TISSUE AND ORGAN TRANSPLANTATION*

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If one removes a portion of tissue from the body, it does not die at once, it retains its viability for a variable length of time. The viability of this removed tissue varies according to the nature of the source and the type of the tissue, the duration of its life depends upon its environment, as the temperature, etc. Plant grafts survive their removal for a long period of time; animal tissues a shorter period, and tissue from the more highly differentiated and organized animals dies sooner than that from the lower species.

Should the removed portion of tissue be replanted into the body from which it was taken, regardless of whether it is replaced on the same site or in a more remote location, it is called autoplastic transplantation. If the tissue is planted into an individual of a like species, it is termed homoplastic transplantation; if into one of another species, heteroplastic transplantation has been performed. On the other hand, grafting of tissues from the cadaver or of dead tissues is known as implantation.

Tissue transplantation has been employed for a long time, but organ transplantation has been made possible only during the last fifteen years, coincident with improved operative technic, namely, the perfection of the blood-vessel suture.

(The author then covers the ground of skin, mucous membrane, subcutaneous tissue, fat, muscle, bone, epiphyseal cartilage and joint transplantation. This portion is omitted since these subjects are also fully treated in the paper of Prof. Lexer, to which reference should be made.)

Blood-Vessel Transplantation.—After the failures of Glück, Exner and Höphner, Carrel and Mosel first were able to transplant veins into arteries. Carrel and Guthrie both made the observation that the vein becomes wider and the walls accommodate themselves to the increased pressure. Since then, due to the investigations of Borst, Enderlen and Stich (with an observation extending over 409 days) the possibility of autoplastic vein transplantation into arteries has been realized.

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Autoplastic insertion of an arterial segment into a vein was followed by thrombosis, in the hands of Borst and Enderlen when performed on a dog.

Homoplastic transplantation of artery to artery was first attempted by Höphner by planting the femoral artery into a resected carotid, and pulsation was demonstrated 45 days later, when the artery was exposed to view. This was done on dogs. Carrel, Stich and others also report good results. Microscopical examination of a case of Borst and Enderlen showed that growth over the suture line arose only from the intima and the connective tissue of the carotid stump of the recipient.

In man, Delbet attempted the above procedure. He wished to repair a defect, eight centimetres in length, of the femoral artery after extirpation of an aneurism, with a piece of femoral artery obtained from a coincident amputation of the thigh. As the artery of the donor was sclerotic, he was compelled to desist, and content himself with ligation of the femoral, because the sutures would not hold.

The first to attempt heteroplastic blood-vessel transplantation was Höphner, who transplanted the aorta of rabbits and cats into the femoral artery of the dog. Hemorrhage or thrombosis followed. These experiments were repeated by Stich in the clinic of Garre; in spite of the theory of Payr, vessel sutures were employed. The first attempt resulted in an astonishing success, following implantation of a cat's aorta in place of four centimetres of a resected carotid of the dog in which autopsy *in vivo* after fifteen days demonstrated pulsation as in a normal artery. Further transplantation of cat's and rabbit's aortas into the resected carotid of the dog after 51 and 52 days, was attended with good healing and function. A segment five centimetres long of the posterior tibial artery, obtained from a freshly amputated leg of a man, was successfully transplanted into the carotid of a dog. The observation period was only fourteen days in this case. Of six heteroplastic transplantations, half were successful. These positive results were soon confirmed by Carrel. He transplanted the segments of the carotid or the jugular veins of dogs into the resected aorta of cats. In three out of five cases the suture lines broke down, while in the fourth case, six days after the above-mentioned extirpation, there was demonstrable functional result. In the fifth case, exploratory laparotomy showed good pulsation in the aorta and in the transplanted carotid segment, and 78 hours after the operation the condition of the animal was good and there was vigorous pulsation in both femoral arteries. Ward, also, sutured a piece of the aorta of a rabbit into the carotid of a dog; up to the seventieth day, the functional result was

good. Borst and Enderlen performed two heteroplastic transplantations from the cat to the dog and from the goat to the dog. In the first instance, examination 74 hours later demonstrated between the obliterated suture lines of the carotid stump a thin, smooth, light brown tissue strand. This was the remains of the completely absorbed implanted cat's aorta. In the second case, transplantation of the goat's carotid into the dog's carotid, the former after 87 days, was found thrombosed and obliterated.

When one examines the transplanted heteroplastic tissue which is functionally useful, it histologically is anything but normal. In Stich's specimens, the transplanted material was completely disintegrated, for in three weeks there was invasion by a rich cellular tissue derived from the vessel of the recipient into the human, cat, or sheep vessel, and in a shorter time the media was represented by rests lying as scattered areas of tissue in the newly formed scar tissue. Together with these changes, thrombus formation in the lumen of the vessel took place. In those parts of the vessel wall which remained free from these changes for a time and which retained their normal endothelial lining, sooner or later the greater portion of the intima became covered with fibrin, soon becoming organized and covered with fresh endothelial cells. Wood, after examining wax preparations under the microscope, found disappearance of the normal construction of the transplant with substitution of the vessel by fibrous tissues.

Material for transplantation was also obtained from the fresh cadaver. This was called by us implantation. Makkas, Dowman and Stich sutured into the circulatory system of animals, vessel segments obtained from animals killed with chloroform, the specimen being removed in from fifteen to ninety minutes after death and placed in physiological salt solution. Out of five attempts, three were successful while two were followed by fatal hemorrhage.

Carrel and Guthrie extirpated portions of vessels from living animals or from animals shortly before death, placed them in Locke's solution in a glass chamber, at from zero to one degree Centigrade, and preserved them for weeks under sterile conditions. Later these segments were grafted into animals (homoplasty) and good results were obtained even with tissues preserved for 35 days. Microscopic examination revealed extensive changes in the vessel walls.

Bode and Fabian preserved portions of vessels in Ringer's solution at from zero to one degree Centigrade for 60 days and implanted them in dogs, using the vessel suture. In the majority of instances, total thrombus formation occurred, while in the minority the lumina re-

mained patent. Bode and Fabian are of the opinion that after preservation of the segments for more than 35 days in the ice box, they become predisposed to injurious changes in the vessel, which they admit cannot be demonstrated microscopically.

