for the calculation when sulphuric acid, or potassium or sodium hydrate are employed. In this formula E represents the potential difference of the element, which is measured by Poggendorff's compensation method; *a* is the original concentration of the acid or alkaline solution employed; *b* the concentration at the close of the experiment of the solution in which the (still living) paramoecia are contained. Without entering into further details of the method employed and the many precautions necessary to ensure accurate observations, which are given at length elsewhere,⁶ some of the results obtained may be here considered. These, which are given in Table III,

TABLE III.—Amount of Acid and Alkali Disappearing from Solution in Per Cent. of the Weight of the Paramoecia Employed.

	Concentration Employed.	Amount of Acid or Alkali Withdrawn by 100 Parts of Protoplasm.
Hydrochloric acid ...	0.00067 <i>n</i>	0.30 HCl
Sulphuric acid..."	0.00067 <i>n</i>	0.13 "H ₂ SO ₄ [= 0.16 HCl]
	0.00067 <i>n</i>	0.24 " [= 0.18 "]
Potassium hydrate ...	0.000330 <i>n</i>	1.95 KOH
	0.000330 <i>n</i>	0.74
Sodium hydrate ...	0.000670 <i>n</i>	1.24 NaOH [= 1.74 KOH]
" "	0.000670 <i>n</i>	1.52 " [= 2.11 "]

confirm the results obtained by the former method, and show, further, that living protoplasm may react with still larger amounts of acid and alkali than are indicated in Table II, reaching in fact during the period of experiment, which varied from eight to forty minutes, as much as 0.3 per cent. in the case of hydrochloric acid and 2 per cent. in the case of potassium hydrate.⁷ With palladium-hydrogen electrodes, however, only the H⁺ ions of the acids and the OH⁻ ions of the alkalis are shown to be used up, and no information is afforded of the part played by the remaining ions. Only in the case of hydrochloric acid has this point been investigated, and condition of the solution employed in respect of the Cl⁻ ions pre-studied. To this end a series of observations were made with calomel electrodes, the arrangement adopted being :

and the potential difference measured being the sum of $E_1 - E_2 + E_3$ obtaining at the three surfaces of contact. From the observed potential difference, the initial concentration of the hydrochloric acid employed being known, the alteration of the Cl⁻ ionic concentration brought about by paramoecia can be calculated from a formula similar to the one given above. In this way the unexpected result was obtained that when paramoecia are added to a dilute hydrochloric acid solution, not only do Cl⁻ ions not disappear, but that an actual increase of these ions takes place. The cause of this increase was found on further investigation to be due to the discharge of chlorides by the protoplasm of paramoecia, when injured by the acid, into the surrounding fluid.

Summary.

By the above-described methods of investigation it is shown (1) that the action of acids and alkalis upon living paramoecia is not a catalytic action, but that (2) a chemical reaction takes place in which H⁺ and OH⁻ ions disappear. Further, it has been shown (3) that when dilute hydrochloric acid acts upon living paramoecia an increase of the Cl⁻ ions takes place.

In conclusion, I must express my indebtedness to Professor Verwor, in whose laboratory this work was carried out, and also to Professor Nernst, who kindly permitted me to make the physical measurements in the Physico-Chemical Institute in Göttingen, and to Professor Cohn, at whose suggestion palladium-hydrogen electrodes were employed.

⁶ Die Addition von Säuren und Alkalien durch lebendes Protoplasma, *Zeit. f. Allg. Physiol.*, 1905. Bd. 5, 8 10.

⁷ It is interesting to compare the amount of acid and alkali reacting with living protoplasm with that taken up by proteids. Cohnheim (*Zeit. f. Biologie*, Bd. 33, 1895, s. 439) found that albumose, protalbumose, deuteralbumose, and antipeptone combined respectively with 4.15 per cent., 4.32 per cent., 5.48 per cent., and 15.87 per cent. of hydrochloric acid; and Bugarsky and Liebermann (*Arch. f. d. ges. Physiol.*, Bd. 77, 1895, s. 51) observed that albumin and albumose combined with 2 per cent. and 4 per cent. respectively of their weight of sodium hydrate.

REPORT XCII.

