rather than diminish. Thus they are taken away from research, the field of work in which their capacity has been proved. The society has deliberately inverted the order of precedence of professorial functions; it has placed its new professors in a position to regard research as their primary duty, and thereby has sought to recognize research as a definite profession, and to advance and to maintain the principle that the laborer is worthy of his hire no less when engaged in research than when he is employed in class instruction.

The need for a definite systematized policy was made the more urgent by the munificent gift of Sir Alfred Yarrow to the society early this year. In his letter of last February announcing his gift Sir Alfred Yarrow said that he would prefer that the money should "be used to aid scientific workers by adequate payment, and by the supply of apparatus or other facilities, rather than to erect costly buildings, because large sums of money are sometimes spent on buildings without adequate endowment, and the investigators are embarrassed by financial anxieties." In arriving at its new policy the council of the society has been advised by a committee of which the donor is a member, so that there can be no doubt that it commends itself to him.

The first indication of the new policy was afforded just a year ago when Dr. E. H. Starling was appointed Foulerton Professor. Down to that time he had held the Jodrell chair of physiology in University College, London, and in that capacity his primary duty was to teach undergraduate students. The series of brilliant researches by which he has laid physiology and medicine under so heavy a debt were, strictly speaking, secondary. At the same time let us recognize that he could not have been so good a teacher of physiology had he not himself been, through all the years of his teaching, an active research worker. He is continuing to work in the Physiological Institute at University College, which was brought into existence mainly through his exertions, and will remain a permanent memorial of the trust his character and achievements have inspired. The two Yarrow professors—the one, Professor Fowler, of the Royal College of Science, South Kensington, distinguished for his research in spectroscopy and astrophysics, and the other, Mr. G. I. Taylor, of Cambridge, whose contributions to the mathematical theory of hydrodynamics and to the physics of crystals are recognized to be of the greatest originality and importance—will both, like Professor Starling, continue their researches in the laboratories of whose traditions, as the president said, their reputations are already a part.

The policy the Royal Society has adopted to guide it in the administration of the funds that have recently come under its control may therefore be regarded as presenting two closely related but slightly different aspects. In the first place it recognizes that certain professors should be relieved from the duty of teaching in order to devote themselves entirely to researches in which they have already gained distinction; in the second place it establishes the principle that a man of suitable temperament and abilities should be able to look upon pure research as a definite calling or profession in itself, which holds out to him a prospect that in the full maturity of his powers he may be placed in a position to give all his energies to following up the line of scientific inquiry in which he has already achieved success. It is a serious adaptation of Disraeli's rather cynical epigram that nothing succeeds like success.—*The British Medical Journal.*

SPECIAL ARTICLES

THE BEHAVIOR OF THE GERMINAL EPITHELIUM IN TESTIS GRAFTS AND IN EXPERIMENTAL CRYPTORCHID TESTES (RAT AND GUINEA PIG)[1]

THE writer and others have shown that rat and guinea pig testes can be transplanted into other rats and guinea pigs and persist for long periods of time. It is generally admitted by all workers who have observed histological preparations of mammalian testis grafts that the germinal epithelium, the lining of the seminiferous tubules, is without exception degenerate or entirely absent. I pointed out in 1921[2] that all testis grafts do not react in the same way, as indicated by the histological picture; thus (pages 379–382), of two guinea pig testis grafts recovered from spayed females seven and nine months after operation, one consisted of seminiferous tubules entirely devoid of an epithelium aside from a few scattered cells along the basement layer of the tubule, whereas the second one possessed tubules in active mitosis and an epithelium of two to three cells in thickness.

Since the publication of the above results approximately one hundred testis grafts have been recovered from operated rats one to seven months after transplantation. Histological preparations reveal a wide diversity of reactions of tissues following transplantation; differences in the condition of the germinal epithelium as well as of the interstitial cells are very marked. These grafts represent subcutaneous, intramuscular and intraperitoneal transplantations and have been recovered from castrated males, spayed

[1] This investigation has been aided by a grant from the Committee on Sex Research of the National Research Council; grant administered by F. R. Lillie.