Carrel performed heteroplastic implantation with segments of dog's carotid and jugular veins, which had been preserved in the ice box as long as three weeks and implanted into the resected aorta. The functional healing was apparently successful, although it could not be proved microscopically that the implanted vessel became part of the recipient's tissue. Carrel also performed implantation of a portion of the popliteal artery of a man, which had been preserved for 34 days in Locke's solution, into the aorta of a dog. Five and one-half months later autopsy *in vivo* demonstrated the implanted human popliteal artery in the same condition as during the implantation, and fourteen months later normal pulse beats were found in both femoral arteries. Guthrie also was able to successfully implant into a dog's artery a portion of cat's aorta which had been preserved for four weeks in formalin; and Bode and Fabian report implantation of human vessels into dog's arteries after preservation in the ice box. Regarding the changes which take place in veins after transplantation into arteries, Carrel states that first on account of the increased blood-pressure there occurs a hypertrophy of the walls followed later by a disappearance of the muscle bundles with sclerosis of the wall by means of infiltration with fibrous tissues. Whether or not there later occurred further changes in the vein is not known, but it is very probable.

Vessel transplantation, however, has been utilized for other purposes than for substitution of vessels. Eiselsberg reports a case of perineal hypospadias in which he utilized a portion of the saphenous vein as a substitute for the urethra, and almost complete healing was obtained one year after the successful transplantation. The sequel of this grafting is a strong tendency to shrinkage of the vein. Bakasch substituted in a case of scrotal hypospadias a portion of the basilic vein for the absent urethra with faultless healing, but he fears that this healing will not be permanent. Other surgeons also have substituted the saphenous vein for congenital and acquired defects of the urethra sometimes with, and sometimes without, success. The gradual disintegration of the vessel segment with subsequent cicatricial narrowing is due to the immediate flow of urine over the endothelium, as proved by Tietze, and Lexer has devised the operation and pleads for the production of a fistula over the implanted vascular tube.

Floercken attempted to plant segments of the carotid into the urethra and observed that the endothelium, even when autoplasty is performed, disintegrates, after which suppuration and necrosis of the wall takes place. Here, also, it is true that the immediate flow of urine causes irreparable injury to the endothelium. Vessels which have been utilized to repair gall-duct defects disintegrate probably because of contact with bile.

Ritter recommends in the repair of injuries of the tendons, where tendon suture is possible, but where the union is uncertain, the use of vascular tubes as shields into which the ends of the tendons lie.

Segments of vessels have been utilized with good results, especially autoplastic transplantation of the saphenous vein, as a bridge in the repair of nerves. Some surgeons have seen good results with homoplastic vessel transplantation for this purpose.

Heart.—Carrel and Guthrie have performed transplantation of the heart. They transplanted the heart of a small dog to the neck of a larger one and united the divided ends of the jugular vein and the carotid artery with the aorta and the pulmonary artery and the vena cava to the pulmonary vein. The transplanted heart after a short time again began to beat vigorously. At first the auricles, finally also the ventricles, began to beat at the rate of 88 to the minute, while the heart of the recipient beat 100 to the minute. Two hours later thrombosis set in so that the observation terminated.

The above authors also extirpated the heart with the aorta and vena cava and both lungs of a kitten one week old and planted them on the neck of a large adult cat. The aorta was united to the peripheral end of the carotid and the vena cava with the peripheral end of the jugular vein. Circulation in the coronary artery was established at once and the auricles began to beat. The lungs became red and in a few minutes visible pulsations of the ventricles set in. Dilatation of the right heart soon occurred because of the occurrence of œdema of the lungs. In two days the animal died of an abscess of the neck.

Thyroid Gland.—Shiff concerned himself with thyroid gland transplantation. He transplanted the thyroid of a dog into the peritoneal cavity of another dog. Some time after the transplantation the animals were killed and it was found that the transplanted glands either entirely disappeared or that only pale red vascular spots were visible at the site of transplantation. Histological examination of these vascularized areas was not undertaken. Thus homoplastic transplantation yielded negative results. Eiselsberg obtained successful results in experiments upon cats. He performed his operation in two steps, removing half of

the thyroid and planting it between the abdominal muscles and the peritoneum. As the second step, a number of weeks later he extirpated the other half of the gland. Tetany did not occur and only appeared when the transplanted and healed thyroid was subsequently removed. In Eiselsberg's researches, autoplastic transplantation of the thyroid only was considered. However, since in these researches the parathyroids were also transplanted the question remained open, whether or not the thyroid in itself functionated. At any rate, two observations speak in favor of the functional ability of the transplanted thyroid gland. First, as shown by Cristiani, that half of the thyroid when transplanted into the ear becomes larger when the other half is extirpated, and, second, the fact shown by Salzer of the rapid encapsulation and enlargement of the autoplastic transplanted half of the thyroid when the second half is removed at the same time.

The question as to where the thyroid should be transplanted, in the spleen after Payr, in the peritoneum, or in the bone marrow after Kocher, or in the subcutaneous cellular tissue after Cristiani, is as yet undecided. As a result of experimental investigation which was undertaken by Carraro, of Ribbert's Institute, it appears that the peritoneum or the subcutaneous cellular tissue hold the preference over all other tissues as implantation sites, while the bone marrow, spleen, and liver are entirely too vascular, since the transplanted portion of thyroid at first is always surrounded by a thick layer of fluid blood which forms a more or less thickened ring and later chokes the transplanted piece by means of cicatricial contraction. Bramann believes that this fear of Carraro's can be overcome in making use of the medullary cavity if one takes the precaution to curette out the marrow down to the compact bone and then to fit the transplanted piece so that very little blood can surround it.

The investigations of Stich and Makkas in autoplastic as well as in homoplastic transplantation of the thyroid, have been attended with marked advances in this field. Instead of bothering with circular sutures of a very small artery, they resected a rhomboid flap of the carotid and inserted it in the respective hole of the other carotid. Also the difficulties of vein implantation, which were greater than arterial implantation, were also fortunately overcome. Of the homoplastic transplantations, none was successful, while two out of three autoplastic transplantations were attended with success. One dog lived 31 days and the other 345 days after operation; they were lively and differed in no way, especially in intelligence, from normal dogs. The anatomically healed thyroid performed normal functions and proof of this was

shown when, after 245 days, extirpation of the healed thyroid was performed, after which the dog became ill and three weeks later he died of cachexia. Thyroid transplantation from man to man has yielded no results. The normal upper pole of the thyroid was transplanted in three cretins by suturing the superior thyroid, artery and vein to the axillary vessels. The grafts healed and after several weeks could be easily palpated, but later became gradually absorbed. The transplantation had no influence upon the intelligence or the growth of the animals.