ON THE ORIGIN AND LIFE-HISTORY OF THE INTERSTITIAL CELLS OF THE OVARY IN THE RABBIT.

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THE majority of investigators agree in considering the germinal epithelium to be derived by a process of differentiation from the peritoneum. There is, however, considerable difference of opinion as to the means whereby the cells of this epithelium come to form part of the ovary, and as to the subsequent fate of the cells.

Pfäfer⁹ considered that the germinal cells grew down into the underlying mesoblast in the form of tubules (egg tubules), the cells thus invaginated giving rise by division to ova, and also probably to follicle cells, some of these latter being possibly derived directly from the germinal epithelium.

Waldeyer¹¹ thought the embedding of the cells was accomplished by the upgrowth of processes from the underlying mesoblast, cutting off groups of cells, which ultimately gave rise to ova (primordial ova) and follicle cells. De Foulis⁸ believed both upgrowths of mesoblast and downgrowth of cells to take part in the embedding of the cells of the germinal epithelium; he differs from the above-named and most observers in deriving the follicle cells from the mesoblast, a view only held by two other observers (Schrön¹⁰ and Wendeler¹³). Balfour⁴ describes the formation of "egg-clusters" by the processes of upgrowth of mesoblast and downgrowth of cells, the cells of the egg-clusters forming either (1) ova by a process of differentiation, and (2) follicle cells, there being a number of cells resembling follicle cells whose destiny he could not trace; he also describes the formation of protoplasmic masses by the aggregation of several primordial ova, of which he thinks one might survive at the expense of the rest. Bühler⁶ has described the streaming inwards from the periphery of germinal cells, which arrange themselves around the primordial ova, forming the follicular epithelium.

V. Winiwarter¹² has described the processes of nuclear transformation connected with ovogenesis. There are three types of cells present in the fetal ovary before birth—protobroque cells of varieties *a* and *b*, and deutobroque cells. The protobroque *a* cells are the original germinal cells; these divide, giving rise to more cells of the same class and also to cells protobroque *b*; these in turn divide, giving rise to more cells of the class *b*, and also to deutobroque cells. These last are the large clear cells seen in the fetal ovary in considerable numbers.

Immediately after birth nuclear changes begin to take place in some of these cells, the ultimate result being a primordial ovum. The changes start in the cells most centrally situated, and pass gradually towards the periphery, the early stages being still seen in this part at the tenth day after birth.

The nuclear changes leading to ovogenesis he classifies into five stages :

1. The leptotenic stage : The chromatin is present in the form of fine filaments spread out over the nuclear area. This stage is very fugitive.
2. The synaptonic : Here the filaments are becoming gradually massed together until they are finally all collected, the chromatin showing as a solid mass lying at one side of the nuclear area.
3. The pachytenic : The chromatin becomes again spread out over the nuclear area, but this time in thick strands, which subsequently show a tendency to a double appearance, thus giving rise to the
4. Diplotenic stage : This is followed by the
5. Final or dielyate condition of the primordial ovum, where the chromatin is arranged in a more or less reticular form, and there are one or two lumps of chromatin as well.

The question of the formation of "ova" in later life is not one upon which the literature throws much light—it consists chiefly of isolated observations of the formation of follicles in ovaries of cats, rabbits, and women, either in the rutting season and at the menstrual periods, or shortly after parturition.

Amann¹ recently published an interesting case of a woman of 63 upon whom he performed double ovariectomy, the ovaries being in a condition of incipient cystic adenoma. He found all stages of ova and follicle formation, all derived by ingrowth of the germinal epithelium. The interest of the

observation lies in the formation of ova and follicles in an ovary which had presumably ceased to function for many years, the process being probably due to the stimulus of the growth.

OBJECT OF THE INVESTIGATIONS.

Changes in the interstitial cells observed during pregnancy led to the investigation into the origin of these cells, this being a subject upon which there would appear to have been no work done. The subject is one of considerable interest in relation to the internal secretion of the ovary (Cf. Andrewes³). By analogy with the interstitial gland of the testis (Cf. Ancel and Bouin²), it would appear probable that the interstitial cells might form the ovarian secretion.

(Throughout the *interstitial* cells are to be distinguished from the *stroma* cells, which are mere connective tissue cells.)

Methods.