[2] *Jour. Exp. Zool.*, Vol. 33.

females, normal males, normal females and females which while possessing the testis graft had become pregnant, delivered and suckled a normal litter of young. So far as a study of these has progressed it is impossible to make a general statement concerning any differential behavior that is correlated with a particular type of animal. It is sufficient to state, at this time, that active cell division may go on in the tubules of grafts in either normal males or in normal females; an epithelium of several cells in thickness, containing many cells undergoing mitosis, is not a rare condition to find. The interesting fact, for the moment, is that grafts taken from the localities mentioned, despite their active mitotic condition, have never contained spermatozoa in the tubules; many cells, apparently spermatocytes, are often found free in the lumen of the tubules, having been loosened from the central border of the epithelium. Some influence is at work that prevents the building up of a completed epithelium with differentiated spermatozoa; instead, the cells near the stage of differentiation either degenerate in place or are cast off into the lumen of the tubules, where apparently they degenerate and are absorbed. No one, to my knowledge, has ever found spermatozoa differentiated from the germinal epithelium of a mammalian testis graft. In birds apparently the smallest nodule of testicular material, grafted or accidentally remaining attached to the peritoneum following castration, may contain an abundance of spermatozoa. Some light is thrown on this condition in mammals by a study of experimental cryptorchidism, a brief discussion of which follows.

Before passing on, it appears desirable to mention again the possibilities of an antagonism existing between the sex glands of the male and the female. Steinach[3] has postulated the sex antagonism idea largely, perhaps, to account for his inability to obtain persistence of testis grafts in females, or ovarian grafts in males, without first having removed the glands of the animal into which the transplantations were made. By transplanting an ovary and a testis at the same time into a previously castrated animal he was able to obtain persistence of each, and considered that the antagonism had been partially broken down by this procedure. Knud Sand, however, was able to obtain persistence of an ovary grafted *into the substance of a normal testis in the male.* Yet he, too, was apparently unable to obtain growth of a subcutaneous graft in an animal of the opposite sex than the graft, without first removing the glands of the host animal. These findings were responsible for his disagreement with Steinach on the question of the *antagonistic action* of the two different sex glands, and to the formulation of his *atreptical immunity* hypothesis. This hypothesis, in brief, supposes that the body produces a specific substance for the nutrition of the sex glands, and that these glands tend to extract this specific nutritive substance from the general circulation and to store the same within its own substance. Thus, should an ovary be grafted subcutaneously into a normal male, the testes would have utilized all this specific substance and none would be available for the graft: hence it would perish. However, should an ovary be placed within the testicle, this specific food principle would be localized at that point and could be utilized by the ovarian graft as well as by the testis itself; thus explaining why subcutaneous grafts do not persist, whereas grafts within the normal gland of the animal are retained.

I have been unable to find justification for either the *antagonism* or *atreptical immunity* hypotheses; no difficulty has been encountered in obtaining grafts one to ten months after transplantation of either testis in females with both ovaries present, or ovarian grafts in males with the two testes present and normal. When the experiments were first begun it was often convenient to operate two animals at the same time, removing one ovary from a female to graft into the male, and a testis from the male to graft into the female. Since in the majority of my reported cases such a procedure had been employed, a certain French reviewer was led to believe that my experiments substantiated Sand's contentions;[4] he has taken for granted the *necessity of the removal of one gland* of the host before the graft (of opposite sex) will grow. Inasmuch as he considers it possible that one gland of the host animal is unable to remove all the specific nutritive substance from the circulation it would follow that the implanted one could obtain sufficient materials for growth and would thus persist.

I wish to emphasize unmistakably that these assumptions are entirely unwarranted. I have recovered many testicular grafts after three to seven months' existence in unbred normal females and in females both of whose ovaries have remained intact and in which pregnancy has occurred, with delivery and the normal suckling period following in the usual manner; yet in such cases the germinal epithelium of the testis graft may be in an active mitotic condition. A student, Mr. N. F. Fisher, has repeated the work of grafting ovaries into males both of whose testes were undisturbed; such ovary grafts, recovered months after the original operation, consisted of typical ovarian tissue in which there were great numbers of active Graafian follicles with normal ovocytes.[5]

In view of the results reported above there should

[3] For a discussion of this question see Moore, *Jour. Exp. Zool.*, Vol. 33, 1921, pages 129–173 and 365–390.

[4] See *Revue Scientifique*, No. 6, 1921 (Bohn).

[5] See Fisher, *Amer. Jour. Physiol.*, Vol. 64, 1923.

no longer be any question of the persistence of a sex gland graft in an animal of the opposite sex with its normal gonads intact. Such assumptions as are implied in the *antagonism and in the atreptical immunity hypotheses* are entirely superfluous and unwarranted so far as my material is concerned.

