

3-1973

## Malignant Histiocytosis of the Robb-Smith Type (Histiocytic Medullary Reticulosis)

Michael F. Macken

Ellis J. Van Slyck

Sheik M. Saeed

Follow this and additional works at: <https://scholarlycommons.henryford.com/hfhmedjournal>

 Part of the [Life Sciences Commons](#), [Medical Specialties Commons](#), and the [Public Health Commons](#)

### Recommended Citation

Macken, Michael F.; Van Slyck, Ellis J.; and Saeed, Sheik M. (1973) "Malignant Histiocytosis of the Robb-Smith Type (Histiocytic Medullary Reticulosis)," *Henry Ford Hospital Medical Journal* : Vol. 21 : No. 1 , 4-10.

Available at: <https://scholarlycommons.henryford.com/hfhmedjournal/vol21/iss1/2>

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.

# Malignant Histiocytosis of the Robb-Smith Type

(Histiocytic Medullary Reticulosis)

Michael F. Macken, MD,\* Ellis J. Van Slyck, MD,\*  
and Sheikh M. Saeed, MD\*\*

*A 60-year-old woman developed high fever, jaundice, anemia with pancytopenia and hepatosplenomegaly. She deteriorated rapidly and died one month later, having shown no beneficial effect from high dose corticosteroids and splenectomy. An antemortem diagnosis of malignant histiocytosis of the Robb-Smith type was made and duly confirmed by autopsy study. This rare disorder of the reticuloendothelial system, heretofore designated "histiocytic medullary reticulosis," deserves recognition and inclusion among the histiocytic diseases and in the classification of the lymphomas. Its proper nosologic designation is suggested.*

THE morphologically descriptive term, "histiocytic medullary reticulosis", was proposed by Scott and Robb-Smith<sup>1</sup> in 1939 for a clinicopathologically distinct, rapidly fatal disorder found in four patients. The disease was characterized by fever, weight loss, generalized lymphadenopathy, and in the terminal stages, severe anemia, jaundice, pancytopenia and purpura. The pathological examination revealed systemic proliferation of histiocytes, some of which demonstrated erythrophagocytosis.

In this paper we present another case of this rare entity, with a review of the pertinent clinical and histological features. The proper place and designation for this disease in the current classification of the diseases of the reticuloendothelial system is offered later in the text and in Table I.

## Case Report

This 60-year-old housewife was well until August 9, 1969, when she was admitted to another hospital with bilateral flank pain of sudden onset. Examination revealed marked bilateral costovertebral angle tenderness and an enlarged spleen, which was palpable two-finger breadths below the left costal margin. The patient received only analgesics and all symptoms subsided within 24 hours. Investigation of the genitourinary tract disclosed only an incidental reduplication anomaly of

---

\* Division of Clinical Hematology, Department of Medicine.

\*\*Department of Pathology.

Address reprint requests to: Ellis J. Van Slyck, MD, Henry Ford Hospital, 2799 W. Grand Blvd., Detroit, MI 48202

**TABLE 1**  
**DISORDERS OF THE MALIGNANT**  
**RETICULUM CELL (HISTIOCYTE)**

1. Reticulum cell sarcoma group.
  - A) Malignant lymphoma, undifferentiated.
    1. Burkitt's lymphoma.
  - B) Malignant lymphoma, histiocytic (Reticulum cell sarcoma).
  - C) Malignant histiocytosis.
    1. Leukemic reticuloendotheliosis (Acute monocytic leukemia).
    2. Malignant histiocytosis, Robb-Smith type.
2. Hodgkin's disease.
3. Differentiated progressive histiocytosis.
  - A) Letterer-Siwe disease (in the histiocytosis X group).
4. Mycosis fungoides.
  - A) Sezary's syndrome.

both collecting systems. Because of the unexplained splenomegaly, evaluation of the hematopoietic system was done, yielding normal results for the following tests: hemoglobin, hematocrit, bilirubin, urinary urobilinogen, Coombs' test, heterophile agglutination, lupus erythematosus preparation, serum lactic dehydrogenase, protein electrophoresis, alkaline phosphatase, bromsulphalein retention, blood urea nitrogen, creatinine and calcium. Radiographs of the chest and lumbosacral spine were normal. However, her white blood count was 3,100 with a left shift of the neutrophils. Platelets were decreased. The bone marrow showed a decreased M:E ratio (1:1) as a result of increased erythropoiesis. Diagnosis on discharge from the hospital was "probable ureteral calculus and hypersplenism of undetermined etiology."