Attempts at heteroplastic transplantation of the thyroid so far have been fruitless, as have been attempts to replant animal thyroids into man extra- or intraperitoneally, and when Kocher obtained improvements in a case of cachexia strumipriva after heteroplastic transplantation, it can be attributed to the subsequent absorption of the thyroid glands. (Beneficial effects being due to absorption of the thyroid secretion.—Translator's note.)

Parathyroids.—The first who transplanted the parathyroid was Waldbaum. He transplanted the external parathyroids autoplastically on to the peritoneum of the stomach and at the same time or at another sitting extirpated the internal parathyroids. He established, as a result of this experiment, that the external parathyroids could not maintain their function alone without aid from the internal ones, since the animals came to a cachectic end.

Kamus in 1905 transplanted by homoplasty the parathyroids from the rabbit into the ears of animals from whom he removed the parathyroids, as well as into animals who had not been so treated. The glands which had first healed finally completely disappeared. Cristiani, laying the cause of Kamus' failure to the fact that the ear of the rabbit was a poor bed for the implanted tissue, was able to microscopically demonstrate after autoplastic transplantation the parathyroids in the ears of cats five years later, and in rats two years later. In 1907 Biedel reported the successful autoplastic and homoplastic transplantation of parathyroids into the spleen of dogs and cats. In the same year Pool reported heteroplastic transplantation of parathyroids in which the rabbit was the donor and the dog the recipient. The external parathyroids of the rabbit were transplanted into the spleen of the dogs and the parathyroids of the latter removed. All the dogs developed tetany. Pool, therefore, discarded the heteroplastic transplantation of parathyroid and believes that even with a successful homoplastic transplantation one is not certain that the homoplastically transplanted parathyroids, even if they heal, are functionally valuable. Iselin is of the

same opinion, as the result of experiments with which parathyroids were transplanted into tetanic rats after parathyroid extirpation. Leischner reports successful autoplastic transplantation of parathyroids, and he also obtained healing in homoplastic transplantation, but in the latter instance, working with Kohler, he admits that the homotransplanted material is of little use, as the foreign tissue, after a short time, is absorbed. Shortly after Leischner's first work there appeared the conclusions of Minkiewitsch that all transplanted thyroids, whether by autoplasty or homoplasty, finally disintegrate even if they functionate for a short time, a fact which is not certain.

Pfeiffer and Mayer obtained a good functional result after autoplastic transplantation and healing of parathyroids. Hermann and Harvey confirmed these results with homoplasty, although success is not always certain. Melinkow reported like results and was able to prevent the development of cachexia. Landois performed transplantation of parathyroids in the dog, autoplastically and homoplastically by artificial emboli in the lumen of the external jugular vein, thus supplying nutrition to the tissue from the circulating blood, and at the same time providing a drain for the secretion of the transplanted organ. It was possible to cause healing with good function of the autoplastically transplanted parathyroids but the majority of the dogs died after a few weeks of inanition and hemorrhage without tetanic symptoms. Homoplastical transplantation of the parathyroids yielded bad results, the animals failing after operation or dying of tetany. Landois therefore concludes that homoplastic transplantation of parathyroids in man for therapeutic purposes is without hope.

Adrenals.—In 1887 Cannalis attempted implantation of small portions of the adrenal glands, without success, as the implanted pieces became necrotic and were absorbed. De Dominicis found in adrenals planted into dog's kidneys, no change after 10 to 15 days, and Pool in his work on rats noted that the medullary portion disintegrated, while the cortex regenerated. This fact was confirmed by Cristiani, and Stilling found in adrenals transplanted into the scrotum of rabbits that it contained typical cortical substance after three years. Monsen and LePlay transplanted the left adrenal into the spleen and after several weeks removed the right adrenal. Rabbits survived for three days, young dogs seven days. While the medulla disappeared rapidly, the cortex survived for a long time. Shiota transplanted the adrenal into the spleen and kidney. The animals survived. The transplanted adrenal loses its adrenalin content in 48 hours quicker in the spleen than in the kidneys. After 24 hours, there was no sign of medulla, while cortex

could be demonstrated 10 to 17 weeks later. The survival of the animals after later extirpation of the second adrenal proved the functional ability of the transplanted adrenal.

The adrenal transplantations of Habraro and Störck were successful. In one-half of their cases there was functional as well as anatomical permanent success. The failures can be accounted for by the insufficient nutrition of the transplanted organs. The microscopical examination of the transplanted and healed adrenal showed that in no case did the organ retain its original structure, but it underwent regressive and necrotic, as well as hypertrophic, changes. In the first few days after the transplantation there occurred regressive metamorphosis of the adrenal so severely that only those portions remained alive which were in contact with the vessels. At this site, there begins in the first few weeks after the operation, a vigorous parenchymatous activity which encroaches upon the degenerated portion of the organ. The hypertrophic tissue may later again regress or even become necrotic. The newly formed cell masses may take on the normal form of the adrenal, but there may be some irregularity not only in the cortex, but also in the ramifications of the medulla. In successful transplantation not only is the cortex preserved, which fact has been the basis of all investigations so far, but the medullary substance also remains alive and is able to regenerate and hypertrophy as well as the cortex. Permanent results five months after transplantation have been obtained, and in most cases a new adrenal was built up in which cortical and medullary substance replaced the regressive and necrotic tissue.

The functional proof of successful adrenal transplantation gave the following results: The unilateral transplantation was borne by all the animals (dogs, rabbits and cats) without ill effect. But one cannot say anything positive about the functions of the transplanted organ, since there is a possibility that this function was performed by the remaining adrenal. In a second series, both adrenals were transplanted into the kidney in two sittings with a considerable interval elapsing between the operations. If the second adrenal is transplanted, while the first is as yet in its atrophic and necrotic stage, no hypertrophy takes place and the animals die of adrenal insufficiency. The functional ability of a transplanted adrenal was proved by extirpating the second adrenal some time after the transplantation. In some cases in which there occurred necrosis of the transplanted adrenal the animals survived the second operation for a very short time only. In 9 cases, however, the animals survived the extirpation of the adrenal for a number of days and months. Microscopic examination here showed healing