EXPERIMENTAL CRYPTORCHIDISM

The varying histological reactions of testis grafts had proven so puzzling a study that it was highly desirable to study the progressive degeneration of a testis and the interstitial cell hypertrophy on controlled material. Ligation or resection of the vas deferens (or both) have been reported to produce such a condition as is desired, and should furnish such graded steps as are necessary. With this in mind Mr. Robert Oslund began such a study at my suggestion somewhat over two years ago. Curiously enough, however, the expected results did not follow; indeed, quite the reverse. Degeneration does not necessarily follow such operative procedures.[6] A second possibility of graded degeneration changes of the testis is based upon a study of cryptorchidism. Since undescended testes of mammals (human, pig, sheep, horse, etc.) are devoid of germinal epithelium, apparently without exception, and contain an excessive amount of interstitial cells, it was thought possible to produce such conditions by operative means.

The guinea pig and rat are among that group of mammals in which the inguinal canal is open and the testis easily retracted into the abdomen. It is a simple matter to free the testis from its slight attachment to the bottom of the scrotal sac and the vas deferens from its mesentery. Thus the testis may be returned to the peritoneal cavity to remain therein with all its blood vessels, the vas deferens and nerve supply intact. Preliminary experiments on the guinea pig showed that a testis free, or held fast by sutures, within the peritoneal cavity for sixty days (with or without closure of the inguinal canals) had completely lost its germinal epithelium and possessed an enormous interstitial cell complex.[7]

Further experiments brought to light the fact that a guinea pig testis retained uninterruptedly in the peritoneal cavity for seven days will show considerable degeneration changes; the epithelium of the tubules is usually highly disorganized and cells have been loosened from it. Spermatozoa are rarely present. By fourteen days the degeneration has progressed considerably: by twenty days usually none of the germinal epithelium remains, excepting possibly a single layer of cells at the periphery of the tubule. Beyond this length of time of retention, the interstitial cell mass becomes the outstanding feature of the preparations.

In the process of this degeneration cells appear to become gradually loosened from the epithelium and to escape into the lumen of the tubules; other cells of the epithelium lose all signs of cell boundaries and coalesce into discrete, multinucleate masses of protoplasm. Such "Giant cell like" masses may be loosened from the epithelial layer and be found in the open lumen, or they may undergo further degeneration in the epithelial layer.[8] Such degeneration follows if the testis is free or fastened in the abdomen; whether the inguinal canals remain open or closed; and when the scrotal sac is completely everted and fastened to the peritoneum within the cavity, the attachment of the testis to the scrotum remaining normal.

Many times the testis, having been placed in the peritoneal cavity without closing the inguinal canals, will return to the scrotum completely or partially. Such a testis may be normal, partially or completely degenerate (as concerns the epithelium), depending upon the length of time it has remained in the abdomen before its return. Should adhesion result in retention of the testis in the upper part of the inguinal canal many normal tubules as well as degenerate ones are found.

Considerable recovery of the epithelium is possible after return to the scrotum. Thus, both testes of a normal guinea pig were confined within the peritoneal cavity for twenty days; by a second operation one was removed as a control for the amount of degeneration, whereas the second was returned to the scrotum and fastened by sutures. The epithelium of the testis removed at twenty days consisted of but a single layer of cells in the tubules in the midst of a fibrillar reticulum. The second testis was removed three months after returning it to the scrotum and it was found to have recovered to such an extent that many of the tubules were normal and contained spermatozoa; the majority of the tubules had not so completely recovered.

Thus it is seen (for the rat and guinea pig) that a normal germinal epithelium is dependent upon nor-

[6] See Oslund, *Proc. Amer. Soc. Anat.*, 1923; *Anat. Rec.*, Vol. 25, page 145.

[7] Before completion of my own experiments a paper appeared by Knud Sand (*Jour. de Physiologie*, '21, Vol. 19, p. 515), reviewing his earlier work on this subject, published in his Danish Monograph 1918. My own work confirms and extends the work done by Sand. Other earlier work will be reviewed at a later date.