A considerable variety of fixatives were used—the usual osmic fixatives as well as several others—but by far the most satisfactory were found to be Gilson's fluid (equal parts CHCl_3 , absolute alcohol, and glacial acetic acid, the whole saturated with sublimate), and a mixture of sublimate (saturated) 4 parts, formol 1 part, and 1 per cent. of glacial acetic. The stains chiefly used for these last were iron, haematoxylin, and haemalum.

The ovaries investigated were those of embryos from the twentieth day onwards and of young rabbits up to about 3 weeks old, as also a large number of those of pregnant rabbits in all stages of pregnancy.

CHANGES IN THE GERMINAL CELLS IN THE IMMATURE OVARY.

Histology.

The embryonic ovary shortly before birth shows two distinct zones—an outer, consisting almost entirely of collections of germinal cells, and an inner, consisting of mesoblast, which sends some processes outwards in between the collections of germinal cells. The germinal cells show a great variety of sizes. The protobroque cells are small, more or less oval in form—I do not propose to make any distinction between the varieties *a* and *b*—while the deutobroque cells are large, round, and very clear. There are also cells of all sizes between these two forms, all of them round.

The arrangement of the chromatin in the different classes of cells gives the clue to their condition. In the protobroque cells it is present in rounded masses, usually rather small, and the whole nuclear area is cloudy, giving the appearance of minute granules. There are no strands or filaments.

In the deutobroque class the chromatin is arranged in a more or less reticulate manner, and there are one or two chromatin masses. The greater part of the nuclear area is strikingly transparent, the cloudy appearance seen in the protobroque cells being confined to the margin. The other rounded cells show nuclei in all stages of transition between these two forms. The nodules of chromatin seen in the protobroque type show at first short projections which gradually lengthen, and finally meet the projections from other masses, forming intersecting chromatin strands, while the number of chromatin masses decreases, there being usually not more than two in the deutobroque cell. Simultaneously with this, the granular appearance has receded gradually from the central part, leaving it clear.

There are a fair number of mitotic figures to be seen; some are in protobroque cells, but the greater number (and this holds especially in the ovary shortly after birth) are in the larger cells of the deutobroque type. I think, therefore, that mitosis has here its normal use, namely, the increase of cells, the changes from one form and another being brought about by nuclear differentiation and enlargement of the cell, the changes consisting in the gradual formation of strands of chromatin instead of nodules, together with the clearing of the central parts.

The deutobroque cells thus formed will many of them pass through the process of ovogenesis, and I would refer any one interested in the subject to v. Winiwarter's paper. The changes of ovogenesis take place much more freely in the cells near the centre, being found in relatively few cells near the periphery, but continuing in these parts in a sort of desultory manner up till three or four weeks after birth.

The formation of egg clusters by means of ingrowing processes of mesoblast proceeds rapidly, and by about the tenth day the clusters are extremely numerous, but the number of cells in each is smaller. In some clusters near the centre a cursory glance would lead one to suppose that all the cells were undergoing ovogenesis, but a careful examination shows

that there are a few in every cluster that retain the deutobroque formation.

By the fourteenth or fifteenth day these cells are no longer to be seen, but instead there are a few small rather dark cells; at the periphery there are now a large number of these small cells scattered thickly amongst cells still undergoing ovogenesis; here there are also a certain number of deutobroque cells, and also some smaller clear cells. The intermediate region shows that the small cells are passing inwards from the periphery, and, together with those already formed, are, some of them, passing towards the primordial ova forming the follicular epithelium, whilst others are lying in groups by themselves and are evidently forming the first traces of the interstitial tissue of the ovary. These features are well seen in the ovary of about the seventeenth or eighteenth day after birth.

These small cells, which form either the follicle cells or the interstitial cells indifferently, are metamorphosed deutobroque cells, the change resembling very much, in the inverse order, those concerned in the formation of the deutobroque cells from the protobroque, and the smaller clear cells near the periphery are in the transition stage.

Broadly the changes consist in the retraction, as it were, of the chromatin strands and the aggregation of the chromatin into lumps, but the strand formation is never completely lost; the whole nucleus and cell become smaller and the granular appearance, which in the deutobroque cell is confined to the peripheral part of the nucleus, becomes again spread out over the whole area, which loses its transparency; cells in all stages of transition can readily be found.