The patient did well for the next three weeks and then developed spiking daily temperatures, a seven-pound weight loss and a feeling of apprehension. Noting icterus, hepatomegaly and further enlargement of her spleen, her physician referred her to the Hematology Division of the Henry Ford Hospital.

Physical examination now revealed an acutely ill, jaundiced female with blood pressure of 120/80, pulse of 84/minute and temperature of 101°F. Head, eye, ear, nose and throat, cardiopulmonary and genitourinary examinations were within normal limits. The significant physical abnormalities were the

presence of a few shotty lymph nodes in the posterior cervical, axillary, and inguinal regions; an enlarged liver, palpable 4 cms below the right costal margin and an enlarged spleen, palpable 8 cms below the left costal margin.

Laboratory studies revealed the following: hemoglobin 7.9 grams/100 ml and white blood count 3,400/cu mm. The differential count showed 54% neutrophils, 5% bands, occasional myelocytes and promyelocytes, 12% monocytes, 25% lymphocytes, 1% eosinophils, and 2% basophils. The reticulocyte count was 15.4% and the platelet count was 77,000/cu mm. The direct and indirect Coombs' tests were negative. The bilirubin was 4.5 mgs/100 ml with 0.16 mgs/100 direct reacting. Additional studies gave the following results: serum LDH 2,000 units/100ml. Prothrombin time 15 seconds with a control of 12 seconds. Partial thromboplastin time was 88 seconds with a control of 61 seconds, and fibrinogen was 125 mgs/100 ml. Urinary hemosiderin test was positive. The fasting blood sugar, BUN, creatinine electrolytes and serum protein electrophoresis were within normal limits. Cultures of the urine, blood, sputum and bone marrow were negative. Right iliac bone marrow examination showed marked normoblastic hyperplasia with an M:E ratio of 1:1. Occasional abnormal neoplastic histiocytes were seen, some of which showed phagocytosis of erythrocytes, normoblasts, leukocytes and even platelets, (Figure 1).

The patient's condition rapidly deteriorated with deepening jaundice and increasing anemia. Daily afternoon temperature spikes reached 105°F. She was treated with prednisone, 60 mgs per day, but showed no improvement. Transfusions with fresh whole blood were given, followed by splenectomy and biopsy of the liver and the periaortic nodes. Following the operation\*, the peripheral blood showed increasing numbers of neoplastic phagocytic reticulum cells (2-4%) (Figure 2), increased polychromasia, spherocytosis, basophilic stippling, Howell-Jolly bodies, erythroblastosis and a pronounced granulocytic left shift. The patient continued to do poorly and died 48 hours later.

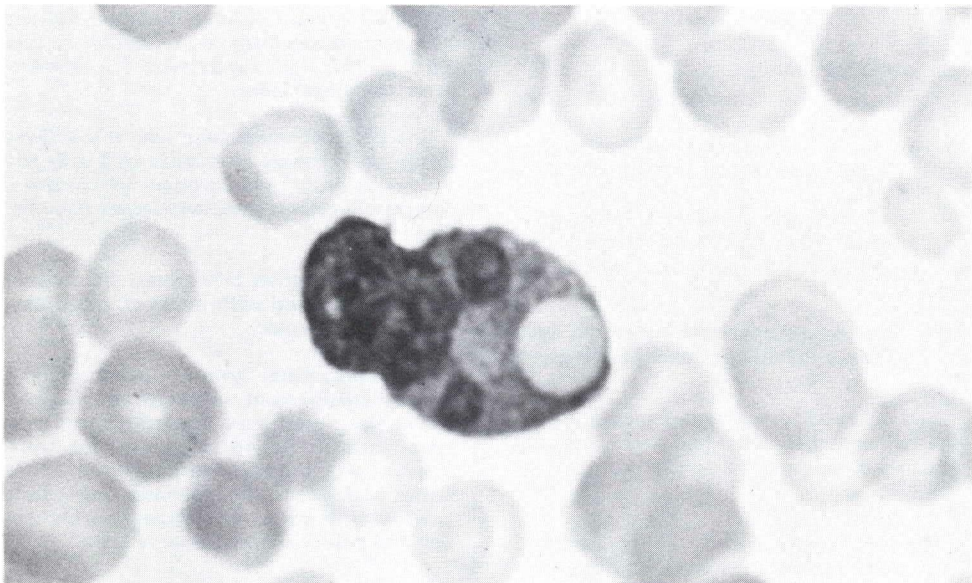
\*Surgical consultation and splenectomy were done by Joseph P. Elliott, Jr., MD, General Surgery II.

