

Rejuvenescence and the Testicular Graft.

By Dr. F. H. A. MARSHALL, F.R.S.

IT has been known from very early times that castration in both man and animals, besides causing the suppression of the sexual instinct, produces marked changes in the bodily conformation and the secondary characters of sex, and that these effects are far more definite if the operation be performed before puberty. There are numerous references to the subject in the works of Aristotle, who remarks on the immense modifications in the general configuration brought about by the mutilation of a comparatively minute organ. The abnormal height of the eunuch, his undeveloped larynx and soprano voice, and the absence of hair on the face and other parts of the body where it is usually present in men are among the well-known effects of testicular deprivation. The domestic animals also furnish striking examples of the consequences of castration, and the same may be said about birds. Thus the testes, besides being responsible for the development of the sexual instinct, are an essential factor in the formation of the bodily characters associated with maleness. The manner in which this influence is exerted, however, has only comparatively recently been ascertained, and there are still many gaps in our knowledge.

According to Berman, the author of "The Glands regulating Human Personality," the first to conceive the idea that the gonads exert their effect through an internal secretion poured into the blood was Bordeu, who was Court Physician to Louis XV. in the eighteenth century. Berthold, however, in 1849 was the earliest to base the idea on experimental proof. This investigator removed the testes from cocks and transplanted them into new positions in the body, and he noted that the birds developed or retained their male characteristics (voice, sexual and combative instincts, growth of comb, wattle, etc.) just as though they were normal males. These results were attributed by Berthold to substances formed by the testes irrespective of their position, and thus he was the first to put on a definite experimental basis the idea of an organ elaborating a hormone which, after being carried in the circulation, acted upon other and distant parts of the body. Little account was taken of Berthold's work at the time, and it was not until much later that the conception of organs having an endocrine function was revived by Claude Bernard, who applied it to the liver. In recent times Berthold's work on the testicular graft has been confirmed for a large number of animals, and the fact that the testis, in addition to producing the semen, gives rise also to one or more chemical substances of the nature of hormones has been established.

The notion that the testis produces an internal secretion which, besides being responsible for the male characters, possesses also a rejuvenating influence, is a somewhat different one. It was originally put forward in 1889 by Brown-Séquard, who injected testicular extract, first into animals and then into himself. He was convinced that in both cases beneficial effects accrued, and claimed that he himself underwent a radical change and regained the force and vitality of former years. The extracts were made from dogs' and

guinea-pigs' testes, and were injected subcutaneously. At this time, Brown-Séquard was seventy-two years old. The supposed rejuvenating effects, however, did not last, and although this form of treatment was extended to some hundreds of patients suffering from various diseases (rheumatism, sciatica, locomotor ataxia, tuberculosis, etc.) by Brown-Séquard and Brainard, who claimed that good results often followed, the practice of testicular injection was soon discontinued and became generally discredited.

In recent years, however, the idea of testicular rejuvenation has been revived in connexion with grafting experiments. In 1913, Lespinasse, an American doctor, recorded a case of testicular transplantation in a man, but gave no evidence of the persistence of the graft beyond that afforded by sexual potency. About the same time Lydston, of Chicago, is reported to have done similar work with human grafts, and the medical department of the California State Prison is said to have organised transplantation experiments in which testicles obtained from executed criminals were grafted on to senile individuals, but there is no satisfactory evidence as to the results obtained.

More recently (1918) Stanley and Kelker have performed the same operation, and in further experiments the testes of animals were substituted for human ones. It was believed, however, that in all cases the grafts became necrotic and were either absorbed or else the site of operation opened up and the necrotic material was discharged. In a later paper, Stanley has described a large number of experiments (more than 1000 had been carried out by 1922) in which men were injected with partially macerated testis by a syringe. With this method the danger of sloughing was much reduced, and the injected substance could be felt under the skin for months, but it was eventually absorbed. From these experiments Stanley concluded that animal testicular substance injected into the human body caused decided benefit for some time. Among those treated were patients suffering from neurasthenia, epilepsy, asthma, tuberculosis, diabetes, and many other chronic diseases, as well as senile decay. Most of the subjects reported increased sexual activity and resumption of virility where this had been lost. It is said, further, that testicular substance often has a beneficial effect in relieving pain of unknown origin and in promoting bodily well-being, and that the power of vision is sometimes greatly strengthened. The testicles used were those of goats, rams, deer and boars.

Three cases have been described by Lyons in which rams' testicles were transplanted on to men suffering from debility and impotence, and in two of these favourable results were claimed, but the fate of the grafts was unknown.