We may then look upon the ovary as consisting of two classes of cells: (1) Cells derived from the germinal epithelium and probably subserving all the true ovarian functions; (2) mesoblast cells, which are merely supporting and vascular.

By far the greater number of germinal cells which become embedded in the mesoblast pass to the deutobroque stage, and are potentially ova; but all cannot become ova, as there are other functions to be performed; therefore when the great wave of ovogenesis has passed and sufficient ova have been formed, the remainder undergo regression and take up the other ovarian functions, becoming either follicle cells or interstitial cells. The protoplasmic masses noticed by Balfour are a very characteristic feature of the young ovary about the seventeenth or eighteenth day after birth, and from the appearance of atrophy of some of the nuclei it appears fairly certain that the fittest ovum will survive at the expense of the rest; it is uncertain whether every ovum must eat up some of its fellows before reaching maturity.

CHANGES IN THE OVARY DURING PREGNANCY.

Naked-eye Changes.

These consist of the formation of the corpora lutea and of general enlargement of the whole gland. The corpora lutea are at their maximum about the fifteenth day (Cf. Fraenkel⁷), shortly after which they begin to decrease in size, and finally by the end of pregnancy they show merely as white circular areas on the surface of the ovary.

The ovary of the non-pregnant animal is about $\frac{1}{2}$ in. long, being wedge-shaped in transverse section. As pregnancy goes on, the whole gland increases very greatly in size, becoming roughly about five or six times as large as it was in the non-pregnant state. The wedge-shape is changed to circular, and the gland may be as much as $1\frac{1}{2}$ to $1\frac{1}{2}$ in. in length, and looks swollen.

Changes in Size of the Interstitial Cells.

The size of the interstitial cells at different stages of pregnancy, and also in a few cases after parturition, have been measured by means of a micrometer eyepiece, gauged against a micrometer slide. A large number of cells were measured, the average of a large number of measurements being given below:

Date of Pregnancy.	Diameter in μ .
0	17.0
14th day ...	23.4
18th day ...	27.2
20th day ...	31.9
22nd day ...	32.6
27th day ...	31.8
Shortly before birth...	29.8
Shortly after birth ...	27.0
3 days after birth ...	26.8
6 weeks after birth ...	17.1

These measurements are not intended to be absolute, but to give an idea of the general change in size. It appears that the increase is at first rather slow, afterwards becoming more rapid, and reaching its maximum about the twenty-second day, the size being sustained until just before birth. In the later stages of pregnancy the cells are very much crushed together; possibly they are still endeavouring to enlarge, but the connective tissue being stretched almost to the full, they are unable to do so.

The Formation of Ova from Interstitial Cells.

About the twentieth day some of the interstitial cells leave their fellows and appear to be pressing towards the periphery, where they become surrounded by connective tissue and pass into a position exactly similar to that of the primordial ova. This process continues more rapidly during the next few days, and multinucleated masses become a marked feature; these are situated near the periphery, and show the same outline as if they had been formed from as many interstitial cells as the mass shows nuclei. Of these last some appear to be undergoing atrophy, whilst one appears to be growing strong at their expense. These multinucleated masses have been noticed by v. Beneden⁵ in the bat. We evidently have here a similar condition to that in the young ovum; there the end-product was a primordial ovum; here the end-product will be similar. In ovaries of about the twenty-sixth day and onwards, it is possible to trace all the transition stages of ovogenesis among these cells thus cut off. According to the description of v. Winiwarter, the leptotenic phase is rare, probably on account of its short duration. There are plenty of synaptenic nuclei to be seen, not many pachytenic, and the diplotenic are not very definite; the dictyate show well.

In connexion with this formation of ova, it may be noticed that the size of a primordial ovum, until it begins to ripen and the follicle begins to grow, does not vary, being about 27 μ , a size reached by the interstitial cells at about the eighteenth day of pregnancy. The interstitial cells are all potential ova, and during pregnancy the ovary probably shares in the general stimulus, causing the interstitial cells to enlarge in size, some of them undergoing transformation into ova.

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MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

ANEURYSM MISTAKEN FOR HARD FIBROMA.