**Malignant Histiocytosis of the Robb-Smith Type**



**Figure 1**

**Marrow aspirate showing two malignant histiocytes. Note ingested erythrocytes and normoblasts. Leishman's stain approximately x2000**



**Figure 2**

**Peripheral blood. Lobulated and multinucleated histiocyte with phagocytized erythrocyte. Leishman's stain approximately x2000**

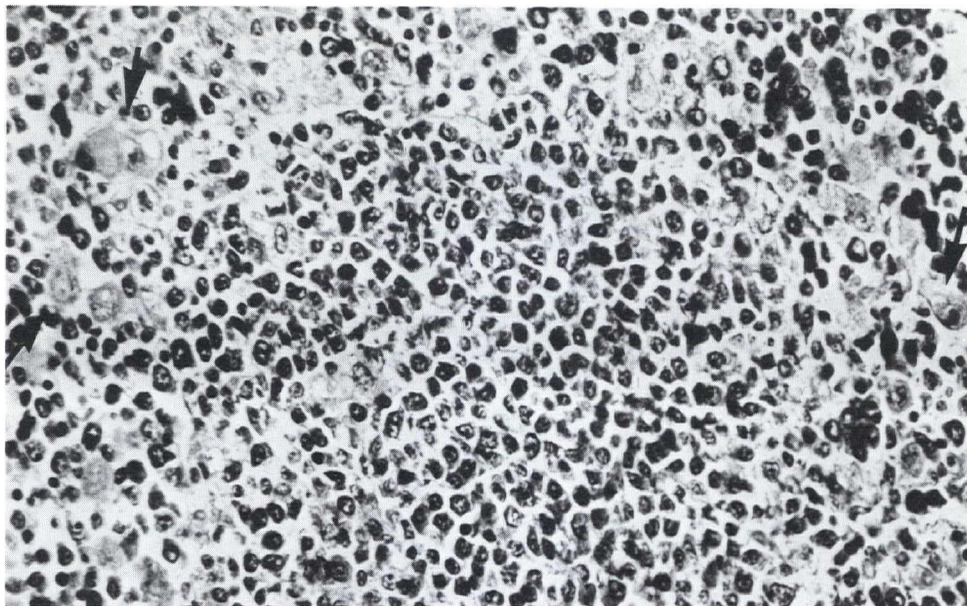


Figure 3

Spleen. Parenchyma is replaced by neoplastic, occasionally multinucleated, reticulum cells some of which show phagocytized erythrocytes (arrows). H & E stain x390

### Pathology

#### *Surgical Specimens:*

The spleen was markedly enlarged, measuring 27 x 15.5 x 8 cms, and weighed 1700 grams. The consistency was moderately firm. Capsule was intact, smooth and dark gray in color. Cut surface of the spleen had a purplish cast with punctate areas of gray-white nodularity. A yellow infarcted area occupied the inferior peripheral part of the spleen.

The liver biopsy specimen measured 1.0 x 0.5 x 0.3 cms and had a granular yellow-green color.

Two enlarged lymph nodes measuring up to 1 cm were also submitted and were both replaced by yellow-gray, soft tumor.

#### *Gross Autopsy Findings:*

The body was markedly dehydrated and jaundiced. Ecchymoses were obvious over the abdominal wall. The right and left pleural spaces contained respectively 200 ml and 150 ml of serosanguinous fluid and 350 ml of serosanguinous fluid were present in the peritoneal cavity.

The right and left lungs weighed 750 and 400 grams respectively. Both lungs were congested. The right lower lobe also showed areas of consolidation.

The heart weighed 380 grams and showed moderate coronary arteriosclerosis with partial occlusion of right coronary artery lumen. Arteriosclerosis of aorta and larger branches was present.

The liver weighed 2600 grams. The cut surface was mottled with areas of red-brown and yellowish color.

The abdominal lymph nodes showed marked enlargement, ranging from 3.0 to 8.0 cm in size. They were located for the most part around the aorta below the renal arteries and around the pancreas. These nodes had a firm, fleshy consistency with a salmon-pink color. The bone marrow was soft and pale. No nodules were seen.

Nothing remarkable was found upon examination of other organs including pancreas, genitourinary tract, endocrine organs, musculo-skeletal system and the central nervous system.

