

OVARIAN ORGANOTHERAPY.

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The organs, tissues, and secretions of animals were extensively employed as therapeutic agents by the ancients, and constituted a prominent part of their disgusting and nauseating medicinal armamentarium. Pliny informs us that the ancient Greeks and Romans ate the testicles of the ass for the purpose of curing impotence, forestalling the later investigations of Brown-Sequard by hundreds of years. In 1852, Dr. Jackson of Philadelphia made a definite attempt to apply animal tissues to the cure of disease by administering the blood of bullocks carefully dried in vacuo, in five to ten grain doses, as a tonic. The use of glandular extracts was revived in 1889 by Brown-Sequard's advocacy of orchitic extract for impotence and certain nervous affections; and the interest was profoundly stimulated by the results which Prof. Geo. R. Murray, of the University of Durham, in 1891, obtained by the use of thyroid extract for the cure of myxedema. Since that period medical literature has been flooded with a deluge of reports of all kinds of extracts. Cerebrine, medulline, cardine, and many others too numerous to mention, have been presented to the profession, tried in the balance of practical experience and found woefully wanting. One would not be surprised to find some enterprising and energetic drug firm vaunting the merits of muscine for pugilists and athletes, or advising political spellbinders to imbibe eloquence and glosio-labial extracts at the same draught.

The popularity of this line of medication depends upon the theory of Brown-Sequard, that all glands, whether provided or not with excretory ducts, have the power to elaborate, in addition to their ordinary secretions, certain materials of unknown chemical composition, which pass into the blood and perform therein definite functions of some kind. The efficiency of thyroid extract in the treatment of myxedema and cretinism has substantiated the theory to a certain extent, but the limitations of its application remain to be determined. The animal extracts which have a particular interest for gynecologists are the uterine, mammary, parotid, thyroid, and ovarian; and of the last of these and its value it is my purpose to speak, hoping to elicit a discussion which may prove valuable to profession and patient.

In studying the action and uses of ovarian extract it is interesting to review the conclusions of Curatulo in regard to the internal secretion of the ovary. 1. The ablation of the ovaries exercises a considerable influence on metabolism. 2. The quantity of phosphates eliminated by the urine is notably diminished after the removal of the ovaries. In reality, this diminution is not due to elimination, which is the same before and after the operation, or to the diminution of the absorbent power of the intestine; for the condition in which the gastro-intestinal tract is found is the same before

as after the operation. 3. The curve of nitrogen, after ovariectomy, ascertained either by Kjeldahl's method or by Yvon's, presents a slight oscillation, without a very distinct tendency to elevation or lowering. 4. After oophorectomy the quantity of carbonic acid eliminated by the respiration, and that of the oxygen absorbed, diminish considerably up to a certain limit, from which time it remains stationary. 5. In animals from which the ovaries have been removed, the curve of the weight is progressively elevated until it attains considerable proportions from 5 to 6 months after the operation. 6. When a certain amount of ovarian juice is injected subcutaneously into sluts deprived of the ovaries, the quantity of phosphates eliminated by the urine, which diminished considerably soon after the operation, tends to increase and even to become superior to that which was ascertained before the operation; when still larger amounts are injected the quantity of phosphates increases in a very marked degree.

Hysterectomy performed in conjunction with oophorectomy does not seem to cause modifications other than those ascertained after simple removal of the ovaries. The author closes his essay with the following theory: The ovaries, like other glands of the animal economy, have, according to Brown-Sequard's general doctrine, a special internal secretion. These glands continually throw into the blood a peculiar product, the chemical composition of which is completely unknown, and the essential properties of which tend to favor the oxidation of phosphorized organic substances, of carbohydrates, and of fatty substances.

It results therefrom that, when the function of the ovaries is suppressed, whether because oophorectomy has been practiced or because the organs do not act, as is the case before puberty and after the menopause, there should be produced, on the one hand, a more considerable retention of organic phosphorus, whence there is a greater accumulation of calcareous salts in the bones; and, on the other hand, the very manifest corpulency which is ordinarily seen after oophorectomy or after the menopause.

This probably suggested the value of substitution therapy, the restoration to the diseased body of chemical substances the removal of which from the normal body gives rise to symptoms of disease. It is not necessary to review the various psychic or vasomotor disturbances which are associated with the natural and the premature menopause; they are too well known to need further comment.

