Since the introduction of therapeutic methods to create small localised lesions in the deep structures of the brain for the treatment of different kinds of neurological disorders, interest has been stimulated in obtaining small biopsies of these regions. Such biopsies are useful to verify by histological methods the accuracy of radiological localisation used for stereotaxic procedures. They also serve to study by histological and histochemical methods the pathology of disease processes.

Housepian and Pool reported on 34 biopsies from 8 patients, using a leucotome technique. The biopsies obtained were specimens of approximately 500 mg. Five of these biopsies were described as negative, being from white matter. The same authors later reported further studies with stereotaxic biopsies from the thalamus. Heath et al. reported biopsies from the cortex of 3 human subjects, obtained by stereotaxic methods. The amount of tissue removed was somewhat smaller. Jinnai and his colleagues referred to stereotaxic biopsies of the thalamo-capsular junction carried out by them. They did not, however, give further details.

Stereotaxic biopsies have been done by us since 1962.

There were 155 biopsies taken from 62 patients during 65 operations. Three of these patients had biopsies from both hemispheres on different occasions. Of these patients 58 suffered from parkinsonism, 1 from disseminated sclerosis and 2 from choreoathetosis. In 1, the pathology causing involuntary movements was uncertain.

**Technique**

The cannula for the biopsy (Fig. 1) was devised by Mr. G. Newell of the University of Edinburgh. The stereotaxic method used was that of Guiot modified by Gillingham. The needle for the biopsy was of the same shape, diameter and length as the other instruments used for insertion into the brain, namely, the coagulating electrode, the opaque-marker carrier and the depth-recording electrode. By adjustment of the shoulders of all these instruments they could be made to correspond exactly to the alignment of the target with the lateral sights of the stereotaxic machine. Thus, biopsies could be taken accurately from the points where previous stimulation or depth recording was done. Coagulation lesions could be done at the same spot and marked radiologically by leaving a small steel ball at the site.

The biopsy needle was introduced to the required depth, the inner piston was withdrawn for 2 mm. and the needle was rotated through one full circle to enable its exposed cutting edge to cut a slice of brain approximately 2 mm. in diameter (Fig. 2). This tissue was sucked into the needle (air-tight suction being provided by a nylon washer) by withdrawing the inner piston for another few mm. The entire biopsy needle was now withdrawn and the specimen ejected out by gentle pushing of the inner piston to the tip of the needle. Usually, with gentle suction, biopsies of 2 to 3 mm. in size, weighing approximately 5 to 25 mg., were obtainable. Often tremor was seen to subside or lessen as soon as a biopsy was taken from the site of the target in the thalamus.

Immediately after withdrawing the biopsy needle, the coagulating needle was introduced to the same point to act as a tampon to prevent any bleeding at the site of biopsy.

The specimens were fixed with formalin and stained with hematoxylin and eosin. Distinction between grey and white matter was relatively easy under ordinary microscopy.

**Comment.** If a biopsy was attempted from a track where another instrument had already been introduced, it was occasionally difficult to obtain good specimens. Sometimes an attempt at biopsy produced only blood clot, especially if it was attempted within 3 mm. of a coagulation lesion done a few seconds earlier. In cases of dyskinesias one was not always successful in obtaining a biopsy from the capsular region. This conformed to our experience that the resistance to the passage of the electrode near the posterior limb of the
internal capsule and through it was greater in dyskinesias than in cases of parkinsonism. Apart from these exceptions it was possible to get a biopsy from the thalamus, capsule or pallidum whenever it was attempted.

No special postoperative complications were encountered in any of the 155 biopsies. There were no cases of haemorrhage at the site of biopsy (as shown by extreme drowsiness with shift in position of steel marker left at conclusion of operation or by transient moderately severe hemiparesis). It is interesting to note that there were 8 cases of haemorrhage as judged by the above criteria in the 388 stereotaxic operations in which no biopsy was taken.

Results

Of the 155 biopsies, 11 were not available for ordinary microscopy either because they were subjected to electron microscopy or because fixation with formalin was not satisfactory. Four biopsies were taken during a leucotomy and are not considered any further. One was from an area of previous electrocoagulation and showed no definite normal tissue.

This report is therefore concerned with the remaining 139 biopsies which were reported upon. A preliminary analysis was first carried out classifying the biopsies according to the histological report.