[8] It should be stated that the effects on rat testes are less extreme than on the guinea pig testis. Often after two months in the peritoneal cavity a rat testis may possess two or more layers of cells in the epithelium, but no spermatozoa are present.

mal relations of the testis to the scrotum; a scrotal testis is normal, an extra-scrotal testis degenerate. Here, then, is a partial answer to the question of why an active epithelium in an intramuscular, subcutaneous or intraperitoneal rat testis graft never possesses spermatozoa. Furthermore, if such a relationship between a normal germinal epithelium and the scrotum holds, it would be expected that a testis grafted onto the walls of the scrotum would develop a normal epithelium.

RAT TESTIS GRAFTS IN THE SCROTUM

In making grafts of testis onto the walls of the scrotal sac one must employ relatively small amounts of tissues in order to permit of vascularization, and preferably testis tissue before the establishment of the germinal epithelium. Testes were taken from just born rats (two to ten days old) and the entire testis grafted onto the walls of the scrotal sac of a sixty-day-old castrated male. Such grafts recovered from the scrotum six months after the transplantation have been found to contain some tubules that were entirely normal and possessing spermatozoa. Most of the tubules were degenerate; many contained an actively proliferating epithelium. To my knowledge this is the only case on record where spermatozoa have been differentiated from a mammalian testis graft.

It is not surprising that all tubules do not contain spermatozoa. Interruption of blood supply is quickly fatal to the germinal epithelium and it must be remembered that the normal testis is vascularized by the internal spermatic as well as by the artery of the vas deferens. The graft is deprived of both these arterial supplies and must depend for its blood supply upon the small vessels of the scrotal sac wall. The limitations of a graft in such a position as this depends upon the amount of blood supply that can be brought to it.

These results confirm our supposition that a normal germinal epithelium and the differentiation of spermatozoa are dependent upon some influence derived from the position of the testis in the scrotum. The factors involved are not fully known but I am inclined to the suggestion of Crew[9] that body temperature may be the responsible agent. The scrotum may act as a local regulator of the temperature of these parts. Details of this work will be presented more fully at a later date.

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[9] F. A. E. Crew, *Jour. Anat.* (Lond.), Vol. 56, p. 98, suggests on hypothetical grounds that the aspermatic condition of imperfectly descended testes may depend upon a temperature gradient locally controlled by the scrotum.

ADDENDUM

Since the above account was written experiments, designed to test the hypothesis that germinal epithelium degeneration in undescended and artificial cryptorchid testes is due to a different temperature relationship established and probably locally controlled by the scrotal sac, have been brought to a close. The writer, in cooperation with Mr. Robert Oslund, using the sheep as the experimental animal attempted to insulate the scrotum from loss of heat by secure wrappings. After a period of eighty days the testes were found to be entirely devoid of spermatozoa. The majority of the seminiferous tubules were decidedly degenerate and presented similar conditions to many of the artificial cryptorchid testes; control testes were in full gametogenic activity.

N. Fukui has shown that local application of heat to the scrotum produces germinal epithelium destruction and the writer has been able to confirm these findings. It thus appears very probable that increased temperature is the operating factor in the degeneration of the epithelium, but it is well recognized that this may not be the only factor.

THE AMERICAN CHEMICAL SOCIETY

SECTION OF CHEMICAL EDUCATION

Edgar F. Smith, *chairman*
Neil E. Gordon, *secretary*

How shall we feed our children? MARIE DYE. The problem of correct food for children may be roughly considered in two parts: first the quantitative, dealing with the amount of food required and second the qualitative, showing the kinds of food. Research in calorimetry has given the basis for the former and enables us to calculate the amount of food required by children of various ages. The qualitative aspect of the food problem necessitates the study of food composition and the research with animals. Fats and carbohydrates are useful chiefly as fuel foods, while proteins, certain inorganic elements and vitamines are needed for growth and maintenance. The amount of protein, calcium, phosphorus, etc., required is determined through balance experiments. It is then a simple matter, when the chemical composition of food is known, to select the kind and quantity to fit the needs of the child. The animal work on vitamines has shown their importance, and our experiments during the war proved that this information may be applied to children. Thus the knowledge of the chemical composition of food and the quantitative needs of the individual give a reliable basis for the selection of food for children.

Some problems in chemical education which are vital to the development of the chemistry in this country: NEIL E. GORDON. Reasons are given for the importance of the twelve following problems in chemical education in the development of the chemistry of this country: (1) Chemical training in the high school; (2) correlation of high school and college chemistry; (3) chemical train-