STUDIES ON THE PHYSIOLOGY OF THE FOLLICULAR FLUID

By

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The formation of the follicular fluid is a phenomenon which is intimately connected with the normal function of the ovary. In spite of this, the physiology of the follicular fluid is very poorly understood at present. It therefore seemed desirable to investigate this question. In the following the author gives a summary of his published and unpublished work in this field.

EARLIER INVESTIGATIONS

There are a number of earlier investigations on the follicular fluid. With regard to the composition of the liquor, it has been claimed that it contains 10–40 per cent of dry substance, mainly proteins and so-called pseudomucin (Oertel, 1924). Cholesterol (Parhon, 1925) and oestrogenic hormone (MacCorquodale, Thayer & Doisy, 1936) are also present. It has further been suggested (Dahlgberg & Akesson, 1930) that the follicular fluid contains a substance which depresses the maturation of other follicles. Both inhibition and acceleration of blood coagulation have been ascribed to the follicular fluid (Mayer, 1919, Wintz, 1920, resp. Palla, 1947). Finally it is well known that the formation of follicular fluid depends on the stimulation by gonadotrophic hormone (FSH) and this has been used as the basis for a commonly used routine laboratory determination of FSH.

OWN INVESTIGATIONS

The author's investigations were performed on rabbits, mainly because their ovaries are sufficiently large and because the rabbit has no spontaneous cycles. The investigations have covered the fields of composition, the physical-chemical properties and function of the follicular fluid.
The composition of the follicular fluid

A few years ago it was discovered that radioactive sulfate was specifically incorporated in the follicular fluid (Boström & Odeblad, 1952). In a more careful study (Odeblad & Boström, 1953) it was shown that the radiosulfate is first accumulated in the granulosa cells and is later on secreted into the follicular fluid. The rate of exchange of the sulfate groups of the follicular fluid (the biological half-life) was found to be about one week. In another study (Odeblad, 1952 a) it was pointed out that there was a correlation between the amount of dry substance (determined with beta radiography), the amount of radioactive sulfate and the degree of metachromatic staining of the follicular fluid. Radioactive phosphate which is accumulated in the follicular fluid to a small extent only (Odeblad, 1952 b) exhibited no similar correlation. The presence of proteins containing \(\alpha\)-amino groups was studied with the ninhydrin reaction according to Berg (1936), and they were found to be present to a moderate extent.

Recently the author has made some attempts to study the elementary composition of the ovary by activation analysis. Histological sections of the ovary were activated in the cyclotron with deuterons (Odeblad & Tobias, 1954) and with alpha particles (Odeblad, 1954 a). In the first case it was possible to reveal the distribution of phosphorus, and in the later case the distribution of oxygen. It was found that only small amounts of phosphorus are present in the liquor as compared with the surrounding tissues. In incinerated sections, mainly containing oxygen as sulfate and phosphate, it was found that oxygen was relatively much more abundant than phosphorus. This supports the view that there is much sulfur in the follicular fluid.

The results of all these studies can be summarized as follows. The follicular fluid seems to contain a sulfo-mucopolysaccharide as an important constituent. Besides this proteins also occur as well as small amounts of phosphorus-containing compounds, and, of course, other materials.

The physical-chemical properties of the follicular fluid

Solutions of sulfo-mucopolysaccharides are often known to be highly viscous. Therefore the viscosity of the liquor folliculi was examined. A special technique suitable for the small quantities which can be obtained, was developed (Odeblad, 1954 b).

A droplet of follicular contents was placed in a thin glass capillary. This was placed at a carefully measured slope, and the velocity of sliding of the droplet was recorded photoelectrically. The same measurement was undertaken with water. The viscosity obtained in this was 120 ± 30 (dispersion), the viscosity of water being taken as a unit. The follicular contents, consisting mainly of fluid with a few cells, are therefore highly viscous.
The function of the follicular fluid

It seemed interesting to do some investigations on the functional significance of the findings described above, mainly with respect to ovulation and corpus luteum formation.

In order to examine the role of the follicular fluid in the formation of the corpus luteum, rabbits were injected with radio-sulfate. Corpora lutea were then allowed to develop after the injection of human chorionic gonadotrophin, which is able to transform unruptured follicles to corpora lutea in the rabbit. Autoradiographs (Odeblad, 1952 c) revealed that the newly formed corpus luteum did not contain radioactive sulfate, which was present in the liquor. It is, however, important to remember that the granulosa cells themselves must be present for the formation of the corpus luteum, as shown by Westman (1929).

In order to study the function of the follicular fluid in connection with ovulation, a number of experimental punctures of Graafian follicles were performed with needles 0.2–0.3 mm. in diameter. It was possible to observe that the follicular contents escaped relatively slowly from the follicle (in 5–30 sec.) and afterwards remained attached to the ovarian surface. The whole liquid contents, including the egg cell and the corona radiata, formed a single viscous body, which could escape from the interior of the follicle through a very small opening and subsequently return to its original form. The granulosa cells in the periphery of the follicle remained inside the follicle.

The same mechanical properties of the body, formed by the liquor, ovum and corona, could also be seen beautifully under the microscope with a micro-manipulator. It was easy to deform the body, but after cessation of the mechanical stress, the body retained its original form. It was difficult to reach the egg cell and touch it directly, but if successful the egg cell was easily destroyed.

**DISCUSSION**

As mentioned in the introduction, it has been known for a long time that the follicular fluid contains a mucinous substance. The author’s investigations support the view that this substance is a sulfo-mucopolysaccharide and that it is an important constituent of the follicular fluid. It seems reasonable to correlate this substance with the high viscosity of the liquor. The high viscosity and the rheological properties of the liquor seem, in turn, important for the mechanism of ovulation. On this last point particularly much work remains to be done, but it does not seem improbable that the liquor with its mucopolysaccharide is of help in the smooth escape of the ovum, protects it and attaches it to the ovarian surface until it is caught by the abdominal portion of the tube.

Westman showed in 1930 that the egg cell is surrounded by a layer of jelly
during its passage through the tube, and good experimental evidence has been presented that this layer of jelly originates from the tubal epithelium. This investigation supports the view that the jelly layer may, in addition, be derived from the follicular contents. This is also supported e.g. by a photograph by Greulich (see Wharton, 1947), showing the egg cell and surrounding granulosal cells, recovered from the tube of a woman.

Thus, the author's investigations show to some extent why the formation of the follicular fluid must take place as a normal physiological phenomenon. Future research will probably adjust many of the views presented here, but the methods used and the results obtained may help to pave the way for future work.

SUMMARY

A series of investigations with autoradiography, beta radiography, activation analysis, histochemical methods, microviscosimetry and experimental follicular functions have led to the following conclusions:

1. In addition to other compounds, the follicular fluid contains a sulfomucopolysaccharide as an important constituent.

2. The liquor folliculi has a high viscosity, probably depending on the presence of the mucopolysaccharide.

3. The high viscosity (and other physical-chemical properties) of the follicular fluid seem to help in the various stages of the ovulatory mechanism, such as the escape from the follicle, the protection of the egg cell and the attachment of the egg to the ovarian surface.

REFERENCES

Odeblad, E.: To be published, 1954 b.

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