THE DIAGNOSTIC RELIABILITY OF FROZEN SECTIONS *

WM. CARPENTER MACCARTY, M.D., F.A.C.P.

(From the Section on Surgical Pathology, The Mayo Clinic, Rochester, Minn.)

The words "frozen sections" have been heard for many years by some pathologists with a certain feeling of reluctance, distrust, or indifference. Certain pathologists who have not had a large personal experience with all methods of preparation of tissues frequently have approached the subject rather apologetically. Despite this attitude of mind, the method of making frozen sections is at least twenty-three years old, and its reliability has been well tried out here on 208,255 surgical specimens including 28,833 carcinomas.

There are several reasons why some pathologists have failed to realize the value of frozen sections. Such sections are made to best advantage from perfectly fresh, unfixed tissues. Their application to necropsy material or to material which has stood longer than half an hour is not very satisfactory. It has been difficult to obtain good stains; the best is Unna's polychrome methylene blue (Gruebler's) or Terry's recent modification of this stain. Before the World War there was no difficulty in obtaining good stain. During and after the War, stain was made in the laboratories of the clinic; for the last three years Terry's modification of this stain has been used. The stain does not make the diagnosis; it merely saves time in finding the cells. A well trained cytologist could make the diagnosis without stain.

It must be remembered that most pathologists see very little fresh tissue. They are quite naturally and justly wedded to paraffin and celloidin sections. With the material they have had, their technique has been admirable but their studies have been limited largely to the low powers of the microscope. Perfectly fresh unfixed tissues, on the other hand, may and should be studied with oil immersion lenses.

There are many tests of the diagnostic and prognostic reliability both of unfixed and of fixed frozen sections: Let us suppose, for example, that a surgeon removes a lymph node from the region of the

* Read before the American Association of Pathologists and Bacteriologists, Chicago, Illinois, March 28 and 29, 1929.

Received for publication May 27, 1929.

cecum or sigmoid and the report, based on a fresh, unfixed frozen section, is that the tissue is malignant. If the condition in the resected cecum turns out to be tuberculosis or the condition in the sigmoid, diverticulitis, how long do you think the surgeon would keep his pathologist? Suppose the surgeon removed a lymph node from the neck and the pathologist reported it to be tissue from a case of Hodgkin's disease or of lymphosarcoma and the lymph nodes were excised and found to be tuberculous; again, how long would the pathologist hold his position? If a specimen obtained by biopsy from a bone tumor were reported to be from malignant tissue and the condition were, after amputation, found to be chronic osteomyelitis, or perhaps syphilis, how long would the surgeon continue to have faith in the pathologist's ability? Suppose the surgeon curetted a uterus and the curetted specimen was reported to be from a malignant growth, and on hysterectomy nothing but a polyp or an hypertrophic endometrium was found, how good would the pathologist's reputation be in the minds of his clinical confreres?

It happens occasionally that a pathological diagnosis that is negative for malignancy is followed by the removal of malignant tissue, but this is no fault of the pathologist since he can examine only that tissue which is given to him and it may not contain anything that is malignant.

Frozen sections of fresh, unfixed tissue are so reliable in the hands of a well trained pathologist that he can make the diagnosis of a malignant condition, correctly, from a single cell. This may seem impossible; in fact a well known pathologist with very little experience with fresh tissue told me that it could not be done. The correctness of the statement that it can be and is being done has been proved. Without the pathologist having any knowledge of the specimen or the patient, a colleague, assistant, or technician may place a single cell under the oil immersion lens and may ask the pathologist to make a diagnosis. Let us suppose the cell is in a peripheral sinus of a lymph node, as frequently occurs. Such nodes are often removed so that the surgeon may know whether or not a mass is malignant and just how extensive it is if it is malignant. The report is that the condition is malignant and the surgeon resects the mass; the resected specimen must show the carcinoma if the original report were correct. In my own experience it has never failed. There are two more examples out of many which might be related. Sup-

pose the test specimen is from the uterus and the report is that the tissue is malignant. I have never seen a benign uterus removed after such a report. Suppose it was from a bone tumor and an amputation followed. I have never seen an amputated leg or arm, or any portion of these, that did not show malignancy to be present after such a cellular diagnosis.

There is another test of the accuracy of the method which unfortunately requires years to carry out. The cytologic method of diagnosis has been used for more than eleven years, and hence there has been enough time to carry it out in many cases. Let us suppose that one, or a few, of the malignant cells are found in a case of chronic mastitis or in a chronic gastric ulcer and are recorded as being malignant and the subsequent histories of the patients are followed. What might be expected? Some of the patients would be cured, or at least would be alive for more than eleven years, and we would not know whether the pathologic diagnosis was correct or not; but some of these patients actually return with recurrence of the malignant condition despite radical treatment. In a study of frozen fresh tissue comprising eight hundred sixty-nine freshly resected or excised gastric ulcers, 4.4 per cent contained the "malignant cell" inside of the gastric tubule and 5.2 per cent, inside, or just outside in the immediate stroma. Seven and five-tenths per cent of the first group of patients are dead of unknown causes and 15.2 per cent of the second group are known to be dead of carcinoma within the eleven-year period of study.