accompanied by regeneration of the adrenal tissue with destruction of the vessels and revascularization from the kidney. Since there were no accessory adrenals in any of these animals, it follows that the transplanted tissue functionated. It was found here, as in bilateral transplantation, that the animals have a better chance for survival if there is an interval of from 11 to 16 days between the transplantation and extirpation, while a longer interval predisposes to failure. One gains the impression that the intact adrenal has so completely undertaken the function of the injured second organ that it hampers the latter's powers of regeneration. If the other adrenal is injured or removed, during the period when regeneration is at its height, a stimulus is given to the regenerating tissue. In a further series bilateral transplantation of both adrenals was done in two sittings and at a third sitting one kidney with its inlaid adrenal was removed. Out of 11 cases, 6 died of adrenal insufficiency. In all these animals the healed hypertrophic adrenal was accidentally extirpated, while the second on section showed regressive changes. Five dogs survived the operation for a year and a day without symptoms. The extirpated transplanted adrenal here also was hypertrophic. Incidental to homoplastic transplantation of the adrenal in man, von Haberer believes as a result of experiments on the cadaver, in the possibility of implanting into the aorta or femoral vein, the adrenals of dead new-born with its vessel and a piece of the aorta. Lately, Busch and Wright reported regarding heteroplastic adrenal transplantation. They transplanted into a 35-year-old man suffering from Addison's disease, the freshly obtained adrenal of a young pig. The organ was freed from both poles and about two-thirds of the freshened flap was implanted into the scrotum (local anæsthesia) after opening of the tunica albuginea and removal of a like piece of scrotal tissue, the tunica then being resutured. The operation was borne without disturbance, the subjective symptoms improved, the appetite increased, the vessel tone was better and the skin pigmentation was lessened. About two weeks after the operation asthenia set in, the blood-pressure fell, and a day later coma, followed by death. Microscopically, the transplant was found to be adherent to the scrotal tissue, and was separated from the adrenal tissue only by new formed fibres arising from the latter. The cortical substance was rich in blood-vessels and stained well, the medulla in greater part was necrotic and only a few cells could be made out.

Hypophysis.—Transplantation of the hypophysis was first performed by Cushing. He was able to prove that the life of an animal in whom the hypophysis was totally removed could be prolonged after

autotransplantation. Crowe, Cushing and Homans report that in 23 transplantation experiments on hypophysectomized dogs, in only 7 cases was the extirpation fatal, while in the remaining 16 cases smaller or larger fragments of the anterior lobe were removed. The transplants were placed in the abdominal muscles, in the bone marrow and occasionally with good results in the subcortical portion of the brain. Out of three cases of the last type, one animal died after 48 hours and the transplanted tissue was found to be completely necrotic. A second adult dog showed no disturbance except glycosuria and was killed on the 18th day. In the transplant there was found a normal peripheral zone, containing well stained anterior lobe cells, the central portion was necrotic and in the surrounding brain tissue were many colloid bodies. In the third case there were mild symptoms of cachexia, and on the second day the animal was in normal condition. This animal was killed on the fifteenth day and the findings were like those in the second case. Crowe, Cushing and Homans conclude from their investigations that transplantation of the hypophysis, after complete hypophysectomy, prolongs the life of the experimental animal. Homotransplantation, one or two days after hypophysectomy, yields better results than transplantation before removal of the hypophysis. Attempts to prove functionating of the transplant by subsequent removal yielded negative results in two cases.

Transplantation after partial hypophysectomy prevented in many cases the development of cachexia. In a young dog, after partial and coincident transplantation of the hypophysis into the rectus muscle, mild symptoms developed, which soon disappeared, and a month later they reappeared in increased severity and after homotransplantation, promptly disappeared. Transplantation investigations were undertaken by Bayer, Biedel, Clairmont and Ehrlich for the purpose of establishing hyperpituitarism without result. Transplanted hypophysis can heal in the spleen and intact cells can be found 10 to 14 days later, which finally become necrotic. Shaeffer's work on dogs, cats, apes and rats, transplanting the hypophysis into the brain substance, the subcutaneous tissue, muscle, peritoneal cavity and kidney, was not crowned with any permanent success. There only appeared a temporary increase in urinary secretion. Changes in development and nutrition were not observed. Very interesting was the investigation of A. Exner, who transplanted 7 to 10 hypophyses of like animals into the retroperitoneal space of young rats, using the weaker mates as controls. In 9 out of 11 cases the experimental animal gained in weight over the controlled animals in from 13 to 30 days. The increase in weight was due partly

through an increase in fat and partly through increase in size of bones. On section it was shown that the transplanted hypophyses were absorbed; in only a few cases could the transplanted hypophysis be demonstrated as necrotic cell masses. Whether or not the increase in weight was due to functionating of the transplanted hypophysis or the absorption of its active substance from the disintegrating tissues, was not decided.

Ovaries.—In 1895, Knauer reported regarding autoplastic transplantation of the ovaries. This was performed on rabbits, the ovary being removed from its normal site and transplanted into the mesometrium of the cornu of the uterus, or between the abdominal fascia and musculature. Where successful healing took place, there was no atrophy of the uterus as is usually noted following castration. These observations were confirmed by a number of investigators. The transplanted ovary retained its normal morphological structure, showing well preserved epithelial cells and follicles with unchanged or only a partially degenerated ovarian and well staining interstitial tissue. No difference was noted whether the transplant was pedunculated or not. The permanency of function and preservation of structure of the transplanted ovaries is not lasting, since after a number of months regressive metamorphosis is noted. Kawasoye found after extirpation of both tubes and ovaries with transplantation of half of one ovary into the broad ligament, that 90 days later there was atrophy and destruction of the follicles, degeneration of the ovum and necrosis of the stroma, while after removal of one ovary and transplantation of half into the remaining tube the degeneration was not so intense. Fogus found, after planting ovary into the spleen, that nine months later there was pigmented cicatricial tissue at the site of transplantation.

In homoplastic transplantation, Knauer and Carmichael were not always successful. The transplant rapidly degenerated completely in the researches of Marchese, Herlitzka, and others, while Vish, Foa, McCone, Basso, Lukaschewitsch, Magnus and Guthrie report successful homotransplantation, with not only preservation of the morphological transplanted ovary, but also later regular and normal ovulation, conception and pregnancy. The possibility of conception was proved conclusively by the researches of Guthrie, who exchanged the tubes of pure white and black hens. When the ovary of a white hen was planted into a black one, and this hen was impregnated by a white male, the offspring were white, black and spotted. The conclusions which Guthrie drew from this experiment have been disputed by Davenport and others, but the fact that the offspring were of the color

of the donor of the tube, is positive proof that the birth of these eggs was from the implanted foreign tube. Foa worked out transplantation of embryonal ovaries and was able to prove that they reproduced in a normal manner. In autoplastic transplantation, it makes no difference where the ovary is transplanted. Halban found in transplantation under the skin, good development of the uterus and genitals, and the transplant did not degenerate. Marschall and Joli, who transplanted ovaries intraperitoneally or into the kidneys, found no sign of degeneration of the uterus, the transplant in the castrated animals healing well, it apparently making no difference whether the epithelium was preserved, or, as happened in most cases, it became absorbed, the follicles disappearing and the implanted organ only remaining as an interstitial remnant.

