opment according to its original orientation. Digits 3 and 4 were formed on the ventral border, indicating that this was the ulnar side, and as development progressed the palm of the graft turned dorsally.

Similar results were obtained at stage 34. In all positive cases the formation of the hand indicated that the asymmetry had not been reversed.

Several limbs transplanted at stages 33 and 34 have been sectioned. The asymmetry of the pectoral girdle was reversed; a harmonic right girdle had developed from a left limb rudiment. The supernumerary appendage was an inverted left limb with a normally oriented right girdle.

We conclude that the dorsoventral axis of the forelimb bud of *A. microstomum* is determined in a manner similar to that of other species of the genus which have been studied. The dorsoventral axis for 3 somite grafts is partially determined at stage 32 and becomes firmly established at stage 33. These experiments are being continued.

HARVEY B. LOVELL

UNIVERSITY OF LOUISVILLE

THE RETICULO-ENDOTHELIAL SYSTEM AND THE CONCEPT OF THE "ANTI-HORMONE"[1]

NUMEROUS investigations have shown that, following prolonged administration of certain endocrine preparations, loss of sensitivity to the injected extract will eventually result. Collip and his associates believe that normally hormonal effects are kept in balance by the presence of specific anti-hormones and that these appear in excess when animals are chronically treated with various endocrine extracts. Another group claims that this response is of immunity reaction nature and believes that the inhibitory substances are antibodies. One way of determining which of the two interpretations is correct would be to administer such hormone preparations to animals from which a large portion of the reticulo-endothelial system, intimately concerned with antibody formation, has been removed. Since the spleen is the most concentrated source of reticulo-endothelial tissue in the body and since the ratio of its weight to body weight is relatively great in the rat, we have compared, in our first studies, the response of young immature splenectomized and normal hooded litter mate female rats to daily injections of 10 R.U. pregnancy urine extract (Follutein or Antuitrin S).

In the controls, the ovary size reaches a maximum after approximately 10 to 15 days of treatment and then regresses, becoming normal in size within two to three months, despite continued injection. The ovaries of the splenectomized rats, however, continue to grow, attaining weights approximately 2 to 3½ times that of the injected controls, 20 to 30 days after splenectomy. This increase in weight is due almost entirely to an increase in the size and, in many cases, the numbers of corpora lutea. With continued treatment the ovaries of the splenectomized animals begin to regress rather rapidly after about 30 days, due, we believe, to the establishment of a compensatory mechanism, in the form of a hyperplasia and increased activity of the remainder of the reticulo-endothelial tissue.

The vaginal smears of the control injected animals show a condition of almost continual estrus for as long as one month after beginning injections. The smears of the splenectomized rats, although indicative of estrus for a few days after the opening of the vaginal orifice, soon become almost of the complete diestrus type and remain that way for at least a month following onset of treatment. We interpret these results as follows. The injected normal immature rat, because its reticulo-endothelial system is intact, soon produces the inhibitory principle for the luteinizing factor believed to be present in the pregnancy urine extracts. The animal's own pituitary, however, is continually producing follicular stimulating substance for which no anti-substance is formed and so the animal remains in constant estrus. This finds corroboration in sections of ovaries of all our treated controls where large follicles are always present for at least 1½ months following beginning of treatment. The splenectomized immature rat, being deprived of a large amount of reticulo-endothelial tissue, produces for a time a smaller quantity of the inhibitory substance for the luteinizing principle. More and larger corpora result, and even though mature follicles are still present, the animal lapses into diestrus because of the greater preponderance of progesterone over estrin in the circulating blood.

It is of extreme importance that the rats employed be completely free of all traces of *Bartonella muris*, a latent infection quite prevalent in rats,[2] since this necessarily affects reticulo-endothelial activity. The following experiments indicate the importance of taking this factor into account.

(1) Unoperated immature Bartonella carrier rats in response to daily injections of 10 R.U. pregnancy urine extract for 20 days develop luteinized ovaries as large as those which are present in 20-day treated Bartonella free splenectomized animals. That this response is due most likely to reticulo-endothelial block-

[1] For chief references on the subject, refer to the papers by: J. B. Collip, *Jour. Mt. Sinai Hosp.*, 1: 28, 1934; G. H. Twombly, *Endocrinol.*, 20: 311, 1936; P. A. Katzman, N. J. Wade and E. A. Doisy, *Endocrinol.*, 21: 1, 1937; K. W. Thompson and H. Cushing, *Proc. Roy. Soc.*, B, 121: 501, 1937; I. W. Rowlands, *Proc. Roy. Soc.*, B, 121: 517, 1937.

