ORGAN TRANSPLANTS: A TYPE OF RECONSTRUCTIVE SURGERY*

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Plastic surgery is second only to obstetrics as the oldest surgical specialty. The concept of tissue replacement or transplantation for diseased or injured parts can be traced back to earliest history. In the basic text of Hindu medicine, about 600 B.C., methods for mending a clipped earlobe and for repairing a mutilated nose by transplanting skin are described.1 Celsus (25 B.C.—60 A.D.) mentioned repair of lips and facial defects with skin and subcutaneous tissue from adjacent areas.2 These were autogenous grafts, that is from the same individual.

It was not until the 15th century, after the Branca family in Sicily successfully introduced the method of nose repair from “the flesh of the arm” that a homologous graft‡ was first mentioned in the fable of “the slave’s sympathetic nose.” The nose cut from a slave allegedly survived in the new recipient only as long as the original donor lived; after his death the nose, now on another person, fell off. Tagliacozzi, a leading surgeon of the 16th century, considered such homografts theoretically possible on the basis of successful grafts in plants. But he wrote that the “singular character of the individual entirely dissuades us from attempting this work (nose reconstruction) in another person. For such is the force and power of individuality . . .”1

Two years ago, while in India, I used the Branca method of autologous nasal repair on a Hindu woman whose nose had been excised as punishment. This somewhat grim experience was a sober reminder of how brief is the span of medical history and, in some respects, how slight its progress.

First Descriptions of Free Skin Grafts

The free transplantation of skin was the major advance of the 19th century.3 French, British and German workers developed operations involving shifting of tissues for all parts of the body. Jonathan Mason Warren performed one of the first free skin grafts in North America in the mid 1800’s in the treatment of a patient with cancer of the face.

These successes with the free skin grafts led, in the 1860’s, to the study of other organ transplants. One method of study was parabiosis (the physical union of two living animals of the same species).4 Permanent success in parabiosis was not achieved because one animal assumes dominance and acts as the recipient while the other (donor) animal succumbs. By the turn of the century embryologists had studied, in cold-blooded animals, the growth of transplanted limb buds, primitive eyes, and other tissues. It was observed that the higher the animal comes in the phylogenetic scale, the greater difficulty there was in successful homotransplantation.

Vascularized Organ Transplants

Having perfected techniques of vessel and organ transplantation in 1900, Carrel5 speculated that successful replacement of diseased tissues and organs would automatically follow. He was wrong. For example, a kidney autograft in the dog survived for a long time but the homograft transplanted by the same technique functioned only for a few days and then was rejected with an intense, local, non-suppurative reaction. Similar reactions occurred in skin and other tissue grafts.

Loeb,6 in 1930 summarized his and other studies on tissue transplantation and concluded that individual “organismal differentials” or complex protein substances within each cell accounted for the rejection of the homotransplant. Because of this basic inherent difference between individuals at the cellular level, he concluded that trans-

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‡Homologous — from another individual of the same species. The currently accepted term, allogeneic, is more precise and should be used.
plantation between individuals would always remain impossible and that work in the field was foredoomed to failure.

IMPLICATION OF IMMUNOLOGICAL FACTORS

Fortunately for subsequent generations some physicians did not share Loeb's pessimism. Dr. Emil Holman, while finishing his residency with Dr. Harvey Cushing, reported studies on skin grafting in 1924. His clear, simple observations demonstrated not only the uniqueness of the individual, but also the phenomenon of increased immunity to a second grafting. Dr. Holman grafted skin from a mother to a child whose leg had been badly mangled. Following the second grafting a general exfoliative dermatitis appeared, probably a manifestation of anaphylaxis or protein intoxication. The second skin grafts were rejected more rapidly than the first and Dr. Holman actually suggested that "each group of grafts develops its own antibody". His observations lay fallow although identical comments by Gibson and Medawar during World War II were to become cornerstones in the development of transplantation biology. Reminiscing in 1963 about his work done 40 years before, Dr. Holman writes: "What an opportunity we missed by not pursuing this further!"