In most cases of heteroplastic transplantation, there was no success, although there are some successful reports. Bucura obtained the best results. He transplanted the tubes of guinea pigs into castrated rabbits and found that not only did they heal, but they were capable of function, in that the follicles matured and prevented post-castration atrophy of uterus. Schultz obtained good results in transplantation of the tubes in different varieties of the same species, as with transplantation of the tubes from common guinea pigs into rosette guinea pigs and *vice versa,* between silver rabbits and land rabbits and *vice versa.* The results were apparently permanent, since the epithelium, the follicles and the ova retained their normal structure six months later. Ovary transplantation to foreign species, from the cat to the mouse, from the Japanese dancing mouse to the white mouse, from the dog to the rabbit, from the guinea pig to the rabbit, from the cat to the rabbit, from the mouse to the cat, from the rabbit to the dog, from the white mouse to the Japanese dancing mouse, healed well, and after 14 days was still well preserved but then began to show signs of disintegration.

Transplantation of the ovaries in the human female probably was carried out for the first time by Morris in 1895, in a woman of twenty, with an infantile uterus and amenorrhœa, good healing took place and menstruation followed two days after ovary transplantation. Transplantation and reimplantation of ovaries in women, especially after oöphorectomy, has been many times performed for the prevention of post-operative disturbances. The castration atrophy was prevented and almost regular menstruation occurred. Halliday, Croom, and Morris saw, after ovary transplantation, pregnancy and birth of a normal child.

In a 32-year-old woman, in whom 5 years previously one tube was

extirpated, while removing the second ovary for a tubo-ovarian cyst, Kayser planted two portions of microscopically unchanged portions of this ovary into the right thigh through an incision so that it lay beneath the vastus externus muscle, fixing it with catgut sutures and covered it with the fascia lata. Menstruation occurred regularly. It appeared after 23 days, was painless and there were no untoward symptoms. Kayser therefore concludes that it is only necessary to implant small portions of ovary in order to prevent symptoms due to ovarian insufficiency.

Testicles.—Testicular transplantation has been carried out for a long time. As early as in 1849 Berchtold successfully transplanted testicles of roosters with good functional results. Regarding the preservation of transplanted testicles, Mantegazza and Bizzozzero, Herlitzka and Zalchas, with frogs, Lode with roosters and Ribberta with nursing animals, showed that the transplanted testicles for a time generate spermatozoa but later undergo a regressive metamorphosis and after a time completely degenerate. Fogus in his researches found after transplanting testicles into the spleen that they became completely absorbed. Foa obtained like results in performing autoplastic and homoplastic transplantations in dogs as well as in new-born animals, even though he used small pieces of testicles as well as entire testicles. Maxikoff and later Cevoloto, after histological studies, came to the conclusion that the epithelial tissue of the seminal canals is very delicate and after implantation, the sperm-generating tissue disintegrates, and that the highly differential cells are replaced by a more simple type of epithelium, so that the canals become obstructed and are lined only by the cells of Sertoli. Anyway Fogus was able to implant small portions of testicles with result that they still contained living spermatozoa after months. Roosters which have been completely castrated and transplanted with functionating testicular tissues, it is true, do not develop all the characteristics of the male, yet they are not typical capon. Whether the absence of these characteristics, as Fogus believes, is due to the scarcity of the transplanted portion of testicle, or to the absence of union between the testicle and the vas deferens, as Nussbaum states, is not yet decided.

Steinach attempted to attain complete development of the epididymis, the prostate and penis in young mammals by means of autoplastic transplantation of both testicles. The sexual desire and potency of the animals were awakened at the proper time and appeared in normal intensity. The development of the male characteristics, the general carriage which this immature animal showed, imitating the adult, was

due to the influence of the testicles. Morphological examination showed that the semen generating portions did not develop but the tissues which manufacture the inner secretion, had developed very markedly.

Castle and Philipps in 33 attempts did not succeed in homoplastic transplantation, as the transplanted testicles always became necrotic. Pogany united two young rats by parabiosis and transplanted their testicles together with the epididymis. The second testicles of both animals were extirpated. After 10 to 14 days, the animals were separated, the pedicles of the organs being divided. Thus each animal had a testicle from the other. As long as the testicle had its pedicle, it retained its structure, but after division of the pedicle, the testicle rapidly broke down and became absorbed. Heterosexual transplantation of the genital glands has been attempted many times. The sex of the recipient has no influence upon the structural preservation of the transplanted gland. In the researches of Herlitzka and Bersca on watermoles, after a few months the testicles remained as fibrous rudiments. Ovaries implanted into males rapidly disintegrated. W. Schultz, after implanting ovaries into male guinea pigs, found that they develop and, even after four months, contained well preserved epithelium and follicles; and Busura found in castrated female rabbits in which testicles had been implanted, after 58 days, well preserved seminal canals, containing spermatozoa. In order to determine the effect of the inner secretions of the heterosexually transplanted genital glands, Fogus obtained positive results in young hens, in that one year after testicular transplantation, they developed the characteristic head and beard growth of the male, while they retained the spurs and feathers of the female. In one case after autopsy, no sign of the transplanted testicle could be found, while in the second case, there was demonstrated at the site of transplantation, a fibrous tumor, rich in blood-vessels. Both hens laid eggs and Fogus himself believes that there was no proof of any influence of a heterosexual gland upon the secondary sexual characteristics.

Steinach castrated young male guinea pigs and rats and implanted them at the same time with ovaries from the females of the same animals. He found that the ovaries transplanted peritoneally or on the inner surface of the abdominal muscles, subcutaneously, healed, developed and functionated in the male organism. The follicles developed into larger follicles with normal ova and in part arrived at full maturity, burst and became in part corpora lutea. The interstitial cells of the stroma also showed a tendency to reproduction. The transplanted ovary

was undersized and did not attain the size of the fully developed ovary in the normal female.

The implanted ovary had apparently no influence upon the development of the male. The male characteristics, which reach their complete development before or with puberty, as the erectile tissue of the penis, the prostate, and the seminal ducts, remained in their infantile states, as after ordinary castration, and the inhibitory effect of the ovary could be noted upon the development of the penis and the erectile tissue in male rats. The transplanted ovary exerted a stimulating influence upon the tube and uterus which had been transplanted with it.