## Malignant Histiocytosis of the Robb-Smith Type

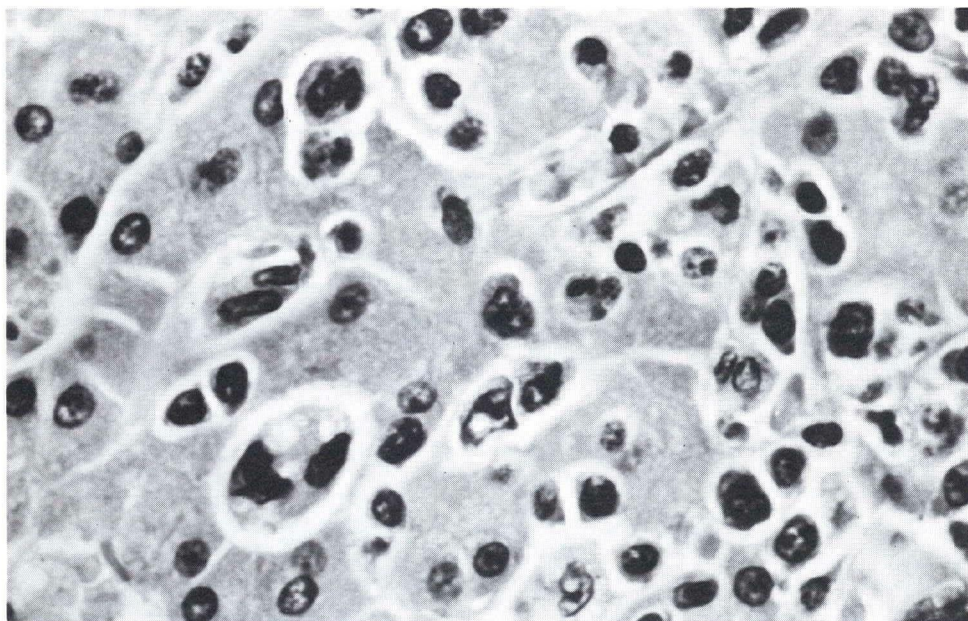


Figure 4  
Abnormal, phagocytic reticulum cells infiltrate the hepatic sinusoids. H & E stain x780

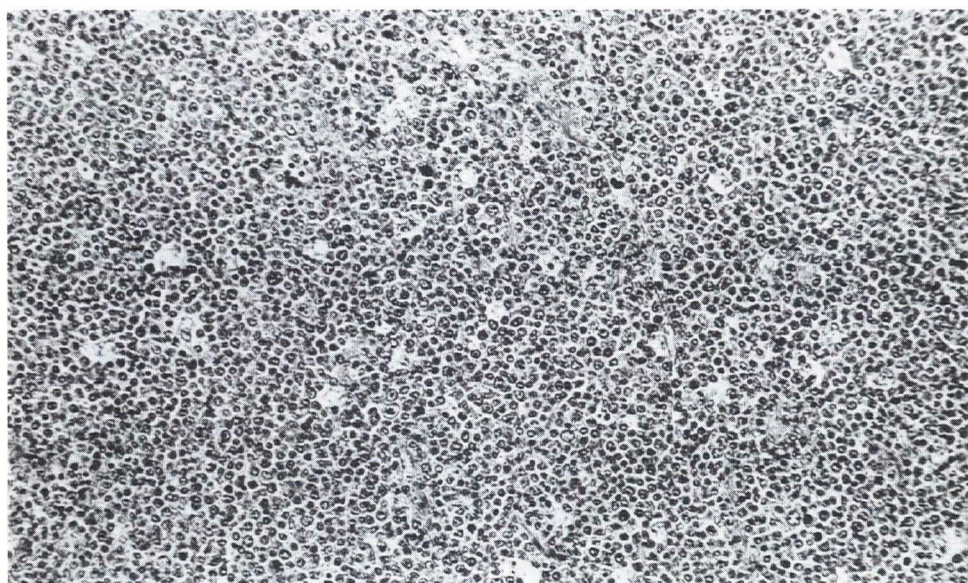


Figure 5  
Abdominal lymph node. Overgrowth of reticulum cells is interrupted by benign appearing histiocytes giving "starry-sky" appearance. H & E stain x150