IDENTICAL TWIN EXPERIENCE

Meanwhile, the remarkable identity of identical twins had long been speculated upon, especially by geneticists interested in analyzing the influence of environment on growth and development. Identical twins are so much alike that minute variations in the form of the hand or fold of the ear, minor abnormalities in the colour of the eyes, and subtle blood group properties, are all shared exactly alike in the two. The two children resemble each other much more exactly than any parent ever resembles a child. From the earliest consideration of any type of grafting it had been suspected that tissues could be exchanged between identical twins. In Germany, in 1927, skin was traded between identical twins to help reconstruct congenital deformities of the hand. It was in 1937 that

Dr. James Barrett Brown (Fig. 1), the noted American plastic surgeon, reported the instance of a child who needed skin to cover a burn. Skin homografts from the mother were rejected, as had been suspected. However, Dr. Brown stated "that for several years I hoped to have the opportunity of using homografts from an identical twin . . . finally I contacted identical twins who donated their time. Both were healthy. Accordingly, I transferred full-thickness skin grafts from the arm of one to the other and obtained primary healing in both, with complete and permanent survival of both grafts for three years" (Fig. 2).

One of the most extraordinary and heartwarming instances of the use of reciprocal skin homografts was by Sir Archibald McIndoe in a medical-legal case of familial identification of exchanged identical twins. "In 1947 the parents of six-year-old twins
became aware of the existence of another small boy who presented a striking resemblance to one of their own twin children. Believing at first that its was simple coincidence, they were surprised to learn that the other child was born the same night and in the same hospital as their own. During a parade, in which the similarly dressed children were participating, the father was so shocked by the resemblance that he decided to contact authorities in order to learn whether or not a substitution of one of his twins could have taken place. After genetic identity had been proven by the exchanges of skin grafts the substituted children were exchanged on the first of July, 1948, to their rightful parents."

**THE INFLUENCE OF WORLD WAR II**

The problem of homografting was on dead-centre until World War II. However, the stimulus for the care of severely burned patients led to the assignment of Mr. Peter B. Medawar, a zoologist, to the Surgical Unit of the Glasgow Royal Infirmary, to undertake a study of the fate of skin homografts along with Dr. Thomas Gibson, who was in charge of plastic surgery. This study was commissioned by the British Government and was an outgrowth of wartime interests in improvement in methods of skin grafting, so much needed for the treatment of burns suffered not only by the troops, but also by the civilian population assaulted by bombing raids.

The two men first made careful observations of a burned patient in whom skin grafts had been placed in an attempt to cover the burn. This was precisely the setting in which Dr. Holman had made his observation in 1924. In this particular instance in Glasgow, the grafts came from the patient and from other persons. The authors concluded, as Dr. Holman had, that homografts were not a practical way of covering burn defects but they discovered a great deal more on the way. They observed the hastened rejection of grafts put on a second time from the same donor and they stated: "The second set of homo-
grants did not undergo the same cycle of growth and regression as the first; dissolution was far advanced by the eighth day after transplantation. The degenerative changes that affected the first set of homografts appear simultaneously in their immediate contemporaries of the second set."

In this quotation is found the first use of the term “second-set” grafts, a term that was to be widely used to describe the immunologic phenomenon of “memory” in homografting, and that later became the basis for studying homotransplant immunology in detail.

Most important, however, was the final conclusion of Gibson and Medawar, as follows: "The time relations of the process, the absence of a local cellular reaction, and the accelerated rejection of the second set of homografts suggests that the destruction of the foreign epidermis was brought about by a mechanism of active immunization."

Stimulated by these results of careful observations in man, Medawar carried forward the investigation after he returned to his zoology department in Oxford. His research, still supported by the War Wounds Committee of the Medical Research Council, consisted of setting up an animal model in which these initial observations could be made repeatedly and under ideally controlled conditions. He used skin grafts on rabbits and by 1944 could establish statistical norms for the length of survival of autografts and homografts and statistical prediction for the accelerated rejection of "second-set" homografts, and could make microscopic pictures showing the phenomena of transplant immunology for the first time in great detail. Again, he concluded: "The mechanism by which foreign skin is eliminated belongs to the general category of actively acquired immune reactions."

**Breadth of Transplantation Biology**

In this brief history of organ transplants I have mentioned, in passing, the role of some plastic surgeons. * Transplantation biology is a common meeting ground for many disciplines and has stimulated workers in the fields of zoology, immunology, genetics, hematology, biochemistry, internal medicine, surgery in all its branches, pathology, irradiation biology and embryology. Only by maintaining open avenues of contact with all of science can any surgeon interested in clinical investigation enjoy the pleasures of the interdisciplinary stimuli required for progress.