Particularly noteworthy was the change of the minor sexual characteristic of the male to typical female organs. In those male guinea pigs which had been castrated and into whom had been transplanted ovaries, there was a remarkable development of the breasts and nipples, their shape and size resembling those of normal females. In normal females, the mammæ begin to develop vigorously at about the third month. The pigmented area about the nipple becomes broad and elevated, remaining free from hair, the pregravid completion of the development progressing gradually. In the operated males this process is accelerated and the male rudiments rapidly are transformed into female organs. The glands attain the size of those of adult females about 8 to 10 months old, and in fact, may even outgrow these. The microscopic examination shows that these breasts which have enlarged because of transplantation, are very similar to the ripe adult female breasts.

The influence of the transplanted ovaries extends over the development, the size and the form of the body and skeleton of rats and guinea pigs. The tendency to rapid, vigorous male growth, after transplantation, is lost in a short time and a transformation toward the gradual weak female development appears. The animals with the transplanted ovaries after a time take on the size and form of females. Growth of hair and fatty deposits bring out the female characteristics, and even psychic changes can be recognized.

Kidney.—The first successful kidney transplantation was demonstrated in 1902, although before this time Lubarsch and Alessenry were able to transplant small pieces of kidney tissue into the spleen and lymph-nodes, in order to demonstrate what changes occur in the kidney tubules. I first automatically transplanted the kidney in a neighboring site in a pig with failure because of the difficulties due to the anatomy of the veins in this animal. The first transplantation on the dog failed, because the dogs scratched themselves in the location of the transplanted

kidneys or because of infection due to licking of the wounds. Only when the kidneys were transplanted into the necks of the dogs were the investigations fruitful. Following the suggestion of Payr, I was able to unite the renal artery with the carotid and the renal vein with the jugular vein. I sutured the ureter into the skin wound. Urinary flow from the ureter was at once established, although in the first dog, the ureter after 5 days became swollen and retracted to such an extent that it became invisible and the urine flowed directly from the wound. Further researches taught me that the kidney itself could be made to preserve its function up to 18 days. Autopsy *in vivo* demonstrated distinct changes in the transplanted kidney which was so densely adherent to the surrounding tissues, that when the capsule was freed, hemorrhage occurred from numerous newly formed blood-vessels.

A. Exner attempted similar transplantation without satisfactory results, as in the old Vienna Physiological Institute strict asepsis could not be observed; in spite of this he was able to note urinary flow from a ureter two days later. Stich, Makkas and Bowman transplanted the kidneys into the necks of a series of dogs. Ten days later the animals died of pyelonephritis. For this reason they implanted, in a second series, the vessels of the kidney into the iliac, and the ureter into the bladder. The other kidney was not removed. On the first day after operation, the urine was somewhat bloody but later became clear. Three weeks later the animal died of infection. Autopsy disclosed numerous abscesses in the region about the transplanted kidney, the latter being macroscopically normal and microscopically showing a well preserved epithelium with no evidence of parenchymatous or interstitial nephritis. Very important were the researches which Zaaijer carried out in 1908. He transplanted the left kidney of a dog into the groin, uniting the vessels with the external iliac artery and vein, and sutured the ureter into the bladder. Eighty-three days later he removed the right kidney. The transplanted kidney functionated, proving the functional value of kidneys transplanted by autoplasty.

Later Carrel extirpated both kidneys in dogs and replanted one into the kidney region. Out of 6 dogs, 5 survived the procedure, one was killed 21 days after operation, 2 developed secondary contraction of the ureteral anastomosis, dying respectively 17 and 31 days after operation, the fourth animal died two months later because of pyelitis. One dog developed minor complications and 8½ months later was in the best of health. That the implanted kidneys carried out their functions was proven by the good condition of the animals until complications developed. Borst and Enderlen performed transplantations of six kid-

neys, joining the renal vessels to those of the spleen, three of the animals being observed for 34, 56 and 118 days. The kidneys were found in faultless condition, macroscopically and microscopically, functionated well, and one animal, in which the second kidney was removed 18 days later, lived in good condition another 100 days.

The first homoplastic kidney transplantation was performed by myself. I was able to prove three months after my first demonstration that I was successful in transplanting the kidney of one dog into the neck of another, the transplanted kidney after a few days secreting normal urine and completely healing in its new location.

In order to test the functional value of homoplastic transplantation of the kidneys, Carrel and Guthrie at first, later Carrel alone, undertook experiments with various methods. They removed the blood-vessels with the immediate portion of the aorta and vena cava and sutured the flaps into respective openings into the analogous vessels of the recipient. Following this method, the operated animals lived for a longer period of time, there occurred in every instance changes in the site and length of blood-vessels which finally led to chronic stasis, and after a number of weeks, to severe disease of the kidneys. Yet, in one cat, three months after operation the transplanted kidney was demonstrated with normal coloring and shape, and the animal enjoyed good health. Finally, the kidney became smaller, and Guthrie one year later found that it was shrunken and incapable of function. Further attempts were designated as transplantation *en masse* by Carrel and Guthrie. This consists of removing from one animal both kidneys with their blood-vessels, the corresponding segments of aorta and vena cava, together with the nerves and ganglia, the ureters, and a part of the bladder, and implanting them into the abdominal cavity of a second animal, in whom both kidneys had been previously removed. An oblique incision had been made into the aorta and vena cava, and the vessel segments of the first animal were sutured into the ends of the aorta and vena cava, and the bladder segments into the bladder of the experimental animal. The successes of Carrel were extraordinary. Twenty days after this operation the cat was in remarkably good health, its urine was normal. She suddenly died 31 days after operation. Microscopical examination demonstrated an acute interstitial nephritis as the cause of death. A second cat, which remained well for 18 days, died 36 days later of a severe arteriosclerosis which Carrel believes was due to the influence of the new kidney. The first heteroplastic transplantation of the kidney was performed by myself, transplanting the kidney of a dog into the neck of a goat. I demonstrated this goat to the Society for

Physicians in 1903, and the 100 present were able to see a distinct flow of urine from the sutured ureter, thus disproving the statement of Villard that this flow was due to œdema. There was no evidence of œdema. On the next day, when I examined the flow of urine, it had ceased because of thrombosis of the blood-vessels. Carrel transplanted the kidney of a rabbit into a cat. After a period of weeks, the rabbit's kidney was completely absorbed. He also transplanted the kidney of a pig into a dog. Fifteen days later the animal died of infection of the kidney, the size of the latter being about normal.