There are many other instances of the subsequent or postoperative history revealing the reliability of diagnosis by means of study of fresh, unfixed and fixed, frozen tissue. I bring the subject to the attention of pathologists merely to emphasize three points:

1. Surgeons and other clinicians know the value of frozen sections and have depended heretofore on professors of pathology to furnish candidates for positions in surgical pathology. Such surgeons are going ahead with the use of frozen sections despite the apathy of many general pathologists and are going to develop their own pathologists who may sooner or later become divorced, unfortunately, from the field of general pathology.

2. Pathologists, if interested at all in tissues, are missing a great opportunity to see cells as they are; they are failing to improve their understanding of their own subject.

3. By their lack of clinical interest and failure to utilize fresh tissues they are rapidly becoming thought to be less efficient as microscopic diagnosticians.

My plea is that pathologists open their eyes to a method which will startle them after a little practice. "I have never seen such beautiful cells" is the usual comment when properly made frozen sections are demonstrated to pathologists who are accustomed to seeing only embedded material.

DESCRIPTION OF PLATES

PLATE 76

Fresh unfixed and formalin-fixed frozen sections.

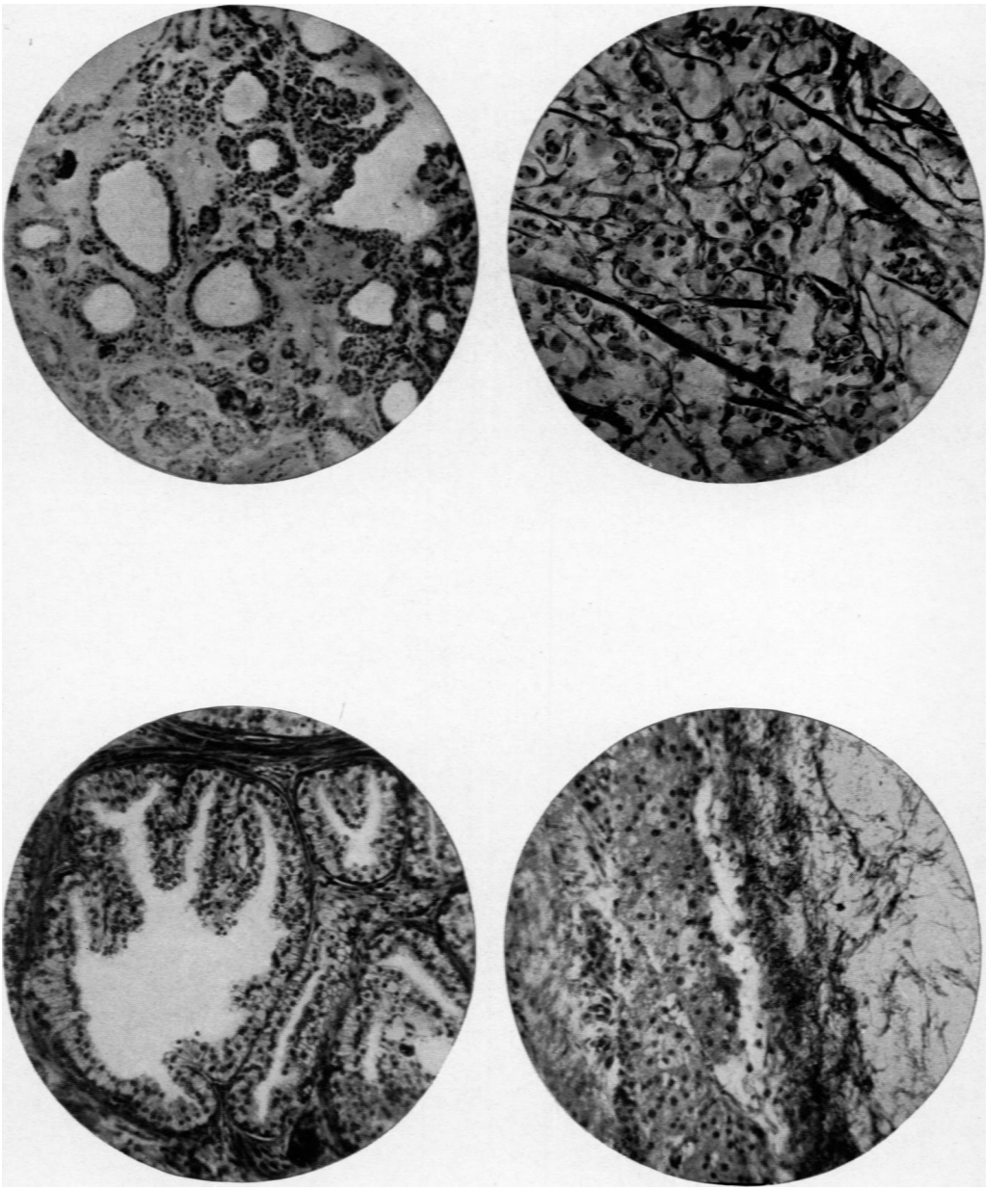

PLATE 77

Fresh unfixed and formalin-fixed sections.

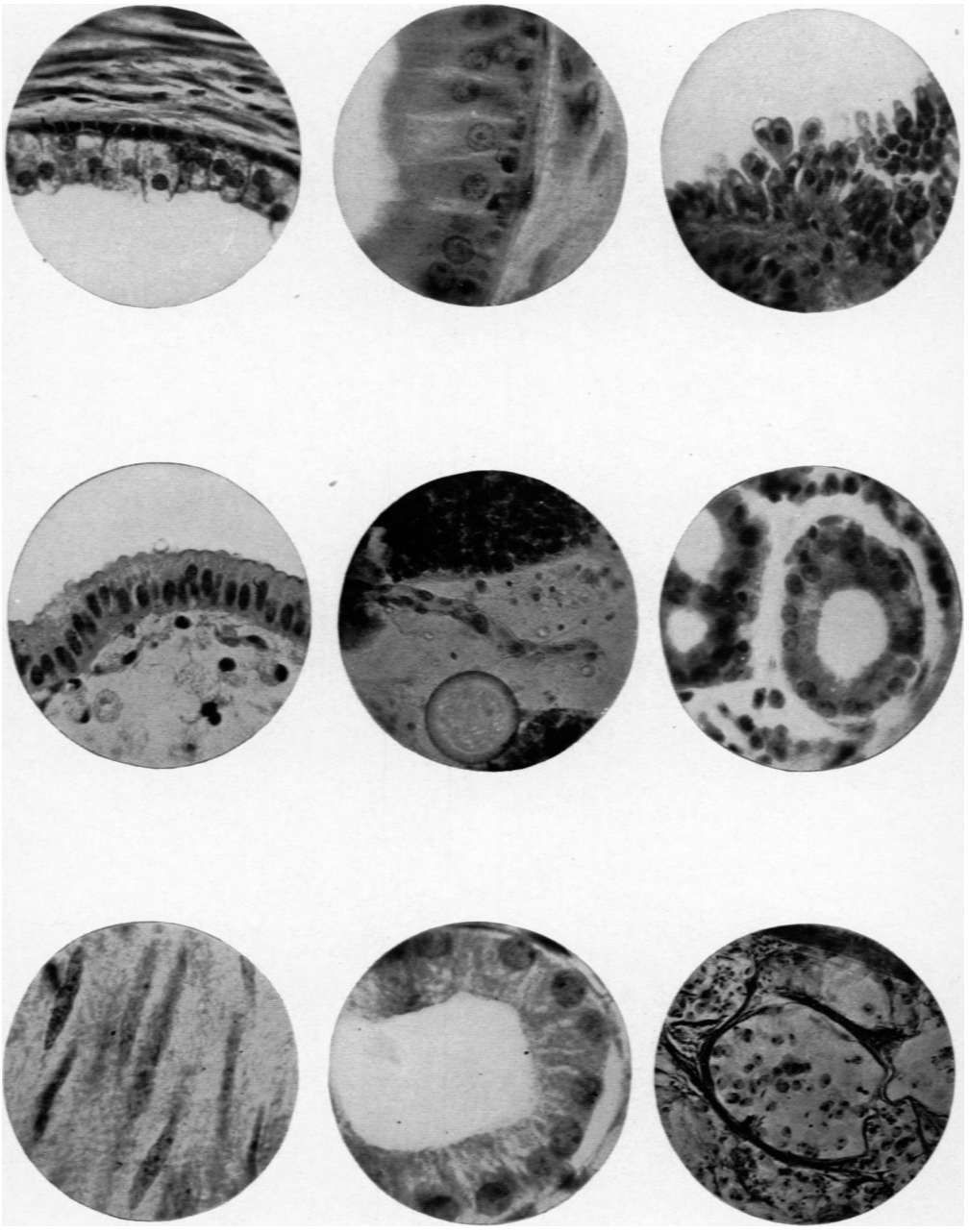

PLATE 78

Malignant cells from fresh unfixed and formalin-fixed frozen sections.