Werth of Kiel was the first who made use of the ovarian treatment in troubles which accompanied the disappearance of the secretion of the ovary following either the menopause or surgical intervention. Out of ten cases, in two only did the treatment fail to bring about any result; in the other eight there was a diminution of general pains, of the headache, of the loss of appetite and sleep, of the palpitation and

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of the feeling of anguish. Mainzer of Berlin obtained a considerable amelioration of the symptoms following double ovariectomy by administering to his patients the raw ovarian substance of the cow or the calf, in daily amounts of from 75 to 150 grains. It has been demonstrated that such large doses are not necessary. Mond has used it successfully in disorders of the natural menopause and in amenorrhea due to atrophy of the genital organs, or to neurasthenia. Spillman and Etienne also obtained good results in *chlorosis* from the administration of the fresh ovaries of sheep, of the dried ovarian substance, and of the ovarian juice. According to these authors, this treatment acted by facilitating the elimination of the toxins, increasing the red globules and causing the reappearance of menstruation. Mairet, Jayle, Touvenant and Jouin have published observations in which this medication has led to favorable results in the treatment of amenorrhea and chloroanemia. Guerder and Vigier have found the symptoms of the natural menopause were relieved. The latter, after freeing the ovarian substance from foreign matter as fat, fibres, etc., mixed it with bicarbonate and charcoal, which preserves it indefinitely without interfering with its therapeutic effects.

Bodon (*Centralblatt für Gynakologie*, August, 1897) reports three cases in which he employed ovarian tablets with good effect. The third was that of a virgin, 18 years old, who had suffered with epilepsy since her first menstruation and had been under treatment for years. Bromides and other drugs had proved utterly futile. She began with one tablet daily and increased the number to ten. In the course of several months the epileptic attacks ceased; but discontinuance of the drug was followed by fresh seizures and its resumption again caused their subsidence.

Jacobs (*Semaine Gynecologique*, June 22, 1897), although skeptical at the beginning of his observations, had confidence in the remedy to continue its use. The extract of the ovaries of recently killed animals was used and he has tabulated 81 cases, of which only 5 are classed as failures. In one case of obesity with amenorrhea of 19 years standing, the obesity diminished and menstruation became regular. Another patient, 21 years of age, with undeveloped genitals, had never menstruated; but after taking ovarian extract for a month, menstruation appeared and has continued regularly ever since. Jacobs believes that suggestion plays a prominent part in some of these cases, though not in all. Landau (*Berlin. klin. Woch.*, No. 25, 1896) believes that this remedy does possess the power of modifying the unpleasant phenomena of the climacteric whether physiologic or anticipated, without producing any evil effects, and that it deserves careful consideration.

Chrobak (*Cent. für Gynak.*, No. 20, 1896) administered ovarian extract made from the fresh ovaries of cows, to a number of castrated women and had good results in two cases reported. Fosburg (*British Med. Jour.*, April 24, 1897) gives the history of a patient who at the climacteric was much troubled with frequent and violent flushing, the face often being in a burning heat while the hands and body were icy

cold. Five grain platinoids of ovarian gland, administered 3 times daily, gave complete relief before 3 dozen were taken; and one platinoid given occasionally prevented recurrence.

Seeligman (*Allg. Med. Centralzeitung*, No. 3, 1898) reports 15 cases treated with extract of the ovaries of sheep and pigs, and concludes that the remedy has a decidedly beneficial effect, not only upon typical climacteric phenomena, but also upon the psychic condition and upon constitutional diseases such as gout, psoriasis, etc., which after long remaining latent develop at the menopause. Bate (*Louisville Journal of Surgery*, vol. v, 1898-99, p. 11) states that "physiologic action of ovarian extract as now observed is vaso-constrictor, nerve sedative, emmenagogue, and anti-anemic"; a combination of qualities which, if it truly possessed them, would make it a most valuable acquisition to our pharmacopeia.