As early as 1902 I transplanted the kidney of a pig into a woman suffering with uræmia in the severe form. The transplantation was attempted in the left elbow region, but I could not surmount the technical difficulties and, also, the animal died from the anæsthetic. Five years later, Jaboulay attempted heteroplastic transplantation in two incurable nephritics, utilizing the elbow-joint as the site for a goat kidney in one case, and a pig's kidney in a second case; anastomosing the brachial artery and the cephalic vein with the renal artery and renal vein respectively; three days later the kidneys became gangrenous and had to be removed. Into a 21 year old girl, suffering with severe hemorrhagic nephritis, Unger attempted to transplant a kidney of a ten year old ape (Macacus Nenestrinus); 32 days after the operation the patient died of œdema of the lungs. Circulation was maintained in the ape's kidney, it apparently was alive 32 hours after the operation, but the question could not be decided whether it functionated or not, since it was not clearly established whether the fluid in the ureters was urine or œdematous fluid. Portions of the kidneys were unchanged, while other portions showed acute inflammatory changes in the renal tubules.

Spleen.—Lüttke transplanted by homoplasty the spleen of rabbits into the peritoneal cavity, and by heteroplasty into the dog, as well as into a pocket of the spleen itself. The transplanted splenic tissue was demonstrated only for four weeks; after two or three months it completely disappeared. The question as to whether or not the transplanted spleen functionated, was studied by examination of the blood. In the first two weeks the hæmoglobin and the erythrocyte contents diminished, while the lymphocytes increased fourfold. The eosinophilic cells after two or three weeks increased in number. Lüttke interprets the increase in lymphocytes as indicative of the functionating power of the transplanted spleen. The functional ability is also proved by the recognition of specific antibodies. In six out of ten cases in which Lüttke transplanted the spleens of rabbits which had been immunized

against typhoid fever, by heteroplasty, into dogs and apes, he was able to demonstrate the presence of typhoid agglutinins. Passive immunity was not conferred simply by transfer, but was the result of an active production of agglutinins by the transplanted splenic tissue. This was proved by the fact that the serum of dogs and apes which had been immunized against typhoid fever by the transplanted rabbit's spleen, contained a great agglutinin content, and retained it for three months; while control animals which had been immunized by the injection of splenic extract from immunized animals, contained less agglutinins, which disappeared in from three to six weeks. Carrel reimplanted a spleen which had been washed in Locke's solution, followed by healing without reaction. Since this operation is relatively simple, Stich believes that the possibility of homoplastic transplantation of the spleen is more likely to be successful than that of thyroid and kidney.

Pancreas.—Autoplastic pancreas transplantation was attempted by Coffey on dogs. Minkowsky successfully transplanted a portion of the pancreas with a vascular pedicle, the latter being later divided. The transplanted segment healed, and it was shown that it was able to prevent the onset of diabetes. Since then Heron was able to transplant pancreatic tissue into the spleen of pancreatized dogs, in the attempt to improve diabetic symptoms and to prolong the lives of the animals.

Intestine.—The idea of enteroplasty occurred to Nicoladoni, who made the suggestion that the construction of an artificial anus after complete resection of the descending colon could be obviated if the removed portion of large intestine could be substituted by a portion of neighboring small intestine which had been lengthened by means of an incision into the mesentery. The borrowed intestine was inserted into the defect of the large intestine and the mobile ends of the small intestine were sutured together. This method was useful in resection of the stomach between the pylorus and cardia, provided that the mesocolon could bear a double incision in order to free the enclosed transverse colon from the gastrocolic omentum. A second method of operation carried out by Nicoladoni was the following: The neighboring small intestine with its mesentery was incised obliquely. The divided ends of the large intestine were united with this incision in such a fashion that the continuity of the intestine was established so that the contents progressed through a portion of the intestinal tract by means of retrograde peristalsis. The success of this second method naturally depends upon the possibility to permanently reverse the peristalsis of a large portion of the intestine, as the contents must, after they pass the first suture line, proceed through the large intestine against the valve of Bauhin, until they find their way

through the reversed, inserted portion of the small intestine, finally being emptied into the rectal extremity of the gut. Digestion must also be reversed. Intestinal digestion must also take place in the transverse colon and fecal bodies must pass through the small intestine shortly before their exit from the body. The principles upon which both operations were founded are very original. The first type of operation will make it possible to insert a substitute for the stomach in resection of that organ, in that the transverse colon, after it has been divided from the descending colon, is implanted in the place of a stomach with its divided mesocolon; the portion of pylorus lying to the left of the operator being sutured into the end of the colon, also lying to the left of the operator, the cardia being sutured on the right side into the other colonic extremity. The success of the operation depends upon the fact that the implanted colon is nourished from the blood-vessels of the divided mesocolon; and, second, that there occurs no disturbance after union of the colon with the stomach, which would be due to a difference in the reaction of the stomach—stomach contents being acid, colonic, alkaline.

I have succeeded in transplanting portions of the intestinal tract in pigs, planting large intestine into the stomach, the stomach into the large intestine, small intestine into the stomach, the stomach into the small intestine, small intestine into large intestine and large intestine into small intestine; the experiments were done on young animals, nursed by their mothers. Three out of eighteen of the animals died, the survivors bore the operations well, they showed no disturbance in digestion, being fed on milk one day after operation, after six days on farinaceous food, and after ten days resumed their normal diet.

Transplantation of the Large Intestine to the Stomach.—The cæcum has been transplanted into the stomach in the following fashion: The blind end of the cæcum was removed and by means of a transverse incision was transplanted into the anterior wall of the stomach so that it formed a little pouch. Silk was used here as well as in the following cases. The sutures were in double rows, the deep layer being seromuscular and the superficial ones serous. The animal survived the operation well and 100 days later was killed. On opening the abdomen, there were present a few adhesions of the stomach to the omentum. The sutured head of the cæcum was completely adherent to the stomach, the peritoneum was even and smooth. The lumen of the caput was not contracted. The differentiation between the inner surface of the stomach from the wall of the cæcum was macroscopically visible, the difference being noticeable, not only in the color, but also in the arrange-

ment of the mucous membrane, that of the stomach being thicker and more massive than that of the implanted segment.

The gastric mucous membrane in the immediate neighborhood of the implanted portion was more wrinkled than that further away, which was smoother. The junction between the stomach and the cæcum in some places only was marked by a light, superficial swelling.

