial paralysis, where restoration of function by nerve repair or nerve grafting has not been possible. In cases of comminution of the petrous bone end-to-end repair cannot be effected, although grafting or anastomosis may still remain practicable; in lacerated parotid wounds the main trunk has already broken up into the parotid plexus, and repair of the diverging branches does not come into the realm of practical surgery.

The deformity is a very terrible one, and any treatment that offers hope of cosmetic improvement should be welcome to surgeons.

Early in 1917 I attempted to do something for these patients by grafts from neighbouring muscles, and in successive cases to employ the method, modifying the procedure by the result of experience.

I describe the operation in the form I finally adopted (Fig. 1):

Preliminary to anaesthesia, the non-paralysed side of the face is inspected, and the position of the lower half of the nasolabial furrow marked in; a second vertical marking is made almost in the centre of the cheek in the position of the dimple that becomes evident when laughing. A third marking is made, beginning below the external canthus and taking the direction of one of the lines of the crow's foot. The side of the head is shaved.

An incision is made through the skin in the hair line from

the zygoma to the upper limit of the temporal fossa, directed slightly backwards so as to be parallel to the underlying fibres of the temporal muscle. The skin is then undermined forwards and backwards to expose the temporal fascia; two parallel incisions are then made, again from the zygoma to the limit of the temporal fossa through the fascia and muscle down to the bone; these incisions should run in the direction of the muscular fibres and should include a strip of muscle as thick as a man's thumb; it is important for the preservation of the nerve supply and for the cosmetic result that fully this bulk of muscle should be used. A smaller slip anterior to this is similarly isolated, and both are detached from the underlying bone.

An incision is now made under the eyelid in the marking representing one of the lines of the crow's foot, the skin is undermined, the anterior smaller slip of muscle drawn through,

made taut, and sutured to the fibres of the orbicularis palpebrarum with catgut (Fig. 1, T, and Fig. 3, T₁).

Incisions are made in the line of the cheek furrow and the lower half of the naso-labial groove, and the skin tunnelled to make a continuous passage from the temporal wound to the corner of the mouth. The large slip of muscle is then drawn down over the zygoma through the channel, sutured with

catgut to the superficial fascia exposed in the cheek wound, and to the muscular fibres of the orbicularis oris below and slightly mesial to the corner of the mouth (Fig. 3, T₂).

The facial incisions are sutured with horsehair: the cut margins of the temporal muscle are brought together as far as possible with catgut (it is extremely difficult to get apposition), and the temporal wound closed with silkworm gut.

Paradism and massage should be employed early, and the patient should daily exercise his facial expression before a glass. The grafted straps of muscle will continue to function.

In the first operation of this kind which I attempted I grafted a slip of the temporal muscle into the orbicularis palpebrarum and a slip of the masseter into the orbicularis oris (Fig. 1, M); Stenson's duct was guarded by a probe inserted and tied to a tooth. Considerable difficulty was

FIG. 1.—2. Denuded area in temporal fossa. T, Slip of temporal muscle inserted into orbicularis palpebrarum. M, Slip of masseter inserted into orbicularis oris.

FIG. 2.—2. Denuded area in temporal fossa. T, Temporal muscle. T₁, Slip of temporal muscle inserted into orbicularis oris.

FIG. 3.—2. Denuded area in temporal fossa. T₁, Slip of temporal muscle inserted into orbicularis palpebrarum. T₂, Slip of temporal muscle inserted into orbicularis oris.