Lymphomas—Troublesome Problems in Management

The Editor interviews Wayne Rundles, M.D., Chief, Hematology and Oncology Division, Department of Medicine, Duke University Medical School, Durham, North Carolina

Editor: What procedures are fundamental in the work-up of a patient with a suspected malignant lymphoma who presents with one or more enlarged lymph nodes which fluctuate in size or progressively enlarge, as well as fever, fatigue, reduced exercise tolerance or general malaise?

Dr. Rundles: The basic work-up includes a thorough medical history and physical examination, a chest X-ray, blood and sometimes bone marrow studies. Proof of diagnosis, however, requires biopsy of an enlarged lymph node from a centrally located or primarily involved site that is free of infection. Imprints from the surface of a freshly cut node help determine cell type and maturity, and cultures are necessary if a bacterial or fungal infection is suspected. Careful fixation of tissue and the preparation of good sections are, of course, essential for an accurate pathologic diagnosis and proper management.

Editor: If the node biopsy is interpreted simply as Hodgkin’s disease or another type of malignant lymphoma, how important is further sub-classification?

Dr. Rundles: Histologic sub-classifications relate more to prognosis than to immediate management. This is fortunate since three or four pathologists, studying the same histologic specimen independently often arrive at two or three different sub-classifications. Of major impor-
tance is determining whether the patient has Hodgkin’s disease or some other lymphoma since this affects the approach to primary treatment.

**Editor:**

Why is clinical staging of lymphomas emphasized so strongly today?

**Dr. Rundles:**

Staging helps the physician decide on treatment, generally a choice between irradiation and chemotherapy. If the disease is localized, as in Hodgkin’s disease, radiotherapy is indicated. All foci must be identified and encompassed in the treatment field, since relapse and recurrence are inevitable if some areas are missed. When the disease is disseminated or located in organs that are impractical to irradiate, systemic chemotherapy should be used as the primary method of treatment.

**Editor:**

What studies are required to stage lymphomas?

**Dr. Rundles:**

This depends on the clinical, laboratory and pathologic findings in a given individual. Following a meticulous physical examination and other basic studies outlined above, lower extremity lymphangiograms are very useful. However, lymphangiograms may not show high para-aortic or mesenteric lymph nodes, submucosal foci of lymphoma or even completely replaced nodes. Aspirated bone marrow, incidentally, rarely reveals evidence of Hodgkin’s disease even when foci are present in needle or open surgical biopsy sections. In non-Hodgkin’s lymphoma and most lymphoproliferative diseases, lymphocytic infiltration in the bone marrow is fairly common and easily demonstrated by aspiration technique. In some instances, inferior vena cavaograms and skeletal survey films, particularly of the thoracolumbar spine and pelvis are necessary. Radioisotope scanning of the liver and spleen may show signs of disease in these organs. Filling defects, irregularity or disproportionate organ uptake of the nucleotide are suggestive findings but are unusual unless there is gross involvement.

**Editor:**

What about surgical staging?

**Dr. Rundles:**

Surgical staging is no substitute for the above studies and lymphangiograms and organ scans usually provide the necessary information on what should be biopsied and where. A number of investigators recommend exploratory laparotomy with splenectomy and multiple liver and node biopsies more or less routinely to stage Hodgkin’s disease and often other lymphomas. But while these studies have been extraordinarily useful in investigating the natural history, origin, pattern of distribution and recurrence of lymphomas, they involve significant risk, discomfort and expense and
should not be considered mandatory or routine procedures. The information gained should contribute in a useful way to the patient’s management.

Following lymphangiography and organ scanning, laparotomy may be indicated to clarify equivocal abnormalities, document the recurrence of disease in previously treated patients or help decide on a treatment regimen. On occasion, treatment may be facilitated by removing an enlarged spleen or marking the extent of disease involvement by placement of silver clips. Splenectomy may be useful finally in some patients who have cytopenias indicative of hypersplenism.

**Editor:** What is the treatment of choice for non-Hodgkin’s lymphoma?

**Dr. Rundles:** Individuals with genuine Stage I or II non-Hodgkin’s lymphoma are rare, but may be cured by radiotherapy given to the involved region. Most patients have more disseminated disease, however, or develop foci within a reasonably short period of time. They usually respond well to chemotherapy regimens employing an orally administered nitrogen mustard derivative such as chlorambucil, often supplemented with 10-15 mg. of prednisone daily. These regimens are safe and effective for most patients, particularly those who have a tumor with a follicular or nodular pattern and a predominance of mature lymphocytes in node sections. At the other end of the scale, patients with poorly differentiated histiocytic or reticulum cell lymphomas tend to be hard to control and require the use of multiagent regimens using cyclophosphamide, vincristine and prednisone. In some instances, local radiotherapy can be a very effective adjuvant in the treatment of bulky, residual or recurrent disease.

**Editor:** Is chemotherapy also recommended for Hodgkin’s disease?

**Dr. Rundles:** Patients with localized Hodgkin’s disease generally respond more completely and permanently to radiotherapy than chemotherapy, although some individuals can be beneficially treated with supervoltage irradiation combined with chemotherapy. Patients with generalized or advanced Stage III or IV Hodgkin’s disease, and particularly those with the ‘‘B’’ symptoms, are best treated by the aggressive MOPP type of chemotherapy regimen.

**Editor:** Is there a risk of inducing new tumors or leukemia with radical radiotherapy or aggressive chemotherapy regimens?

**Dr. Rundles:** There probably is, but it is much less than the risk of not using these agents and allowing the disease to remain active and progress. As a general principle, we use the least therapy that will do the most good and hope that there will be no iatrogenic complications.
Editor: Has immunotherapy advanced to the point where it can be considered a standard treatment for malignant lymphomas?

Dr. Rundles: The value of immunotherapy is fairly well established in the treatment of some acute leukemias, but it is still being investigated for other conditions.

Editor: Can anything be done to prevent lymphomas from developing?

Dr. Rundles: No. One should avoid the unnecessary use of agents or hormones that might modify immune responses and either magnify or suppress sensitivity reactions, but there is no assurance at present that lymphomas can be prevented.

Editor: Is there any risk of contagion in a family if one member has a malignant lymphoma?

Dr. Rundles: There is no increased risk for the family, spouses, nurses, doctors or technicians who might have contact with these individuals.

Editor: There has been recent concern as to whether some lymphomas and leukemia may be transmitted from pets to humans.

Dr. Rundles: There is no reason for anyone to fear contact with animals or pets, even those with a diagnosed lymph node disease or leukemia.

Editor: Thank you, Dr. Rundles.

Cancer Cells . . . The Key to Immortality?

"Whenever cell ageing is discussed there is always the unavoidable conundrum of cancer. Cancer cells appear to be immortal—they go on dividing forever. How? If cell life is normally limited by a built-in programme, the immortality of cancer cells is easily explained by postulating a change in this mechanism. "If the error theory, which states that the number of errors in defective proteins that are responsible for the production of more proteins mounts to the point that cell function breaks down, is correct then one needs to suggest that "those cancer cells that contain a potential error catastrophe are selected out, leaving error-free cells to replenish the population. Whatever is the answer, cancer cells may hold the key to life. "—Dr. Roger Lewin. Is Ageing Part of the Plan? New Scientist 60:617, 1973.