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OVERVIEW

Premalignant Lesions in the Upper Aerodigestive Tract

In this session, morphological, biological, and some clinical characteristics of precancerous lesions of the upper aerodigestive tract are described, as are the results of some cancer detection screening studies. Dr. John D. Crissman distinguishes between keratinizing and non-keratinizing dysplasia. Keratinizing dysplasia is identified clinically as the white lesion of leukoplakia, and occurs in the thick mucosa of the hard palate, alveolar ridges, and vocal cords. Non-keratinizing dysplasia is identified clinically as the red lesion of erythroplakia and histologically resembles the classic CIN lesion of the cervix. It is found in the thin mucosa of the floor of the mouth, undersurface of the tongue, inner cheek, pharynx, and upper larynx. Interestingly, in keratinizing dysplasia, individual cells undergo a disregulated switch from small to large molecular weight keratin production and histologically begin to show premature keratinization while still in the lower epithelium. Dr. Crissman presents a useful glossary of definitions used by pathologists when they describe preinvasive neoplasia, and emphasizes that while "dysplasia" refers to morphological changes at the cellular level, "squamous intraepithelial neoplasia (SIN)" refers to the entire biological phenomenon of neoplasia at all levels, including the genetic and molecular level.

Dr. Leopold G. Koss presents an inclusive review of important aspects of neoplasia of the upper aerodigestive tract, concentrating on the characteristics and benefits of cytological screening. Ten percent of 2,758 patients with visible oral lesions screened by cytology were found to have invasive cancer, 28% of which had not been recognized clinically. In another study of 2,297 patients, 3 of 11 cancers identified were clinically unsuspected. In a study of 81,187 patients in Henan Province, China, screened for esophageal cancer with the balloon brushing technique, cancer was found early enough in 1% of the cases to allow survival of most of the patients for five years, in stark contrast to the five-year survival of only 5% in the United States. Dr. Koss suggests that in high-risk patients such as those with prior cancers of the larynx and pharynx, and alcoholics who are also heavy cigarette smokers, a major effort at balloon screening may be indicated.

Dr. Myron R. Melamed reviews the early lung cancer screening project undertaken at Johns Hopkins Hospital, Memorial Sloan-Kettering Hospital, and the Mayo Clinic. Over 10,000 patients were screened at each center with sputum cytology every four months and chest X-ray every year for a total of 10 years. Overall, 35% of patients who were diagnosed as having lung cancer survived 5 years. For patients with asymptomatic lung cancer diagnosed by their private physician outside the study, the survival rate was a similar 35% at 7 years. The survival of patients with symptomatic cancer diagnosed by their private physician is only 13% at 7 years. Dr. Melamed therefore recommends that screening for early lung cancer be carried out by including a chest X-ray in the annual physical examination of asymptomatic high risk patients. The study also yielded information concerning multiple lung cancers. The probability of a second lung cancer at each of the 3 centers was 5–7%. Of a total of 82 second primary lung tumors, 40 were synchronous, 37 were metachronous, and 5 were both.

Dr. Charles W. Boone describes the biology of intraepithelial neoplasia in terms of clonal evolution through 5 stages: predysplastic, starting with the first critical mutation; clonal expansion of normal-appearing cells forming an abnormal disorganized tissue pattern; abnormal-appearing cells (dysplasia); invasion; and finally, metastasis. Dr. Boone stresses the need to use surrogate endpoint biomarkers (SEBs) to avoid the high cost of clinical trials which use cancer incidence reduction as their endpoint. Following a review of the ongoing quiet revolution in diagnostic histopathology due to computer-assisted cytomorphometry and cytophotometry, Dr. Boone describes how computerized cytometry can markedly increase the sensitivity, precision, and accuracy of SEB assays based on the morphological and staining properties of dysplasia. Finally, he discusses the need for careful quality control of SEB assays and outlines some Phase II trials of chemopreventive agents in which dysplasia-based SEBs are used as the endpoint.

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