the diagnosis. T-cell lymphomas constitute a diagnostic challenge for FNA; this diagnosis has to be supported by the identification on flow cytometry of an aberrant phenotype expression and T-cell receptor rearrangement by ISH and should, in our opinion, be confirmed by biopsy.

Hodgkin's disease is usually easy to diagnose by FNA, except for the lymphocyte predominant subtype where we usually see smears with a monomorphic pattern suggesting low-grade non-Hodgkin's lymphomas with a polyclonal phenotype; because of this discrepancy a careful search of Reed-Steinberg cells is advised and, if negative, a biopsy suggested. Immunocytochemistry should always be performed in diagnostic smears for Hodgkin's disease to prevent a misdiagnosis with anaplastic Ki-1 non-Hodgkin's yinphomas, although in many cases this distinction is feasible by morphology. One should think of Ki-1 non-Hodgkin's lymphomas when examining a smear suggestive of Hodgkin's disease that shows too many Reed-Steinberg cells, and should therefore look carefully for cells with the ring nucleus characteristic of this lymphoma. Although some attempts have been made to cytologically subclassify Hodgkin's disease, we do not think this it is prudent or even necessary, since the most relevant prognostic information is the clinicopathological staging. Therapy may be initiated based on FNA diagnosis in cases where node excision is not easily available.

In summary, like Buley, Young and Tani, we think that the accuracy of FNA in the diagnostic workup of lymph node pathology has been greatly enhanced due to ancillary techniques, allowing the diagnosis and subclassification of lymphomas in most cases and thus being sufficient for establishing therapy. Except for difficult cases, which always occur both in cytology and in histopathology, the decision to conduct a surgical biopsy shall be taken, not for the mere confirmation of diagnosis, but with the aim of preserving archival material frozen or in paraffin blocks, for further studies that may contribute to advances in treatment.

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Aspiration cytology of soft tissue tumors

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SamDling

The preoperative diagnosis of soft tissue tumors (STT) should always be established in a manner that does not compromise the radical surgical treatment. Fine needle aspiration cytology (ENAC), when applied with respect to anatomic compartment boundaries, is the least invasive method to obtain diagnostic material for microscopy and other cell-based techniques (1). Our routine procedure is to identify and mark (by a tattoo) the aspiration site(s), if possible together with the surgeon and/or radiologist.

Often the aspirations are performed under radiographic or ultrasound guidance. We usually aspirate with a 21-gauge needle attached to a 20 nil syringe in a Cameco syringe-holder. We prepare both air-dried and ethanol-fixed cell smears, but also rinse the needle with physiological, phosphate-buffered saline (PBS) to obtain material for cytospins. In order to check the representativity, we routinely perform a Diff-Ouick staining on the spot. This is also very helpful to disclose areas of the tumor that may be totally or partly necrotic. It is, indeed, an advantage if the cytopathologist samples the lesion him- or herself in order to assess the representativity of the cell material. It is more difficult to evaluate a submitted specimen in this respect.

When aspirating pediatric STT tumors, where international protocols demand histopathological diagnoses, we use FNAC to select representative areas for core needle biopsies. The procedure will then also allow us to make a preliminary assessment of the type of

lesion we are dealing with, for selection of further, special techniques. We will also get an impression of tumor heterogeneity by comparing aspirates from different parts ot the tumor.

Staining

The air-dried smears are routinely stained according to May-Grunwald-Giemsa and the ethanol-fixed ones according to Papanicolaou. Both types of smears can also be used tor special stains, e.g., Alcian blue at different ionic strength or pH to disclose the nature of myxoid material (2).

Only occasionally do we fix part of the aspirated material in paratormaldehyde for electron microscopy. It has a proven value in demonstrating, for instance, mesothelial and rhabdomyoblastic differentiation (3).

Assessing the specimen

In general, some main features to be noted are listed below.

Background

The background needs to be determined, *e.g.,* necrosis, myxoid, mucoid, chondroid, osteoid material.

Cellular arrangement

It needs to be determined whether cells are arranged in a special way *(e.g.,* tascicular, papillary, alveolar, or only dissociated cells.) and their relation to normal stromal components, including vessels.

Cell size

Cell size is an important parameter, often given in relation to the size ot an erythrocyte or a lymphocyte. Small round blue cell" tumors represent a concept, which comprises important pediatric tumors (neuroblastoma, nefroblastoma), but also rhabdomyosarcomas, especially the alveolar type, and the various types of lymphomas.

Giant cells are seen in many typos ot mesenchymal tumors, both clearly neoplastic ones and reactive ones (foreign body type or osteoclastoma-like).

Cell differentiation

Cell differentiation is very important parameter, since the classification (4) is based on histogenic criteria. The identification of lipoblasts, for instance, in an otherwise undifferentiated sarcoma will have obvious diagnostic impact, as will the identification of rhabdomyoblasts in a small cell sarcoma. A simplified WHO's classification can be used, as follows: tumors of fibrous tissue; fibrous-histiocytic tumors; and tumors of adipose tissue muscle, blood vessels, synovial tissue, peripheral nerves.

Grading

It is often difficult or impossible to grade sarcomas without an identification as to type. There are malignancy-related criteria, however, that support the diagnosis of a malignant tumor, even though the type may not be evident. Lack of differentiation, high nuclear/cytoplasmic ratio, nuclear abnormalities and atypical mitoses belong to this category of cellular changes.

SDecial techniques

Immunocytochemistry

The cytospin specimens are prepared fresh and allowed to air-dry over night, allowing a first micromorphologic assessment on cytology. A potential problem with the cytospin technique for cytochemistry is the fact that the antisera have to be titrated especially for this purpose. It is not always possible to use the same concentrations/procedures as for histopathology. This is particularly true if automated machine is used for immunostaining.

Cvtogenetics

Cytogenics has become an important adjunct in identifying certain SSTs since the tirst specific translocation was described for alveolar rhabdomyosarcomas t(2q; 13q) (5). Further examples are Ewing's sarcoma t(IIq -22q), myxoid liposarcoma t(12q,16p) and synovial sarcoma t(X, 18).

Fluorescence *in situ* hybridization

Fluorescence *in situ* hybridization (FISH) is a technique that lends itself to application on cytological material. It is technically easier to use tor detection ot translocations than a cytogenetic analysis, since it can be performed on interphase nuclei. The method also lends itself to detection of amplifications. One example is the N-myc amplification in neuroblastoma. The cytological material, adequately preserved, can also be used tor any other DNA- and RNA-based technique.

Diagnosis

The diagnosis should indicate if the material is sufficient for diagnosis. Only diagnoses from WHO's list should be used. If the diagnosis is one of several possible alternatives, differential diagnoses should be given.

In cases where there is uncertainty as to the benign or malignant nature of the lesion, additional diagnostic suggestions should be given, *e.g.,* type of additional biopsy required, excision, special techniques, etc.

Examples of common soft tissue lesions will be given, both benign and malignant ones.

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Aspiration biopsy of bone tumors

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Cytological diagnosis of bone lesions by fine needle aspiration (FNA) biopsy is by no means a new approach; it is employed to