[2] D. Perla and J. Marmorston, "The Spleen and Resistance." Williams and Wilkins Co. 1935.

age by the Bartonella organism can be seen from some of our experiments, which show that if Bartonella carrier injected rats are splenectomized on the twentieth day of treatment, those which have developed the largest ovaries die within a few days, evidence of the disease being very readily revealed in the blood during this time and, in most cases, in histological sections of the excised spleen. Autopsy of these animals shows only a slight compensatory hyperplasia of the lymph and hemolymph tissue. We have had a few Bartonella carrier treated animals which did not succumb after splenectomy performed on the twentieth day of injection, but these rats are almost invariably those which have developed smaller ovaries in response to the treatment. They survive and produce the inhibitory substance to some extent, due most likely to the marked hyperplasia of the remainder of the reticulo-endothelial system, noted as an increase in the numbers and size of the lymph and hemolymph glands at autopsy of these animals sacrificed a few days after the operation.

(2) Nearly all our immature Bartonella carrier rats, if splenectomized at an early stage, are capable of surviving for at least a month. Daily doses of 10 R.U. pregnancy urine extract cause such animals to go into a condition of constant estrus. The ovaries of such animals after 20 to 25 days of injection are, in many cases, even smaller than those of the non-operated treated Bartonella free rats. Histological sections of these ovaries show large follicles and relatively few and smaller corpora lutea. Removal of the spleen serves as a stimulus for increased development and activity of the remaining reticulo-endothelial elements. Our results show that in the treated infected animals, removal of the spleen, coupled with the presence of the Bartonella organism, has evoked much greater reticulo-endothelial compensation, and in a shorter time, than in the injected splenectomized uninfected animals. The injected splenectomized Bartonella carrier immature rat, because of this vigorous rapid compensation, may therefore produce as much or even greater quantities of the inhibitory principle than similarly treated Bartonella free control rats. This would explain the constant estrus condition in such animals.

This work has theoretical importance because (1) it demonstrates a connection between reticulo-endothelial activity and the development of refractoriness to heterozoic endocrine extracts. This strongly supports the contention that the antagonistic substances produced in response to chronic treatment with such extracts are antibody-like in nature. Experiments dealing with a comparison of the neutralizing effects of serum from injected splenectomized, "reticulo-endothelial blocked" and normal animals are now being conducted. (2) It suggests that, by depressing reticulo-endothelial activity either by excision of portions or experimental blockade, it may be possible to evoke from endocrine organs physiological responses of greater magnitude than ever before. (3) It points to the necessity of taking into account the factor of latent infection prevalent in laboratory animals, in interpreting the responses from the endocrine organs. This factor may possibly account, to some extent, for the sometimes exceedingly variable results obtained with prolonged injections of endocrine principles.

ALBERT S. GORDON
WILLIAM KLEINBERG
HARRY A. CHARIPPER

WASHINGTON SQUARE COLLEGE
NEW YORK UNIVERSITY

SCIENTIFIC APPARATUS AND LABORATORY METHODS

A NEW TYPE OF RELIEF MAP

IN many fields maps are absolutely indispensable in recording, understanding and demonstrating the lay of a land. Relief maps, too, have their special purpose, and contractors, architects and engineers are using them more and more the better to understand the problems depending on terrain. Even with the specialist himself, contour lines alone do not make the picture stand out in its full meaning.

It is easy to think of a contour line as the edge of a terrace or of a horizontal board; indeed, it is common practice to cut out cardboard to represent contour lines, and these are piled one on another to give actual relief features. Even without smoothing the "terrace" edges to give a uniform slope the original map may be drawn in place to represent the geographic units—roads, streams, cities and such.

Now we offer a plan of map making by which all the features may be brought into relief as if stamped out of sheet metal, and with it the streams, roads, etc., may be retained in their correct positions. This makes for accuracy and for ease in construction, since it is purely a mechanical reproduction of the original.

The procedure may be as follows. Take the regular government topographic map and have it enlarged, perhaps to four inches per mile. Secure the cardboard that happens to give the desired vertical elevation, and lay the map on a piece of board of suitable size; place this on a jig-saw and cut along the lowest contour. (For convenience mark this board No. 2.) The piece of map thus cut out represents an area of one elevation and may be pasted upon a new board (No. 1) in its proper place and put to one side.

The rest of the map should in turn be fastened to a