Dr. Ray Owen, a teacher of veterinary science at the University of Wisconsin, was the first to prove that two genetic types can live together in the same organism without any signs of antagonism or disease. He showed this to be true in cattle twins. Dr. Owen knew that identical twins in cattle almost never occur. He likewise was aware of the previous studies of Dr. F. R. Lillie who, in 1916, had reported that in bovine twins of opposite sexes there was often a union of the circulatory system between the two placentas in the uterus of the mother cow. The female twin was then born with abnormal sterility and was termed by farmers and veterinarians a "freemartin".

Dr. Owen reported, in 1945, that in some cattle twins each member of the pair carried blood cells of two different types. He postulated that at some time prior to birth, with the circulation of the two placentas intertwined, the twins seeded down each other’s bone marrow with primitive cells from which blood cells would grow. This cross-colonization of the bone marrow, before birth, permitted the two different blood types to live together without any rejection battle. Evidently the two genetic types of blood cells got used to each other at an early age and became mutually “tolerant” (Fig. 3).

This important contribution formed a significant background to many subsequent experiments and demonstrates how the various fields of science contribute to each other. Dr. Owen concluded that if living cells were exchanged before birth, tolerance would be achieved; then the twins should be able to trade skin grafts successfully. Such indeed was shown to be the case. A few years later kidney grafts, as well as skin grafts, were successfully transplanted between “freemartin” twins.

*Other plastic surgeons who have made major contributions to transplantation biology are Peer, Conway, Edgerton, Converse, Stark, Rogers, Peacock, Ashley and many others.
This controlled and reproducible breach in the homograft barrier excited activity along other lines. Total body x-radiation and bone marrow infusion produced radiation tolerance; a high titre of circulating antibody allowed prolongation of tumour homograft survival, a process called “enhancement”; and immunological tolerance to purified proteins in rabbits treated with the antimetabolite 6-mercaptopurine was applied to kidney transplants in dogs and man.

The scientific life and productivity of Dr. M. Simonsen of Copenhagen, is an apt conclusion for this historical resume of transplantation biology. Dr. Simonsen embodies the cross-fertilization of many ideas and laboratories. He was the first, along with Dr. J. Dempster of London, to study dog kidney homografts and note that the second-set response applied to kidney as well as to skin. Stimulated by Owen’s observations on the “freemartin” cattle, Simonsen exchanged kidney transplants between a pair of these cattle twins with success, thus completing the experiment of nature suggested by Lillie in 1916. During the 1950’s Simonsen refined the criteria for determining the interaction between donor and recipient, especially when donor tissue was immunologically competent and capable of reacting against the host.

Meanwhile, Sir Archibald Mclndoe, at the Queen Victoria Hospital in East Grinstead, England, had maintained his international centre of plastic and maxillofacial surgery, a major portion of which dealt with the healing of wounds and the surgical reconstruction of missing parts. Over the years a succession of young plastic surgeons from various countries, under training at the hospital, required research facilities to follow up a variety of clinical problems. It was felt by Sir Archibald that basic research in tissue transplantation was of fundamental importance to the advancement of surgery as a whole. It was recognized that such research even if of an academic nature without immediate clinical application should form the background of research and training in a hospital primarily concerned with wound healing in all its practical aspects. Thus arose his conception of the research unit which, opened in
1961, has rapidly become a leading centre of transplantation biology. To head this unit organized by a plastic surgeon as a training for all surgeons he selected Dr. Simonsen and enticed him to England. Thus in one person the circle runs full.

**Current Evaluation**

The rest of this report is restricted to a single topic, namely, clinical and experimental kidney transplantation at the Peter Bent Brigham Hospital, Boston, Mass., and the Harvard Medical School. The project involves the major disciplines of surgery, medicine, pathology, and radiology. The responsibility of each research project is individualized but patient care is shared. We decided in 1950 to use the kidney rather than skin as a test graft in studying the homograft problem for several reasons: Renal disease is widely prevalent; it afflicts young people; kidneys are paired organs and one alone can be life-sustaining; kidneys have solitary vessels large enough for anastomoses, and function can be determined easily.

In the laboratory, using Carrel's techniques, we demonstrated first that the canine autograft without nerve supply and relocated into the iliac fossa could function normally for the lifetime of the animal. Concurrently, in humans, we occasionally transplanted kidneys from cadavers or from elective nephrectomies in order to observe the natural history of such grafts in these severely ill, uremic patients. Surprisingly, some of the unmodified human transplants functioned better than anticipated. In addition, the management of the seriously ill patient was not an insurmountable problem. From these experiences came the observation that uremic recipients could not reject homografts with normal vigour.