Of these, 81 were identified as grey matter because of the presence of ganglion cells (Fig. 3). There were 15 identified as white matter because of the predominance of fiber bundles with absence of ganglion cells (Fig. 4). In 28 specimens there was a mixture of both grey and white matter. Fifteen biopsies could not
be classified definitely as grey and/or white matter since they consisted largely of blood clot with only a minute quantity of neural tissue. Out of 155 attempts 15 therefore produced inadequate material for examination—a biopsy failure rate of less than 10 per cent.

Of the 81 biopsies which were identified as grey matter, 61 were from the thalamus and 20 from the pallidum. All postoperative lesions were charted on the atlas of Schaltenbrand and Bailey, working back on the roentgenograms showing the opaque steel marker left at the conclusion of the operative procedure. It was seen that all the 20 pallidal biopsies corresponded to the pallidum on the stereotaxic atlas.

Of the 61 thalamic biopsies 52 conformed to the corresponding site on the atlas. Of the 9 cases which did not, 5 biopsies were taken after withdrawal of another instrument in-
introduced in the track before the biopsy cannula. One was known to be a case of abnormal anatomy in that region and another patient has had 2 previous stereotaxic operations on the same hemisphere. Out of 54 biopsies, therefore, 52 coincided with the atlas in the thalamus after these cases had been excluded.

Since all the thalamic and pallidal biopsies were taken at or very near the thalamic or pallidal targets defined radiologically, this information gave us very good confirmation of the great accuracy of the radiological methods used.

Of the 15 biopsies reported as white matter, 11 conformed to the internal capsule on atlas charting. One was probably a bit of subcortical tissue pushed in by the needle. Three were from the capsule although we intended the biopsy to be from pallidum. One was from the capsule although we intended it to be from the thalamus. Individual anatomical differences between the patients probably accounted for this.

At the junctional tissue between grey and white matter the greatest degree of lack of correlation with the atlas of the brain occurred. In only 5 out of these 28 cases, the biopsy was intended to be from junctional tissue. In 23 cases the biopsy was intended to be from grey or white matter as per the atlas.

These biopsies which were taken when the biopsy cannula was the second instrument to be introduced along the track were considered separately. It was seen that in this group of 34 biopsies only 18 conformed to the corresponding site in the atlas. Of these 18, 9 were from the thalamus. The direction of the electrode track in this operation made it difficult to evaluate which part of the thalamus these 9 were from and how accurate they were with reference to the atlas. The observed difference between the proportions of correct correlation in cases of biopsy with and without previous insertion of instrument is statistically significant.

These results therefore could now be classified in a different way to assess the correlation between the atlas and the histological report. In this final analysis all biopsies taken when the biopsy cannula was not the first instrument to be introduced were omitted. The biopsies which were after a previous operation and also the piece of subcortical tissue were excluded. This left 88 cases shown in Table 1, which suggests that the degree of accuracy with radiological localisation with this method decreases in the following order for targets in our method of stereotaxy—thalamus, pallidum and capsule.

**Conclusions**

From this study, therefore, the following conclusions are suggestive. (1) Stereotaxic biopsy appeared to be a safe method of obtaining tissue for examination from intended sites from the depth of the brain. (2) When properly carried out the rate of failure was less than 10 per cent and accuracy of the order of 1 to 2 mm. (3) In order to get reliable results, the biopsy cannula should be the first instrument to be introduced along the planned track. (4) The thalamic target and to a less extent the pallidal target as defined radiologically in the Guiot-Gillingham method were reasonably accurate. (5) The borders of the internal capsule, however, could not be predicted with the same accuracy by this method because of individual anatomical variations.

When depth recording is not used to define the borders of the internal capsule, biopsies could serve as a useful guide to confirm the site of the lesion as well as to plan a revision of the lesion, if needed later. From the research point of view, confirmation of the site...

**TABLE 1**

<table>
<thead>
<tr>
<th>Intended Site</th>
<th>Histological Report</th>
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<tr>
<td></td>
<td>Grey Matter</td>
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<tr>
<td>Thalamus (46 biopsies)</td>
<td>44</td>
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<tr>
<td>Pallidum (25 biopsies)</td>
<td>14</td>
</tr>
<tr>
<td>Capsule (11 biopsies)</td>
<td>2</td>
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<tr>
<td>Junctional tissue (6 biopsies)</td>
<td>1</td>
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</table>
of the lesion is valuable since the amount of autopsy material available in this class of patients is very small.

This biopsy method could also be used with benefit for deep-seated tumours before and after irradiation. The possibilities of histological, histochemical and electron-microscopic studies of many diseases of the brain are unlimited using this harmless and accurate technique.

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References