FROZEN SECTION SERVICE IN THE GENERAL HOSPITAL, SINGAPORE

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The first utilization of frozen section was attributed to Welch of John Hopkins Hospital in 1891. This rapid method of diagnosis has suffered innumerable attacks of criticisms in the last 75 years. Most of these criticisms have been levied by the pathologists themselves, whilst surgeons have accepted this method much more readily. In America, this is a routine facility in most laboratories, whilst in England, only relatively few centres have accepted it.

In Singapore, this method was introduced as a routine service by Dr. B. Gellei in 1961. In the latter nine months of that year only 29 sections were examined. This method was found to be so valuable that the number of sections had increased to 155 in 1964.

THE METHOD

The Pathologist is called to the theatre as soon as the biopsy is about to be removed. When the pathologist has arrived he is told briefly of the patient's history and is given the specimen. The specimen is inspected in the Frozen Section Room, just next to the operating theatre. The steps are:—

1. Either the whole piece or a representative piece is boiled in Formal Calcium for a quick fixation.
2. The tissue is then cooled in tap water before it is blocked with freezing carbon dioxide which is released from a gaseous cylinder.
3. The sections are cut at about 15 mu to 25 mu thick.
4. Thence it is dipped into a metachromatic stain (we find 1% Toluidine Blue highly satisfactory) for about 20-30 seconds.
5. It is then differentiated for 1 to 2 seconds in 1% acetic acid. This step can be omitted if your tap water is already acidic.
6. The section is mounted in water and a cover-slip is placed over it.

From the time of examining the gross tissue and up to the time of making a decision it usually takes about 3-5 minutes. In the case of Hirschsprung disease, it takes much longer.

The metachromatic Toluidine Blue stains the nuclei blue and the cytoplasm pink. Under the microscope the diagnosis is based mainly on the grouping of nuclear patterns and the unruliness of cancerous growth rather than on subtle cytological atypism. Therefore, the pathologist must be an experienced one before he embarks on this frozen section method. It is more prudent if a beginner apprentices himself with some one else who is already familiar with the frozen section technique until he is competent enough to read it alone. Even a pathologist of considerable histopathological experience will encounter some difficulty when he first embarks on this method of diagnosis.

What is left of the frozen piece of tissue is then passed with the rest of the tumour (if any) for a routine paraffin section diagnosis. The only malignant portion of the whole specimen may be in this piece of frozen section.

RESULTS

In the short span of $4\frac{1}{4}$ years (April 1961 to July 1965) we examined a total of 443 frozen sections on 33 different types of tissues (Table 1). 51.8% were diagnosed as benign, and 42.7% were malignant. This gave an overall accuracy of 94.5%. 2.5% were deferred diagnosis (doubtful), 0.7% were false positives and 2.3% were false negatives. There was a trend of improvement as the years went on (Table 2), and up to date this year (1965) we had an accuracy of 98.5%. This figure could be further improved if only one man was responsible for all the frozen sections. The deferred diagnoses and false negatives indicated to a small extent the infancy of the service. The false positives were actually 3 (0.7%) in number: two of these were not of a serious nature and one (breast) was due to a misunderstanding between the surgeon and the pathologist (see below). The first false positive was reported as an astrocytoma (Grades I & II) at frozen section, and it turned out to be a meningioma. The second and third false positives would be discussed in their appropriate sections.

The breast (151 sections), the lymph node (48 sections) and the thyroid (44 sections)

TABLE I

NUMBER OF FROZEN SECTIONS FROM 30th MARCH 1961 TO JULY 1965

Specimens	Benign	Malignant	Doubtful	False +	False —	Total
Adrenal	2	-	-	-	-	2
Appendicular Mass	1	-	-	-	-	1
Bladder	3	1	2	-	1	7
Bone and Marrow	1	1	-	-	-	2
Brain	10	6	-	1	2	19
Breast	74	72	1	1	3	151
Cervix	-	3	-	-	-	3
Colon	15	9	1	-	-	25
Eye and Lids	3	2	1	-	-	6
Joints and Synovium	1	-	-	-	-	1
Gall bladder	4	4	-	-	-	8
Intestine	1	-	-	-	-	1
Kidney	6	3	-	-	-	9
Liver	5	5	1	-	1	12
Lung and Bronchus	13	10	-	-	1	24
Lymph node	28	18	1	-	1	48
Oesophagus	-	1	-	-	-	1
Mediastinal Mass	1	-	-	-	-	1
Omentum	1	2	-	-	-	3
Ovary	2	3	1	-	-	6
Pancreas	3	2	-	-	-	5
Parotid Gland	7	5	-	-	-	12
Peritoneum	1	3	-	-	-	4
Prostate	1	-	-	-	-	1
Skin & Subt. Tissue	6	9	-	-	-	15
Stomach	8	4	-	-	-	12
Submandibular tumour	-	1	-	-	-	1
Spinal tissue	-	1	-	-	-	1
Testis	3	5	-	-	-	8
Thymus	2	2	-	-	-	4
Thyroid	27	13	3	1	-	44
Tongue	1	2	-	-	-	3
Ureter	-	2	-	-	1	3
Total	230	189	11	3	10	443
Percentage	51.8%	42.7%	2.5%	0.7%	2.3%	100%