During 1954 the first identical twin was referred for a question of transplantation. After serious soul-searching the decision to proceed was made, and following the transplant the moribund patient was restored to normal health. The success with the identical twin experience stimulated increased activity in our laboratory program. We tried to make dogs uremic, we injected embryos with cells from some prospective donors, we infused bone marrow into x-radiated dogs, all without success. Meanwhile, individuals with clinical problems appeared on our doorstep clamouring for help. These included patients from whom a solitary kidney had been removed and those children and young adults who were in terminal uremia from a variety of causes. We performed regular but infrequent transplants to test any promising leads.

In 1959 the first non-identical twin transplant succeeded following the use of sub-lethal total body x-radiation without bone marrow infusion. This patient is alive and well today, the only survivor from a dozen patients treated with x-radiation in varying doses. In 1960 we began to test the effect of antimetabolite drugs on dog-kidney homografts. The longest previous laboratory survival, from hundreds of dog-kidney transplants, had been 14 days; however, using 6-mercaptopurine on the day of the transplant a 45-day survivor resulted, a clear intimation of a brighter future. With current drug regimens we can achieve 90% 50-day survivals in dogs and 50% 100-day survivals. Most animals surviving for 100 days go on to live a normal life span.

Next, these drugs were tested cautiously in man. The program using immunosuppressive drugs was started in April 1960 and, by October 1964, 42 transplants in 40 drug-treated recipients had been performed at the Peter Bent Brigham Hospital (Table I). In the 11 instances in which cadavers were used as the source of the donor kidney, seven functioned well but only one is surviving at present, to date almost one year. Of the "free" kidneys, i.e., those removed from elective therapeutic
nephrectomies, seven were used and six functioned well.

Eighteen of the individuals with transplants from 24 living volunteers are surviving at present. From an analysis of the 24 transplants in Table II, it will be

| TABLE II.—P.B.B.H.: 24 Transplants From Living Volunteer Donors (Oct. 1, 1964) |
|---|---|---|---|---|---|---|---|---|---|
| Donor | Months post-transplant |
| | Mother | Father | Sibling | Unrel. vol. | Dizyg. twins |
| | 1-2 | 3-6 | 6-12 | 12-18 | 18-24 | 1-2 | 3-6 | 6-12 | 12-18 | 18-24 | 1-2 | 3-6 | 6-12 | 12-18 | 18-24 |
| Mothers | 1 | 1 | 8 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Fathers | 3 | 0 | 2 | 1 | 0 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Siblings | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Unrel. vol. | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dizyg. twins | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *alive | 18 | 6 |
| dead | |

noted that 12 of 13 maternal donor kidneys are surviving; two between one and six months, eight between six and 12 months, and two others between one and two years. Three out of six paternal donor kidneys and one from a sibling are surviving. The two attempts to use kidneys from unrelated volunteers, one from a spouse and on another occasion from a friend, failed between one and six months. The recipients with kidneys from dizygotic twins are surviving. The variabilities and unpredictabilities of renal transplantation are discussed more fully elsewhere.21

The establishment of a Registry of Human Kidney Transplants has resulted from a National Research Council Conference on human kidney transplantation.22-24 The following tables utilize some of the data from the Registry. This Registry allows all investigators to share experiences and minimize duplication of effort and error. Table III shows the status on September 15, 1964 of 143 transplants which were surviving on March 15, 1964, six months previously. These include 10 of 11 transplants performed before March 16, 1961, eight performed between March 15, 1961 and March 15, 1962, 16 of 17 the following year and 98 of 107 during the last year. Therefore, only 11 transplants out of the 143 functioning on March 15, 1964 had ceased to function on September 15, 1964. This is encouraging because probably if patients survive beyond the first six months a drastic mortality rate during the ensuing months is unlikely. However, more data and time will be required to establish this point completely.

