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AN ATTEMPT TO INOCULATE HUMAN LEPROSY TO LEPERS BY HETEROPLASTIC DERMO- EPIDERMIC GRAFTING¹

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Attempts to inoculate human leprosy to man have not, until now, been followed by convincing results. It occurred to me that skin grafting from one patient to another might be more successful. This method was first tried with patients suffering from tuberculoid leprosy. In many of these cases the lesions are not numerous, and sometimes they are confined to a single segment of the body, the healthy skin not showing any apparent signs of the disease. These patients are susceptible to leprosy, as proved by their lesions, while healthy subjects might be refractory.

In heteroplastic grafting the transferred graft remains alive only for from eight to fifteen days. That period, however, is ample for exchanges to occur between the graft and the tissues of the carrier, in which some of the germs should be carried to his organism under the best possible conditions.

This attempt has been made in three such cases. In one instance the graft was taken from one of the cutaneous type of leprosy, and in the other two the grafts were from tuberculoid cases. The lesions produced in these three cases are described.

Observation No. 1.—This man, B. K., presented only a small lesion, 1 cm. in diameter, at the interior corner of the right eye. His skin was very dark from exposure to the sun. On December 22, 1937, a dermoepidermic strip was excised from the left paravertebral groove and in its place was

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implanted a slightly smaller dermoepidermic graft obtained from a very active tuberculoid lesion of another patient (A.M.).

On December 24 the grafted piece was satisfactorily adherent and alive. It was of a lighter shade than the skin of the recipient. On December 31 it appeared as a small, clearly distinct element.

On January 4, 1938, a dry, adherent crust had replaced the graft. In the following days it was difficult to tell if there still remained any part of the graft at the place of the scab.

A month later the scar was exuberant, and it remained in this condition for many months. On June 18 a new scab, small and dry, was found in the center of the scar. Around the scar the skin showed a linear zone of infiltration that was slightly raised, yellowish in color, and of papular nature due to coarsening of the spaces between the folds. This condition was easy to distinguish on a cold day. On June 26 a biopsy was made of this infiltration. On July 7 the ring of infiltration was still slightly raised and of a yellowish-pink color.

Histological examination of the biopsy specimen reveals islands of infiltration throughout the depth of the dermis. This infiltration is made up of lymphocytes, monocytes, histiocytes, fibroblasts and scanty polymorphonuclear leucocytes. In places it extends as a sheath along the vessels. In these sections rare microfilaria are found, naturally outside of these foci of infiltration.

From these findings it appears that this graft produced around itself a new focus of infection which developed six months after the transfer was made.

Observation No. 2.—Patient La., with only a small papular spot 1 cm. in diameter upon the right supraspinal fossa. On February 4, 1938, a dermoepidermic graft was placed on the left side, in place of a piece of skin excised from the same location. This graft was taken from a patient (O.S.) whose lesions were in a state of tuberculoid reaction.

On February 14 the graft was firmly adherent, although it remained smaller than the area of excision. On the 16th it seemed to be dry, and to be shrinking more and more. On the 22nd it was no more than a scab, dry and raised. On the 26th it had dropped off and the skin was healing, with scar formation. On March 24 the scar was slightly exuberant.

In May it was almost flat, and on the same level as the surrounding skin. At its upper and outer angle, however, there was a purplish-red triangle, formed by three small papules. On June 9th these component parts were clearly larger and broader. On June 30 two of them were merged; these papules had become yellowish in color. The largest one was excised at this time.

Sections of the biopsy specimen show an essential infiltration of the dermis, under a smooth and thin epidermis. The granulomas are composed of numerous histiocytes, monocytes and lymphocytes.

On July 5 the papule which remained was yellowish-pink and of the same appearance as some of the isolated component parts of the original macule in the right supraspinal fossa. It had none of the appearance of a

reaction due to any of the common germs. During the entire month of July it continued to spread a little more.

In this patient, therefore, the graft produced a new focus of infection.

Observation No. 3.—This patient, M. T., had only a large, slightly active macule which covered his lumbar regions. On February 14, 1938, a piece of skin was removed from the supraspinal fossa and the place filled with a graft of the same area, 1 sq. cm. This graft was taken from a patient (B.F.) with lepromatous leprosy, the lesions very rich in bacilli.

On February 16 the graft had adhered well. On the 18th the epidermis had detached from the dermis, leaving a yellowish tissue. On February 21 the graft was less colored, having the appearance of leprous tissue, but it was no longer adherent. On February 23 it came off with the dressing. The wound, which was now left open, was irregularly granulomatous.

On February 26 the border of the wound was pink and infiltrated, with a small elevated nodule at the external angle. A part of this nodule was excised and crushed on a slide. In this smear there were quite numerous staphylococci, but also some fine lepra cells containing globi of bacilli, most of which were well stained. Following this a swelling, more or less elevated, reddish in color, developed around the wound, which healed slowly, scabs forming over the center.

A biopsy was made of this swelling, which surrounded the ulcerating wound, at its external angle. In smears made of one-half of the specimen there were found abundant mononuclear cells and several leprosy bacilli. In sections of the other half there is seen an infiltration of the dermis composed of coalescent granulomas made up of numerous epithelioid and giantiform cells.

In the following weeks the ulcer was again covered by a scab, while the swelling partly subsided; the scab then came off, revealing a deep-red surface. On March 29, besides the cicatrix, there was observed another swelling, 2 mm. in size, in the skin which was not involved in the excision. This point was slightly elevated and in color a little different from the healthy skin. In the meantime the cicatrization progressed and the scar became flattened.

Another biopsy specimen was taken from the border of the scar, where there still persisted several foci of infiltration. No bacilli were found in a smear, but in the sections there is seen a very marked infiltration of histiocytes, mononuclears, lymphocytes, quite rare polymorphonuclears, and some masses of epithelioid cells.

In May the scar became nearly uniform, with some spots more rose-colored than normal. Besides the elevation limiting the scar, the ring described above stood out more clearly, yellowish-red in color, its elevation perceptible to the touch. In the months of June and July the scar took on an ordinary aspect; it was then not possible to attribute to a leprous origin the manifestations present at this place.

In this patient, therefore, a month after the placing of the graft, and three weeks after it fell off, it was possible to find

leprosy bacilli in the infiltration of the border of the ulcer. It was six months before this ulcer took on the appearance of an ordinary scar. The reaction of the skin around the ulcer, and later of its scar, gave rise to a tuberculoid infiltration.

CONCLUSIONS

Patients who have few macules of tuberculoid leprosy are certainly subjects that permit attempts at inoculation, by heteroplastic grafting, more readily than apparently healthy subjects, who might be refractory to the infection and with whom it might not be permitted to make the attempt.

In the first two experiments described there was observed, surrounding the grafts of tuberculoid leprosy tissue, the appearance of new lesions of tuberculoid leprosy after periods of from four to six months.

In the third experiment, about one month after transferring a graft of a lepromatous lesion to a tuberculoid case, some leprosy bacilli were still found in lesions at the border of the ulcer. Around the wound which limited this ulcer there was produced a reaction of tuberculoid leprotic nature.