TABLE 2

TOTAL NUMBER OF FROZEN SECTIONS

Year	Actual No.	Benign	Malig-nant	Accuracy	Doubtful	False +	False —
Apr.-Dec. 1961	29	13	13	89.8%	1 (3.4%)	1 (3.4%)	1 (3.4%)
1962	66	27	34	92.4%	-	-	5 (7.6%)
1963	126	66	53	94.4%	4 (3.2%)	2 (1.6%)	1 (0.8%)
1964	155	86	61	94.7%	6 (4%)	-	2 (1.3%)
1965 1st 6 mths.	67	38	28	98.5%	-	-	1 (1.5%)
Overall Total	443	230	189	94.5%	11 (2.5%)	3 (0.7%)	10 (2.3%)

TABLE 3

FROZEN SECTIONS (BREAST)

Year	Actual No.	Benign	Malig-nant	Accuracy	Doubtful	False +	False —
Apr.-Dec. 1961	6	4	2	100%	-	-	-
1962	26	11	13	92.3%	-	-	2 (7.7%)
1963	49	25	22	96%	-	1 (2%)	1 (2%)
1964	51	26	24	98%	1 (2%)	-	-
1965 1st 6 mths.	19	8	11	100%	-	-	-
Overall Total	151	74	72	96.7%	1 (0.7%)	1 (0.7%)	3 (1.9%)

TABLE 4

FROZEN SECTIONS (THYROID)

Year	Actual No.	Benign	Malig-nant	Accuracy	Doubtful	False +	False —
Apr.-Dec.							
1961	4	1	2	75%	1 (25%)	-	-
1962	7	4	3	100%	-	-	-
1963	8	5	1	75%	1 (12.5%)	1 (12.5%)	-
1964	14	11	2	92.8%	1 (7.2%)	-	-
1965 1st 6 mths.	11	6	5	100%	-	-	-
Overall Total	44	27	13	90.9%	3 (6.8%)	1 (2.3%)	-

TABLE 5

FROZEN SECTIONS (LYMPH NODE)

Year	Actual No.	Benign	Malig-nant	Accuracy	Doubtful	False +	False —
Apr.-Dec.							
1961	4	1	2	75%	-	-	1 (25%)
1962	2	1	1	100%	-	-	-
1963	16	11	5	100%	-	-	-
1964	13	6	6	92.3%	1 (7.7%)	-	-
1965 1st 6 mths.	13	9	4	100%	-	-	-
Overall Total	48	28	18	94.2%	1 (2.9%)	-	1 (2.9%)

would be considered in a little more detail because they were the most frequent organs examined. Hirschsprung's Disease also needed particular mention.

Breast (See Table 3)

The most frequent organ examined was the breast. Out of the total of 151 breast frozen sections examined, 1 (0.7% was a deferred diagnosis, 1 (0.7%) was a false positive, and 3 (1.9%) were false negatives. The one case of false positive was really due to a misunderstanding between the pathologist and the surgeon. At frozen section it was thought that the tissue was malignant, but diagnosis was better deferred to the next morning when a paraffin section would then be examined to exclude hyperplastic intraductal epithelicsis. However, in the next morning before the paraffin section came through, the surgeon thought that by 11.00 a.m., no news was bad news and he went ahead with the radical mastectomy. At noon when the pathologist rang up to the surgeon, he was told that the radical mastectomy was already completed. The actual paraffin diagnosis of the breast here was multiple fibroadenomas with mammary dysplasia. The latter showed marked adenosis and profuse epitheliosis, and in spite of the ductal and atypical epithelial hyperplasia, it was still within the limits of benignity.

From Table 3 it can be seen that there was a general improvement in the accuracy rates: there was only one doubtful in 1964 (98% accuracy), and in 1965 hitherto there was a 100% accuracy. "IT IS RECOMMENDED THAT EVERY SUSPICIOUS LUMP OR LUMPS IN THE BREAST MUST HAVE A FROZEN SECTION EXAMINATION AS A PRELUDE TO ANY SURGICAL TREATMENT."

Thyroid

Out of the 44 frozen section examinations of the thyroid, 27 were benign and 13 were malignant giving an overall accuracy rate of 90.9% (Table 4). There were 3 (6.8%) cases of deferred diagnosis and one (2.3%) case of false positive. The lower overall accuracy rate of 90.9% was due to the inherent difficulty in differentiating a benign from a malignant tumour in the thyroid. This is true even with paraffin sections. The one false positive case was in a thyrotoxic goitre, (who had been treated with neomacazole) which was diagnosed by the pathologist as a tumour—? adenoma, ? carcinoma. If the pathologist had known the history and had seen the cut surface of the whole lobe of thyroid, this mistake (although it did not alter the course of treatment here), might not have been made.