The above recorded experiments were all carried out in America in the last decade. In the same period, numerous operations of a similar order have been carried out in Europe. In 1915, Lichtenstern, of Vienna, operated on a soldier who had lost his testicles as a result of being wounded in the War. After a few months, the patient showed all the usual signs of

complete castration and suffered from want of vigour and general apathy. Lichtenstern then engrafted an undescended testicle from another individual, and as a consequence the symptoms of castration disappeared and the man became normal. Two and a half years later he was still normal, having been married fifteen months. Further cases of testicular transplantation in men are recorded by Lichtenstern as well as by Kreuter and Mühsam, the operation being performed for eunuchoidism and homosexuality, as well as for debility and impotence, and successful results are claimed. In none of these cases does there appear to be definite evidence as to the fate of the graft, but it would appear almost certain that it must have persisted for some time.

Voronoff, whose work on the so-called "monkey gland" has attracted so much attention, began his experiments on the testicular graft at the Collège de France in 1917. His earlier work was upon sheep and goats, in which he grafted young testes into old animals and into animals castrated before puberty. The best results were obtained by grafting the testes into the scrotal sacs, or in the case of aged animals, upon the testes already present. Retterer and Voronoff, in a paper published last summer, tell us that some of these animals are still under observation at the Laboratory of Experimental Surgery of the Collège and that they continue to display sexual vigour and ability to copulate. The success attending these experiments led Voronoff to attempt testicular transplantation upon aged men. In connexion with this work, two points are strongly emphasised; first, the advantage of making the graft in a suitable position and preferably the natural position of the organ; and secondly, the importance of biological affinity between the individual from which the testis is taken and the recipient of the graft; consequently, in carrying out testicular transplantation from animals to men, Voronoff selected the chimpanzee as the most suitable animal from which to obtain the graft, since of all the anthropoid apes this species is believed to be the nearest akin to man. The result of the operation in many instances is claimed to be entirely successful. The walls of the arteries are said to have become softened and the capacity for work increased, and, in short, a complete restoration of mental and muscular vigour is stated to have been attained. In the majority of men so operated upon sexual potency also is said to have been revived.

In some of Voronoff's experiments there is definite evidence concerning the persistence of the graft, and Retterer and Voronoff have described microscopic sections of graft tissue after several months of transplantation. Thus the figure of a section of a goat's testis a year after grafting shows cells which might

reasonably be supposed to have had an internally secreting function, though the tissue as a whole had undergone considerable degeneration and neither spermatozoa nor interstitial cells can be detected. The authors state that the condition of the transplanted chimpanzee's testis is similar, but they do not appear to have recorded the duration of the graft. On the other hand, Thorek, an American surgeon, who has recently confirmed Voronoff in regard to the persistence and efficacy of the chimpanzee graft when made upon man, has described and supplied photographs of sections of such grafts when removed four months after transplantation, and these show an abundance of secretory cells and every evidence of active life, though the seminiferous tubules had undergone incomplete regression. The good results are attributed to a new technique whereby the vascularisation of the graft was greatly improved.

There is one point of importance on which Retterer and Voronoff differ from most physiologists, and this relates to the elements which are responsible for producing the internal testicular secretion. The bulk of the experimental evidence is strongly in favour of the view that the testicular hormone is elaborated by the interseminiferous or interstitial cells, and Steinach, who has called this tissue the "puberty gland," attributes the supposed rejuvenating effects of vasectomy to the hypertrophy of this gland, pointing out that the spermatogenetic tissue after this operation undergoes degeneration as noted by former observers. According to the French investigators, however, the testicular graft does not contain interstitial cells, the rejuvenating function being due to the epithelial cells which continue to discharge the problematical secretion into the circulation notwithstanding the fact that they become converted by poverty of nutrition into "young connective tissue." On the other hand, in Thorek's preparations, the interstitial cells have proliferated and appear to have been functionally active.

In conclusion, it must be emphasised that the work is as yet in the experimental stage. In many of the cases recorded the effects of "suggestion" are not satisfactorily excluded, and the evidence as to the persistence of a functional graft is still meagre. That the histological results are conflicting and that those of Voronoff are contrary to the usual view as to the source of origin of the hormone, are valid reasons for reserving judgment. Nevertheless, it must be pointed out that the accumulation of evidence in support of the contention that a testicular graft obtained from another individual, and even from another species, may exert a definite physiological influence upon the recipient, is considerably greater than many men of science have so far been disposed to admit.

Some Aspects of the Physical Chemistry of Interfaces.¹

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LET us now inquire how far the phenomena which are characteristic of a gas-liquid interface occur also at the interface between two immiscible or partially miscible liquids. Many years ago it was shown by Gad and by Quincke that a fatty oil (such as olive oil)

is very readily dispersed in the form of an emulsion by a dilute solution of caustic soda. Some experiments which I once made showed that a neutral hydrocarbon oil could be similarly emulsified in a dilute aqueous solution of alkali if one of the higher fatty acids was dissolved in it, whilst the lower fatty acids do not

¹ Continued from p. 870.