Three portions of this tissue were utilized for microscopic examination, first, the swelling; second, the portion of the cæcum; third, the border without swelling. The swelling was confined to the large intestine. The enlargement was due to hypertrophy of the lymph follicles of the implanted intestines, no other changes in the mucosa being observed. The muscularis in the middle of the implanted portion, as well as in a swollen and normal portion, is thickened, this being probably due to ring formation. The stroma is no more vascular than that of the normal intestine, while the submucosa is distinctly richer in vessels than the normal, as well as thicker and richer in connective tissue. Of interest is the fact that the number of ganglion cells in the submucosa is unchanged; the intestinal plexus is apparently intact. It was noted regarding the finer structures of mucosa that the superficial epithelium which covers the spaces between the gland mouths is unchanged, and that they are covered by columnar cells as in the normal gut. The beaker cells in the depths of the glands are not as numerous. It is noteworthy that the implanted large intestine gave a distinct acid reaction, showing that it came in contact on all sides with the gastric juice.

Transplantation from the Stomach Into the Small Intestine.—A portion of the wall of the small intestine opposite the mesenteric attachment was removed from that part of the intestine which could be brought in contact with the stomach without difficulty. The extirpated piece was six centimetres in length and 3½ in width. Into this defect was planted a portion of the gastric wall. The stomach wound was then sutured. The animal, which remained under the influence of the anæsthetic for a long time, bore the operative procedure well, soon began to eat regularly and with a good appetite, digesting its food well. Seventy-seven days after operation it was killed. On macroscopical examination, a distinct difference between the two varieties of mucous membrane could be recognized. The mucous membrane of the stomach was continuous with that of the intestine, it is true, but that of the intestine was thicker and protruded more prominently into the lumen of the gut and its color was a deeper red. It must be admitted that the implanted segment became smaller in size. Examination with a magnifying glass as well as under higher power reveals a reflection of the

gastric mucosa over that of the intestine. The mucous membrane of the stomach is lined by one layer of columnar epithelium as usual.

Transplantation from the Stomach Into the Large Intestine.—Implantation of a rectangular piece of stomach into the transverse colon. The animal after the operation was in good shape and gained in weight. On examination 53 days after operation, the transplanted stomach is readily found, and the different varieties of mucous membrane are easily made out. The gastric mucous membrane protrudes somewhat into the lumen of the gut, it is thicker and redder and there are present on its surface definite elevations and depressions. Even with the naked eye one can perceive a swelling at the junction of the mucous membranes, which with the magnifying glass is found to be present in the intestinal wall. This swelling affects only the mucous layer and in the submucosa is present a cellular infiltration, although there is no evidence of abscess formation or disintegration. At the site of the swelling there is a wealth of vascular tissue.

Transplantation from the Small Intestine Into the Stomach.—From the anterior wall of the stomach a portion five by three centimetres is excised. A low lying loop of the small intestine is selected and a portion about six centimetres in length is removed, and by means of a generous incision, the mesentery is mobilized. The open lumina of the loop are then resutured and on the wall opposite to the mesenteric attachment a long incision is made. The small intestine is then fitted over the wound in the stomach like a cap. At the same time the continuity of the gut was re-established by means of sutures. The pig was killed 99 days after the operation. At autopsy was found a swelling on the anterior wall of the stomach which was found to be the transplanted intestine. On opening the stomach one finds in this intestinal pocket the same food contents as in the rest of the stomach.

Transplantation of an Unpedunculated Gastric Flap Into the Small Intestine.—A rectangular portion of the anterior gastric wall 4½ by 3 cm. was excised and sutured in the place of a small piece of small intestine which had been removed. The animal was killed 13 days after. On section the stomach was found to be healed. No adhesions. The gastric mucous membrane was easily differentiated from that of the intestine. Microscopically the section appeared normal.

Insertion of Small Intestine Into the Colon.—The grafting is performed in such a manner that the direction of the peristaltic waves was not changed. A portion of small intestine 8½ cm. long was implanted into the colon, by my method of intestinal anastomosis. One hundred and ten days after the operation, the animal was killed, it weighed twice

as much as at the time of operation. On section, a difference between the small and large intestine was distinctly visible. Externally there was seen a contraction corresponding to the line of union, although there was no difference in color. The mesenteries were united, somewhat thickened, and folded over one another. The mucous membrane everywhere was normal, at the most, there was a slight thickening at the site of junction.

The conclusions that I derived as to transplantation of the intestine was, that it is easily performed on the pig and that these animals survive the operation for a long time and gain in weight after it. I have been asked by Dr. Exner in what manner the foreign piece of mucous membrane protects itself against digestion by the intestinal juices. Many theories have been advanced to answer this question. From the result of my researches it appears that each portion is able to protect itself against the foreign digestive juices, and that when the two varieties of membrane unite, the one of least resistance undergoes swelling.

Rosenberg resected a loop of intestine in the dogs, opened the gut longitudinally and planted it into the incised urinary bladder or into the bladder, the upper half of which had been removed. The transplanted intestine healed and after 2, 4, and 15 weeks did not contract. The intestinal epithelium disappeared and was replaced by bladder epithelium. Transplantation of the intestine as a substitute for the œsophagus has been performed in a number of cases and the intestine healed in its entire length in the subcutaneous tissue between the sternum and the skin.

Prostate.—Scrralach and Parre attempted prostatic transplantation by implanting small or large pieces of the prostate subcutaneously or intraperitoneally. The transplanted tissue changed, in that the glands atrophied and the connective tissue hypertrophied.

The hopes which were entertained 15 years ago regarding tissue and autotransplantation have been partially fulfilled; in heteroplastic transplantation it appears that the obstacle to success lies in anaphylaxis, while in homoplasty inherent biochemical characteristics interfere with healing. On this ground only can be explained the unsuccessful results of these types of transplantation as compared to the more favorable and more permanent results in autotransplantation. In heterotransplantation relatively successful results have been obtained, as it is finally replaced by the bone of the recipient. The cell protoplasm, specific for each organism, varies with the individual.

There are as many protoplasms as there are individuals. Thus in homotransplantation the appearance in the body of a foreign protoplasm calls forth ferments into the circulation which destroy the transplanted tissue. The statement of Roux which he made in 1895 that a part of an organism will accustom itself to the surroundings in another organism cannot in this era be accepted. Whether it is possible or not to artificially alter the bloods of two individuals so that homotransplantation will be successful, is questionable. For this purpose, one could resort to parabiosis.