Table IV shows the number of transplants performed during four time-periods.

| TABLE IV.—Kidney Transplants |
|---|---|---|
| Date | Total (as of 9/15/64) |
| | Living |
| Before 3/16/62 | 94 | 18 |
| 3/16/62-3/15/63 | 60 | 16 |
| 3/16/63-3/15/64 | 230 | 98 |
| 3/16/64-9/15/64 | 111 | 64 |
| 495 | 196 |

It will be noted that 94 transplants were performed before 1962, 60 during the year 1962 and 1963. Following the first report on the use of drug therapy18 there was an increased interest in the problem and 230 transplants were performed in 1963 and 1964. One hundred and eleven have been performed in the last six-month period tabulated. Table V indicates the most discouraging aspect of the current work in the field. In the past six months, during which presumably the most advanced techniques have been used, only
TABLE V.—Transplants Performed Between March and September 1964

<table>
<thead>
<tr>
<th>Donor</th>
<th>Total</th>
<th>Living</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother</td>
<td>32</td>
<td>19</td>
</tr>
<tr>
<td>Father</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Siblings</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Unrelated</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Cadaver</td>
<td>41</td>
<td>22</td>
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</tbody>
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19 of 32 maternal kidneys survived. In other words, 13 failed immediately or within the first six months, indicating the unpredictability of the operation.

A more encouraging trend, however, is noted in the use of the cadaveric donor. The cadaveric donor, of course, has the major advantage of circumventing all the ethical and moral factors involved in the use of living volunteer donors. Twenty-two out of 41, or more than 50%, of cadaveric donors survived during this six-month period. This indicates improved methods of organ procurement and preservation, as well as improvement in the techniques of surgery and in the care of the ill patients. Table VI indicates that during the past

TABLE VI.—Current (September 15, 1964)
Status of Transplants Performed Between 3/15/63-9/15/64

<table>
<thead>
<tr>
<th>Donor</th>
<th>Total</th>
<th>Living</th>
<th>%</th>
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<tbody>
<tr>
<td>Mother</td>
<td>88</td>
<td>47</td>
<td>53</td>
</tr>
<tr>
<td>Father</td>
<td>30</td>
<td>20</td>
<td>67</td>
</tr>
<tr>
<td>Siblings</td>
<td>61</td>
<td>41</td>
<td>67</td>
</tr>
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18 months about one-half of all maternal donor kidneys are still functioning, whereas two-thirds of those from fathers or siblings are still functioning. These figures are analyzed more completely elsewhere.24

One of the most important unsolved questions is how these drugs work. An effort to analyze the mechanism of immunosuppressive drugs in renal homotransplantation25 indicates that the animals on prolonged drug therapy are immunologically competent. The drug therapy could be stopped successfully in some but not in all animals. The long-surviving kidney was apparently protected in some way in the new environment because a second donor kidney could be rejected while the first survived. Retransplantation of a long-surviving kidney to its original host did not lead to a decrease in renal function. Long-surviving kidneys successfully transplanted back to their original donors are rejected. They likewise are rejected if transplanted to third parties, non-drug-treated recipients.

One of these experiments is illustrated in Fig. 5 in which immune paralysis does not seem to account for the prolonged survival. In this experiment a second donor kidney, which constitutes a double dose of antigen, is rejected while the first continues to survive.

The fact that the drug-treated animal is not an immunological cripple is of prime importance. The drug-treated hosts are able to withstand ordinary environmental infection in most instances and can lead normal lives without strict aseptic precautions. The drug-treated host not only can survive after the drug therapy has stopped but also can reject skin homografts from the kidney donor while retaining the kidney in situ. Fig. 6 shows that three such skin grafts were placed and all were rejected while the kidney continued to survive.

CONCLUSION

Renal transplantation is beginning to approach realization but a conservative attitude should be maintained so that we retain the proper relationship and motivations among doctors and donors in human kidney transplantation. Renal transplantation must be considered primarily experimental, and not predictably therapeutic. Any group performing transplants should consist of clinicians from many disciplines who, in addition to their basic knowledge, should be participating in basic laboratory investigations. In selecting any human volunteer donor we must be clear and careful about our motivations. When we take a healthy living donor and make him sick by offering him a potentially fatal operation, we are reversing completely and qualitatively the very essence of our medical motivation which is to make sick people well. The decision to subject a living volunteer donor to a major operation requires serious reflection and soul searching.
**Fig. 5.**—This experiment in the dog illustrates that a double dose of donor antigen, in the form of a second kidney transplant on day 267, does not insure survival of the homografted kidney. Therefore, it is unlikely that the principle of immunoparalysis activated by steady release of donor antigen from a long-established kidney graft accounts for drug-induced immunological tolerance (courtesy of Annals of Surgery, 160: 449, 1964, p. 458).