The following case, which I saw in consultation with my colleague, Dr. H. Scott-Russell, of this town, may be of interest as illustrating one of the most serious mistakes in surgery. Its history was as follows:

The patient, the wife of a native minister of Ethiopian persuasion, first noticed a small, hard lump in the groin about ten years ago, painless, but growing slowly until it reached its present dimensions—the size of a coconut. Advice was sought, because pain was present recently and a soft spot was noticed. Upon examination it presented the following features:

The growth was situate in the right groin; it was roughly oval in shape; its long axis in line with the sartorius muscle, of the size noted, its upper portion on a level with Poupart's ligament, its anterior aspect bulging on the front of the thigh. No pulsation could be felt, and the femoral artery could not be located above it. It gave the impression of great hardness, except at one point, where a small fluctuating protrusion existed; it appeared to be fairly movable, except along the line of Poupart's ligament. I concurred in the diagnosis of hard fibroma undergoing in its softer portion some form of cystic degeneration. The operation for its removal was commenced, but in the early steps of enucleation the wall ruptured, and a quantity of black tarry matter

escaped, followed by copious bleeding. It was immediately evident that an old-standing aneurysm had been opened; the wound was at once closed temporarily, pressure applied, a tourniquet placed over Poupart's ligament, and the patient sent into hospital. The treatment decided upon was ligature of the external iliac, with subsequent excision of the aneurysm if feasible. The external iliac was reached in the usual way with little difficulty, its ligature (kangaroo-tail tendon) at once controlling the haemorrhage. The aneurysmal sac was then freely opened up, all clot removed, the sac dissected out from below upwards, and the distal portion of the vessel ligatured. Its formation was as follows:

The greater part of the sac was superficial to the fascia lata, the neck having traversed the facia in the region of the femoral ring, as illustrated in the diagram.

What probably occurred was this:

A small sacculated aneurysm of the superficial femoral, after enlarging in the direction of least resistance, that is, through the cribriform facia, commenced to leak with the formation of a so-called false sac, as described. The points of interest are as follows: The entire absence of pulsation; slow growth; great hardness with softening and fluctuation at one spot, due to disintegration of old clot and the formation of watery fluid—the fact that it had advanced towards a natural cure and then remained stationary until sepsis (several enlarged glands were present in the inguinal region, two of which were breaking down) supervened; the contained clot was like hard putty, inky black in colour and of greasy consistence, except in the softened area described; the error in diagnosis, which, I venture to think, was excusable on our part. Although a definite history of the case was unobtainable, it was probably primarily traumatic in origin, as the external iliac was comparatively healthy. The case is progressing favourably, a good collateral circulation evidently being established and the wound healing by primary union.

Transvaal.

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A FEW ILLUSTRATIVE CLINICAL NOTES ON THE TREATMENT OF DIPHTHERIA.

In illustration of my article on the Treatment of Diphtheria appearing in the *Practitioner*, April, 1905, the following clinical notes of a few cases may prove of interest:

CASE I.—W. P., aged 7, admitted December 3rd, 1901, on the sixth day of disease with extensive membrane and enlarged glands, and marked toxæmia. First sound impure in pulmonary area.

Treatment.—Antitoxin 6,000 units. Strychnine 42 minims per diem (18 minims hypodermically). This for two days. Then 52½ minims per diem (30 minims hypodermically) for two days. Then 42 minims per diem (20 minims hypodermically) for two days. Then 37 minims per diem (15 minims hypodermically) for one day. Then 32 minims per diem (10 minims hypodermically) for two days. Then 27 minims (5 minims by skin) for a day or two. Then 20 minims per diem by mouth for a week. This patient averaged half a fluid drachm of liq. strychninae per diem for a period of three weeks.

CASE II.—M. C., aged 6, admitted December 4th, 1902, with much membrane, subnormal temperature, rapid pulse, and wax-like pallor; was given 7,000 units of antitoxin in the course of forty-eight hours. She was given 56 minims of liq. strychninae (15 minims hypodermically) the first twenty-four hours; 66 minims the second day (30 minims hypodermically); [owing to her becoming collapsed and almost pulseless, with vomiting; in short, all the signs of fatal toxæmia]. Rectal