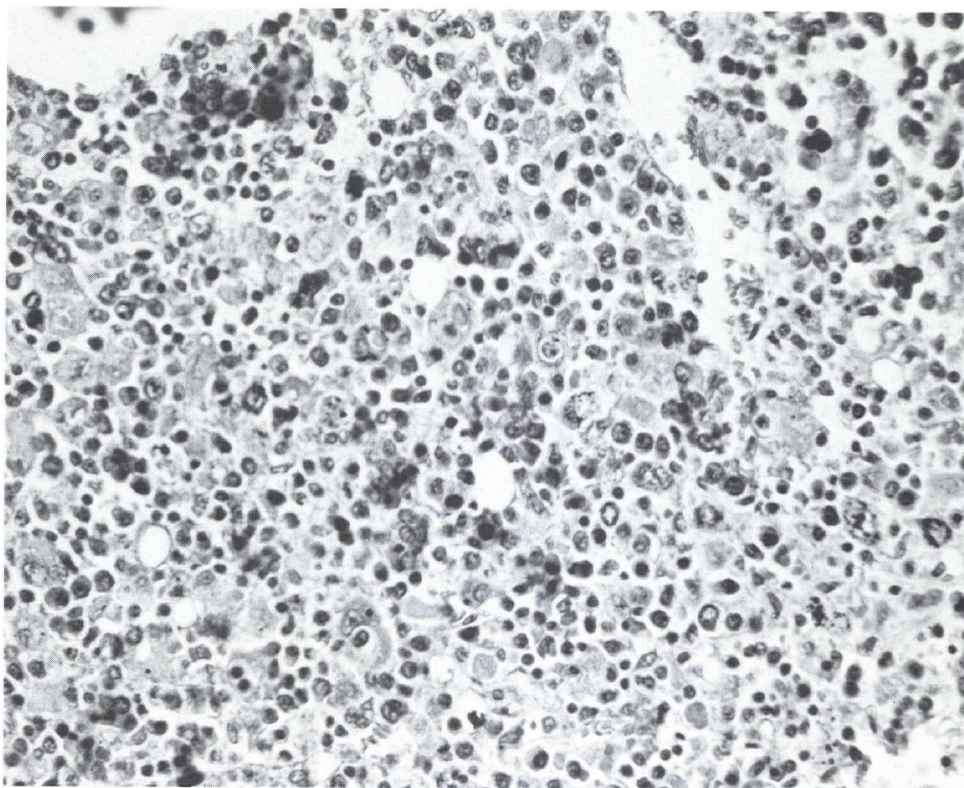


Figure 6  
Bone marrow. Infiltration by phagocytic, benign appearing reticulum cells. H & E stains x780

*Histologic Examination:*

Sections of the spleen revealed almost complete destruction of normal splenic architecture. Massive proliferation of large, bizarre tumor cells infiltrated the cortex, medulla, trabeculae, germinal areas and the sinuses, (Figure 3). The tumor cells generally had abundant cytoplasm with large, frequently lobulated, vesicular nuclei and prominent nucleoli. Binucleate and multinucleate giant tumor cells were also seen. Cells in mitosis were frequent. Several of the tumor cells had frothy, irregular cytoplasm and phagocytic activity was noted. Within the phagocytic vacuoles karyorrhectic nuclear debris or erythrocyte fragments could be seen.

Sections of the liver and lymph nodes also showed histiocytic malignant reticulum cells. In the liver, these tumor cells aggregated in the periportal areas, and from these ag-

gregates individual cells radiated and infiltrated along the hepatic sinuses between cell cords, (Figure 4). Modest Kupfer cell hypertrophy and bile stasis were noted. Tumor tissue involving the lymph nodes broke through the capsule and infiltrated perinodal fat. Scattered among the masses of neoplastic reticulum cells were large benign histiocytes giving a "starry-sky" appearance to the lymph nodes, (Figure 5).

Autopsy material showed the histologic pattern of the tumor involving the lymph nodes and liver was similar to the biopsy specimens described above. The character of the tumor involving the bone marrow, however, was considerably different. Among islands of intense erythroid hyperplasia were large clusters of histiocytes with abundant cytoplasm and phagocytic vacuoles, but with reticular nuclei exhibiting minimal pleomorphism. The chromatin pattern was

## Malignant Histiocytosis of the Robb-Smith Type

fairly uniform and nucleoli were of modest size. These histiocytes showed more intense erythrophagocytosis than the undifferentiated histiocytic tumor cells in the other organs, (Figure 6).