Several factors emerged out of our experience with thyroid frozen sections:—

1. Either the whole nodule or the whole lobe is preferred by the pathologist at frozen section examination.
2. Only the suspicion of malignancy warrants a frozen section. That means obvious cases of thyrotoxic goitre, and multinodular goitre should not need a frozen section. In a case of a well encapsulated thyroid adenoma, it is most difficult for the pathologist to detect a malignant change at frozen section.
3. If there are nodules or lymph nodes outside the thyroid, these should be sent for frozen section in preference to tumour within the thyroid gland itself. This is due to the inherent difficulty in diagnosing a well differentiated follicular carcinoma within the thyroid gland at frozen section. So any thyroid tissue within lymph nodes outside the thyroid gland signified metastasis. There is no such entity as a lateral aberrant thyroid.

Lymph nodes

Except for the frequency, (48 occasions) there is nothing much to comment on this section, but for a rare abuse of the pathologist. This is usually done late in the day when a proven carcinoma (*viz.* oesophagus or stomach) warrants a long and major operation. The pathologist is called up to examine lymph node after lymph node. If one of them were to have a tiny focus of secondary the surgeon would immediately close the patient up and classify the case inoperable.

Table 5 shows that the accuracy rate here is 94.2%, and there is only 1 (2.9%) deferred diagnosis and 1 (2.9%) false negative.

Hirschsprung's Disease

A frozen section is routinely called for to study the presence or absence of ganglion cells in the large gut in these cases. Recognising ganglion cells, especially in an infected gut wall, is the most difficult exercise in frozen section. It

is not universally known that besides absence or paucity of ganglion cells in Hirschsprung's Disease, "abnormal" nerve bundles are also present in the submucosa and between the muscle layers. These nerve bundles are normal in appearance, but they are abnormal by their mere presence in these situations. This latter finding helps to confirm the diagnosis. It is also not commonly known that in Hirschsprung's disease, there is a variable zone of transition between abnormal and normal segments of gut. In other words, there is a zone of variable length in which an occasional ganglion cell is seen, but abnormal nerve bundles are also present in that same segment. Therefore there must be abundant ganglion cells as well as absence of nerve bundles before a segment can be pronounced absolutely normal.

Observations and Recommendations

1. A frozen section service is very valuable and essential. The total equipment does not come up to more than M$1,500—and it takes only about 5 minutes per section. Every laboratory should strive to provide such a service.
2. The frozen section should be performed beside the operating theatre: the pathologist may then go into the theatre to view the gross specimen for himself (if necessary) and he may ask for many more samplings from different areas of the tumour without inconveniencing anyone.
3. It must be understood that a 100% accuracy is almost impossible, and no pathologist can achieve this even with paraffin sections. However, if the surgeon is not wholly confident with the paraffin diagnoses of his pathologist, he should not ask for a frozen section.
4. This service however must not be abused, one instance of which is quoted above. A frozen section should not be asked for, if the operational findings are obviously inoperable, or if the surgeon has no intention of proceeding to radical surgery if the pathologist's diagnosis is malignant. It must not be done to satisfy the whims of the surgeon who wants to know the diagnosis 2 minutes after closing up the patient, so that either his records can be completed promptly, or that his macroscopic diagnosis may be confirmed in the presence of an audience.
5. In a case with unusual features, the pathologist must be called to examine the patient before the operation and a discussion on the possible diagnoses and the site of biopsy is then held.
6. If the pathologist's opinion of the frozen section is malignant in spite of overwhelming clinical evidence to the contrary, the patient must be treated conservatively until paraffin sections are available for further study.
7. The pathologist must have only 3 opinions on a given section: "Malignant", "Benign" and "I don't know". If he sincerely cannot come to a decision he must ask for help from his superior officer. If he is the Chief himself, the surgeon should not harass him into one of the other diagnoses.

SUMMARY

A routine frozen section service was started in April 1961 in the General Hospital of Singapore. This service is performed by a pathologist in a room beside the operating theatre. Except in cases of Hirschsprung's disease, it normally takes 3 to 5 minutes for the pathologist to come to a decision from the time of receiving the specimen. The method is described.

In this short span of $4\frac{1}{4}$ years, 443 frozen sections were performed on 33 different types of tissues. It has an overall diagnostic accuracy of 94.5% and this figure improved as the years went on, until in 1965 it reached a figure of 98.5%. The overall doubtful (2.5%), false positive (0.7%) and false negative (2.3%) reports were discussed. Out of the three false positives, two were of not a serious nature. and the third was due to a misunderstanding between the surgeon and the pathologist. With experience, the false positives should be completely eradicated.

In conclusion, a frozen section service should be included in the normal routine curriculum of a pathological department. It must be performed by a pathologist experienced in frozen section beside the operating theatre. It must be done on every suspicious lump in the breast and in the thyroid. It is also most valuable in looking for metastases in a lymph node, in Hirschsprung's disease as well as in parathyroid disorders.

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