**Fig. 6.**—Example of an experiment designed to analyze the mechanism of immuno-suppressive drug therapy. This demonstrates that animals successfully tolerating a kidney homograft can discriminate against skin from the kidney donor, indicating that the animal is not an immunological cripple (courtesy of Annals of Surgery, 160: 449, 1964, p. 453).
References


Résumé


La seconde partie du travail rapporte l’expérience du Peter Bent Brigham Hospital et du Harvard Medical School, sur les transplantations expérimentales et cliniques de rein. Conjointement avec d’autres disciplines, la greffe de greffe rénale en 1950, il fut décidé de choisir le rein comme organ donneur à transplantant au lieu de la peau, pour étudier le problème des greffes rénales. En 1954, un premier succès avec une greffe rénale prise chez un jumeau identique, stimula l’intérêt. En 1959, la première greffe chez un jumeau non identique, fut réussie après avoir utilisé une dose d’irradiation subléthale. L’établissement d’un registre de transplantation rénale humaine subventionné par le Conseil du Conseil National de Recherches, a permis à cette nouvelle science de faire des progrès rapides et d’éviter la duplication des efforts et des erreurs. En septembre 1964, on collectionna 143 transplantés qui avaient survécu six mois. La survie de six mois donne de meilleures garanties pour une longue et définitive survie. L’auteur rapporte ensuite l’analyse de ses propres résultats, utilisant des reins prélevés chez les cadavres; près de 50% des greffons, ainsi transplantés, survécurent plus de six mois. Il semble que cette technique offre des possibilités.
très intéressantes éliminant les problèmes d'éthique et de morale qui sont soulevés lorsque le donneur est un humain volontaire.

En conclusion l'auteur remarque que la transplantation rénale est encore à ses débuts et doit encore être considérée au stade expérimental. Il insiste pour faire remarquer qu'il exige un travail d'équipe intéressant plusieurs spécialités et qu'il doit toujours être associé à la recherche en laboratoire. L'auteur signale enfin le problème moral suscité par l'utilisation de donneurs vivants en bonne santé que l'on soumet à une opération potentiellement mortelle et à qui on risque de donner une nouvelle maladie. La décision d'utiliser des donneurs vivants doit être prise après mûre réflexion.

POSTMASTECTOMY LYMPHANGIOSARcoma IN THE LYMPHEDEMATOUS ARM:

A Review of Four Cases*

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LYMPHEDEMA of the arm is a common complication of radical mastectomy for carcinoma of the breast. Treves,1 discussing its etiology, reported that it occurred in 41% of patients with primary operable breast cancer who were subjected to radical mastectomy. In 1948 Stewart and Treves2 first described a new entity, lymphangiosarcoma, developing in a lymphedematous arm after mastectomy. This is a rare complication of a common condition. In 1959 McConnell and Haslam3 reported five cases of this neoplasm and reviewed the literature. In 1962 Taswell, Soule and Coventry4 reported 13 cases of their own, the largest series to date, and reviewed the literature. This report brought the number of accepted cases to 64. Of the 64 cases of lymphangiosarcoma, 58 occurred in a postmastectomy lymphedematous arm, four developed in an edematous leg unassociated with a previous malignant neoplasm, one of congenital origin occurred in an arm, and one in a lymphedematous leg was unknown etiology. Since 1962 occasional single cases have been reported.

The purpose of this paper is to draw attention to this neoplasm so that it will not to be confused with recurrent mammary cancer, to point out the dangers inherent in the lymphedematous arm, and to review briefly four cases of postmastectomy lymphangiosarcoma that have come to my attention.

CASE REPORTS

CASE 1.—A 67-year-old single retired female school teacher had a left radical mastectomy for carcinoma of the breast on April 9, 1940. Following mastectomy, radiation therapy was administered, the details of which are not available. Some time later (the exact time is uncertain), the left arm became edematous and remained so. Eight years after mastectomy a blue-black nodule appeared in the skin of the arm just above the elbow, which on excision was diagnosed hemangiendothelioma. A month later she reported to the London Cancer Clinic because of recurrence of similar blue-purple nodules in the skin of the arm. On the following day wide excision of the affected area was carried out. Eleven days later a suspected recurrence was noted closely adjacent to the operative site and 13 days later radiation therapy was begun. On October 16, 1948, the left arm was disarticulated at the shoulder because of neoplastic recurrence. By December 1, 1948, neoplastic nodules and appeared close to the surgical incision in the left shoulder. Once again the patient received radiation therapy. In June 1949 she complained of cough, fever and sweat-