Study of the patient's saliva after irrigation of the mouth with Gey's balanced salt solution may be a useful screening test for squamous cell or epidermoid carcinoma in the oral cavity. Likewise, the topical application of toluidine blue, an acidophilic metachromatic nuclear stain, helps differentiate areas of carcinoma in situ or invasive carcinoma from normal tissue. However, these two procedures—the mouthwash technique and the toluidine blue test—while helpful, are not a substitute for biopsy and a negative smear does not preclude the presence of cancer.

The Mouthwash Technique

A large majority of oral neoplasms are squamous cell or epidermoid carcinomas. Since these tumors continually exfoliate malignant cells, it was felt that examination of saliva specimens taken from the entire oral cavity following irrigation with some form of mouthwash might be an effective screening test for oral cancer.

Numerous mouthwash solutions have been tested: Normal saline solution, which is not truly osmotic, was found unsatisfactory for oral irrigation; cells suspended in this preparation generally absorbed the fluid and burst within a few minutes, making cytologic evaluation impossible. Then, at the suggestion of the late Dr. Charles M. Pomerat, Research Director of the Pasadena Foundation for Medical Research, Gey's balanced salt solution—a simple culture fluid containing various amounts of salts normally found in most cells—was tested and found to be a successful mouthwash irrigant. (Table 1.)

Although a direct biopsy is the most accurate means of diagnosing a...
suspicious oral lesion, the mouthwash technique has proved valuable in two specific situations: (1) in the diagnosis of patients with extensive leukoplakia who have negative biopsies, and (2) in the follow-up of patients after surgical or radiation therapy for oral cancer. Experience at two dental schools and a large county hospital suggests that this method may also be useful as a screening technique in asymptomatic patients. However, if malignant cells are seen in a specimen, further attempts to discover the area of malignant change, such as repeated careful examinations of the oral cavity and multiple biopsies, must, of course, be carried out.

The technique is simple: have the patient vigorously irrigate his mouth for 60 seconds with one ounce of Gey’s Solution at room temperature. A specimen with a cell population typical of the entire oral cavity is obtained, placed in a large-mouthed jar and refrigerated to prevent growth of organisms. Mix the specimen with equal parts of 95 percent alcohol. Spin it down in a centrifuge and smear and stain the specimen in the usual Papanicolaou method.

Malignant cells will usually appear singly—not in clumps—and present little problem in identification. (Figs. 1 and 2.) Occasionally, however, more anaplastic and small cell types may be difficult to recognize. The leukocytes, plasma cells and red cells seen so prominently in specimens from oral scrapings are less common in mouthwash smears.

Although epidermoid carcinomas as small as 3mm have been detected by the mouthwash technique, only about an 85 percent yield has been obtained from patients with known oral cancer; there is no accounting for those instances in which carcinomas were missed. However, despite the fact that the study of smears is somewhat time-consuming and requires an experienced examiner, this technique has proved useful in the diagnosis of patients with diffuse oral leukoplakia in whom previous biopsies have been negative and in the follow-up of patients previously treated with surgery or radiation.

The Toluidine Blue Test

The topical application of toluidine blue, yet another technique in the diagnosis of oral cancer, will stain an area of carcinoma in situ or invasive carcinoma. Toluidine blue will not stain normal mucosa. Earlier reports by Shedd and Strong demonstrated that this test can detect squamous cell and
Fig. 3. Exophytic squamous cancer of the tongue.

Fig. 5. Sharply demarcated squamous cell carcinoma in the soft palate stains vividly.

Fig. 4. Ulcerated squamous cancer of the tongue stains vividly while the surrounding mucosa-covered malignant tissue does not stain.

Fig. 6. Deeply ulcerated malignant melanoma. Surrounding normal mucosa does not stain.

Fig. 7. A large, ulcerated squamous cancer of the floor of the mouth with two small satellite areas posterior to the main tumor.
epidermoid carcinoma (Figs. 3, 4, and 5) as well as the usual benign oral lesions, such as leukoplakia, lichen planus and traumatic ulcerations.\textsuperscript{3-5} Myers has demonstrated that toluidine blue can also identify melanoma, fibrosarcoma and lymphosarcoma, in addition to epidermoid cancer.\textsuperscript{6} (Fig. 6.)

In large, advanced cancers of the oral cavity, inspection and biopsy will generally provide sufficient information for diagnosis. However, toluidine blue may be indicated to diagnose leukoplakic lesions or dysplasia; differentiate a traumatic or inflammatory ulcer from cancer; determine the margins of resection prior to excision; and demonstrate a small second primary or satellite lesion adjacent to a larger lesion. (Fig. 7.) However, since toluidine blue does not stain normal mucosa, it is of value in the diagnosis of tumors which spread without involving the overlying mucous membrane.

To perform this test, have the patient first rinse his mouth with water and then swallow several sips of water. Aspirate excess saliva with suction and apply one percent acetic acid, a mucolytic agent, with a cotton applicator. If there is a large deposit of fibrin or debris in an ulcer, also remove this by suction. Next, place a small amount of one percent toluidine blue on the entire lesion as well as on some of the surrounding oral mucosa. Instruct the patient to rinse his mouth with water thus washing away the excess toluidine blue. If the lesion is stained, the test is positive; biopsy immediately. Of course, you may also biopsy many lesions which do not take up the stain in order to document their precise nature. Keep those negative lesions which are not biopsied under close supervision.

The efficacy of this procedure has been tested in several series: Myers demonstrates no false positives in his study of 70 patients,\textsuperscript{6} although false positives have been reported by other investigators.\textsuperscript{3-4,7} Even though such results are controversial, toluidine is, nevertheless, a valuable preliminary screening technique.

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