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Report of the Committee on Hodgkin's Disease Staging Procedures

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The evaluation of previously untreated patients with Hodgkin's disease must be done with great care if current staging designations are to have usefulness and meaning for the care of the patient, for prognostic purposes, and for comparative clinical investigations. There have been numerous procedures and tests developed, studied, and proposed for these purposes. In consideration of current available evidence and data, the Committee recognizes those procedures which it considers necessary for all previously untreated patients with Hodgkin's disease, those procedures which it considers necessary under certain conditions, those procedures which it considers as ancillary but useful, and those which it considers promising but requiring further clinical study and application.

Required Evaluation Procedures

1. An adequate surgical biopsy must be obtained and reviewed by a pathologist competent and experienced in the field of hematopathology. (Inguinal nodes should not be biopsied, if equally suspicious nodes are present elsewhere.)

2. A detailed history must be obtained and recorded including the duration of signs and symptoms of the disease. Specifically, the following should be recorded: (*a*) the presence or absence of unexplained fever and its duration; (*b*) unexplained sweating, especially at night, and its severity; (*c*) unexplained pruritus, its extent, and severity; and (*d*) unexplained weight loss, its amount compared to normal body weight and its duration.

Other historical facts which are desirable to record include a family history of Hodgkin's disease, other lymphomas and autoimmune disorders, a history of infectious mononucleosis, a history of tonsillectomy, the use of hydantoin-type anticonvulsant drugs, and alcohol-induced pain.

3. A careful and complete physical examination must be performed by a physician experienced in the evaluation and care of patients with Hodgkin's disease. Special attention must be directed to the usual areas where lymphadenopathy occurs, to the lymphoid tissue of Waldeyer's ring, to determination of the size of the liver and spleen, and to determination of sites of bone tenderness.

4. Necessary laboratory studies are as follows: (*a*) a complete blood count, including a white blood cell count, and differential hemoglobin and/or hematocrit level, platelet count, and erythrocyte sedimentation rate; (*b*) serum alkaline phosphatase level; (*c*) evaluation of renal function; and (*d*) evaluation of liver function.

5. Radiological studies advisable are: (*a*) chest roentgenogram, posteroanterior and lateral views; (*b*) intravenous pyelogram; (*c*) bilateral lower extremity lymphogram; and (*d*) views of the skeletal system to include the thoracic and lumbar vertebrae, the pelvis, proximal extremities, and any areas of bone tenderness and/or pain, supplemented by tomograms if necessary. (Usually, these osseous sites are adequately evaluated with films obtained during the lymphographic study.)

Required Evaluation Procedures under Certain Conditions

1. Whole-chest tomography, in the frontal view with or without lateral planes as necessary, if there is abnormality noted or suspected on the routine chest roentgenogram. Appropriate filters should be used to balance radiographic density for simultaneous mediastinal and pulmonary parenchymal evaluation.

2. Inferior cavography to supplement equivocal lymphographic or pyelographic findings.

3. Bone marrow biopsy, by a needle or open surgical technique in the presence of any of the following: (*a*) an elevated serum alkaline phosphatase; (*b*) unexplained anemia or other blood count depression; (*c*) roentgenographic or scintigraphic evidence of osseous disease; and (*d*) generalized disease of Stage III category or greater.

4. Exploratory laparotomy and splenectomy, if management decisions will depend on the identification of abdominal disease (see "Comment").

Useful Ancillary Procedures not Definitive for Diagnosis

1. Skeletal scintigrams should be performed in selected patients with roentgenological osseous abnormalities, unexplained osseous pain, or elevated serum alkaline phosphatase, but biopsy and/or typical roentgenological abnormalities should be utilized to confirm the findings.

2. Hepatic and spleen scintigrams are of very limited value except when large, filling defects are noted or to estimate the size of the spleen. Scintigraphic abnormalities cannot be

considered diagnostic of Hodgkin's disease involvement of the liver, spleen, or bone.

3. Serum chemistries to include the serum calcium and uric acid for overall management of the patient.

4. Estimates of the patient's delayed hypersensitivity of the tuberculin type are of interest but cannot be used for prognostic or therapeutic considerations.

Procedures and Tests Promising for Clinical Study at Selected Centers but Experimental at This Time

1. Whole-body gallium and selenium scintigrams, especially for the demonstration of mediastinal disease.

2. Determinations of: (*a*) serum iron and iron-binding capacity; (*b*) serum copper and ceruloplasmin; (*c*) serum zinc; (*d*) serum haptoglobin; (*e*) serum fibrinogen; (*f*) serum α_2-globulin; (*g*) urinary hydroxyproline; (*h*) leukocyte alkaline phosphatase; (*i*) absolute lymphocyte count; (*j*) antibodies to Epstein-Barr virus; and (*k*) human lymphocyte antibody typing.

Comment on the Indications for Exploratory Laparotomy and Splenectomy

The major value of exploratory laparotomy and splenectomy is to determine with accuracy the involvement of the spleen in Hodgkin's disease. Approximately 25% of spleens, unsuspected as involved clinically, when studied carefully by the pathologist, will contain Hodgkin's disease. Conversely, approximately 50% of spleens judged to be clinically enlarged will not contain Hodgkin's disease when examined pathologically. Of lesser value, as a result of laparotomy, is the evaluation of Ethiodol-filled lymph nodes, of lymph nodes in sites not surveyed by the lower-extremity lymphogram, and the liver.

The surgical sampling of abdominal lymph nodes, even when directed by equivocal or positive lymphographic findings, is still inadequate. All lymph nodes cannot be removed and, occasionally, the most radiographically abnormal lymph node cannot be identified surgically for pathological confirmation. In contrast to the reliable evaluation of this involvement of the spleen, the laparotomy findings judging lymph node involvement must be considered in the context of lymphographic findings, the 2 procedures being complementary, one neither substituting for nor necessarily superseding the other.

The demonstration of liver involvement by laparotomy is uncommon of the order of 5% or less, for all patients with no consideration of extent of disease. The demonstration of liver rises to approximately 15% in the presence of clinical involvement of the retroperitoneal lymph nodes and spleen. Peritoneoscopy performed by those skilled in the procedure has a similar yield of positive liver biopsies and is an alternative to exploratory laparotomy for the demonstration of Hodgkin's disease of the liver.

In view of the known and possible complications of exploratory laparotomy and splenectomy, the procedure should be considered required for diagnostic purposes if the therapeutic philosophy is to limit radiotherapy to only the known sites of disease, or to patients with disease of Stage I and II extent only. The procedure should be considered desirable but not required in attempting to exclude involvement of the liver in those patients who have the highest risk of liver involvement, those with apparent involvement of the paraaortic lymph nodes and spleen, or those who have marked splenomegaly. In these circumstances, peritoneoscopy with liver biopsy is a suitable alternative procedure. Laparotomy is not considered required and is probably not justified if the risk for liver involvement is minimal *and* it is the therapeutic philosophy for an individual patient or, as a general rule, is to treat the paraaortic lymph nodes and spleen with radiotherapy even in the absence of identified abdominal disease.