Stimulated by such enthusiastic and gratifying clinical reports I began the use of ovarian extract, employing capsules prepared by a reliable firm, since the ingestion of raw ovaries or nauseous doses is not usually appreciated by the average American woman. For the past three years, in selected cases, in dispensary and private practice, the effort has been made to obtain some definite result from the use of this carefully prepared ovarian extract, in 3 classes of cases: (1) Those suffering from amenorrhea, dysmenorrhea and other forms of pelvic disease; (2) those suffering from symptoms following the removal of the uterine appendages, for the relief of the vasomotor changes, the flushes and cardiac neuroses which, with indescribable depression, are so often produced by the premature menopause; (3) the disturbances associated with the natural menopause. My first case was that of an intensely neurotic patient suffering from artificial menopause. Marked relief was noted for a brief period; then there was a recurrence of the symptoms. Later the patient became an adherent of Christian Science and has obtained more relief from auto-suggestion than from inspissated ovaries. Many other disappointing instances were met with. Patient after patient would faithfully take the extract to the exclusion of other remedies without any perceptible result, although occasionally the effect would be apparently so marked and the results so satisfactory as to encourage its further use. For instance, such a history as the following, taken from the case-book at St. Joseph's Hospital, would incite to renewed confidence in the efficacy of the preparation. Jan. 9, 1901, Mrs. A. C., aged 26 years, had had double ovariectomy performed by Dr. Joseph Price; general condition good, pelvic examination negative, but complained of hot flushes every few minutes and extreme nervousness. Five grain capsules of ovarian extract, 4 times daily, were ordered. The patient returned in 3 days stating that the nervousness was better and the hot flushes decreasing in frequency. In one week the nervousness had disappeared and hot flushes occurred only on exertion, two or three times daily. Another case in point was that of Mrs. J. W., patient of Dr. Chas. B. Smith of Newtown, Pa., who was operated upon for double pyosalpinx. Within 2 months after leaving the hospital she began with the usual vasomotor phenomena and relief was secured by the administration of 5-grain doses

of ovarian extract 3 times daily. Time and a regard for your patience prevent my giving a detailed history of more cases; besides the recital of our failures is never pleasant; yet it seems unfortunate that more of those who have been disappointed in their use of this product have not given their experience; only a few seem to have done so. Montgomery (*International Med. Mag.*, Nov., 1900) states that he has never seen the slightest influence from the use of ovarian extract although he has found the thyroid especially valuable in the treatment of cases of myxedema, obesity, and in some forms of sterility; and Baldy says that "a careful consideration of this subject forces one to the conclusion that it is destined quickly to follow in the steps of the testicular injections urged several years ago with the object of renewing youth." Johnstone of Cincinnati may give the correct explanation of the failure to secure more definite and satisfactory results from the use of ovarine. He says: "There is not an iota of proof that the ovary has any other function than the manufacture of eggs. The ovary is in no sense a gland. Its epithelium is arranged for the purpose of being cast out and lost, and is not placed so that its secretions, if it has any, could be absorbed either by ducts or blood-vessels. Anatomically, the ovary does not resemble the suprarenal, the thymus, or the thyroid gland. The thymus is a lymphatic gland, the thyroid and the suprarenal have a rich supply of blood-vessels so arranged that each epithelial cell is closely approximated to a venous radical, thus providing for a rapid absorption of whatever secretion its cells may make. The ovary has a true duct, through which its epithelium, when cast out, passes off en masse to the outer world."

Probably Jacobs struck the keynote when he said that "suggestion plays a prominent part in some of these cases"; for this might explain why we have successes and failures under the same conditions without apparent cause. Not-

withstanding the many brilliant results referred to in this paper, experience leads me to the following conclusions based upon the use of the American product upon American women: (1) The employment of ovarian extract is practically harmless, as no untoward effects beyond slight nausea have been noted even when full doses have been administered. (2) In the treatment of amenorrhea and dysmenorrhea no good results were secured. (Although in some cases of amenorrhea of obesity, remarkable results have been obtained by the use of the thyroid extract.) (3) The best results were seen in the second class of cases, for the relief of symptoms of artificial menopause, when in a few instances the congestive and nervous symptoms were apparently ameliorated. (4) No appreciable result was noticed in the use of ovarine in the natural menopause. (5) No definite or exact reliance can be placed upon the drug, as it often proves absolutely valueless where most positively indicated. (6) It is extremely problematic whether, in those cases in which relief was noted, the effect was not due to mental suggestion rather than to any physiologic action of the drug. The neurotic type of individual demanding this treatment will often be relieved by any simple remedy. (7) In those instances in which effects were noted increase in dosage seemed to have little influence in maintaining the effect or preventing the patient from becoming accustomed to its use. (8) In conclusion, the theory which suggests the use of this extract seems to be at fault, and the administration of ovarine or ovarian extract is based upon a wrong assumption as to the function of the ovary. In organotherapy, the best results have been obtained from the use of the thyroid and adrenal glands, and the ovary in function is in no sense analogous to these organs. Its principal function is ovulation, and if any peculiar product is coincidentally manufactured, the isolation of this product has not yet been accomplished.