Sections of the lungs showed edema, congestion and focal bronchopneumonia. The heart contained small scars in the left ventricular wall. The kidney sections showed bile casts but were otherwise unremarkable. Changes were inconsequential in other organs including pancreas, genital system, endocrine glands and central nervous system.

### Discussion

This case typifies the major clinical and histologic features of malignant histiocytosis of the Robb-Smith type (MHRS). Data from a review of 49 cases by Greenberg et al<sup>2</sup> indicates that MHRS most commonly occurs in the 4th through 6th decades, affecting men more than women in a ratio of 3:1. Generally, it is rapidly fatal. However, two cases of survival greater than three years following splenectomy have been reported recently.<sup>3</sup> Symptoms and signs almost universally present are weakness, malaise, weight loss, pyrexia, splenomegaly and anemia. Less frequent findings are edema or serous effusions (82%), hepatomegaly (78%), leukopenia (69%), purpura (61%), jaundice (53%), and lymphadenopathy (52%). Skin lesions have been described in several cases.<sup>4-7</sup> These have had varied appearances, including diffuse maculopapular rashes, reddish-purple plaques and diffuse petechiae, but there is no skin lesion characteristic of MHRS.

The anemia, universally manifest during the course of MHRS, may be in part due to impaired red cell production secondary to marrow replacement by tumor cells.<sup>8</sup> The predominant and characteristic type of anemia, however, is hemolytic, an observation which has

been demonstrated by a number of authors.<sup>2,3,8,9,10</sup> Increasing jaundice, high serum LDH, urinary hemosiderinuria, altered red cell morphology and erythroblastosis all indicated rapid red cell destruction in our patient. Marrow erythroid hyperplasia excluded tumor induced myelosuppression. Rappaport<sup>10</sup> has stated that the anemia in MHRS is probably due to hypersplenism, but cytochemical and ferrokinetic studies seem to suggest that it is due in large part to erythrophagocytosis by histiocytes in the bone marrow and reticuloendothelial system generally.<sup>5,9</sup> Lack of improvement in the anemia following splenectomy would also speak for a mechanism different from hypersplenism.

An autoimmune component has not been shown to play any significant role in the hemolysis. The Coombs' test has been positive in only three of the previously reported cases. In two of these it became positive only after multiple transfusions.<sup>8,11</sup> Thrombocytopenia and leukopenia, when present, also appears to be due in part to abnormal phagocytic activity by histiocytes.<sup>12</sup>

There seems to be little doubt that MHRS is a distinct clinical entity, characterized histologically by a proliferation of malignant histiocytes which demonstrate a marked degree of erythrophagocytosis. It should be noted, however, that the descriptions of the histiocytes have varied in different cases, from benign-appearing cells to obviously malignant reticulum cells. Commenting on the benign appearance of the histiocytes in their case, Friedman and Steigbigel<sup>8</sup> likened the entity to Letterer-Siwe disease rather than a true malignancy. Our case is of interest in that islands of histiocytes, with variable morphologic degrees of malignancy, could be demonstrated in all bone marrow sections at autopsy.



In keeping with the concept proposed by Rappaport,<sup>8,10</sup> it seems proper to us that this disease be included as a member of the malignant histiocytosis group of diseases, (see Table 1). As such, it requires a more decisive and descriptive name than "reticulosis". Proliferation of reticulum cells (histiocytes) is the underlying common feature of such diverse conditions as Hodgkin's disease, malignant lymphoma of the histiocytic variety (reticulum cell sarcoma), Burkitt's lymphoma, histiocytic (monocytic)

leukemia, Letterer-Siwe disease, and mycosis fungoides. Clinically and pathologically these conditions are separable and should be dignified by a proper designation. The old term "histiocytic medullary reticulosis" is confusing and inaccurate, while the purely eponymic "Robb-Smith disease" conveys no information about the nature of this disease entity. We suggest, therefore, a more informative compromise term, namely, "malignant histiocytosis of Robb-Smith type".

#### References

1. Scott RB and Robb-Smith AHT: Histiocytic medullary reticulosis. *Lancet* 2:194, 22 July 1939
2. Greenberg E, Cohen DM, Bease GL and Kyle RA: Histiocytic medullary reticulosis. *Proc Staff Meet Mayo Clinic* 37:271-83, 1962
3. Scamps RA, O'Neill BJ and Purser BN: Histiocytic medullary reticulosis. *Med J Aust* 2:956-60, 6 Nov 1971
4. Anderson RG: Histiocytic medullary reticulosis with transient skin lesions. *Brit Med J* 1:220-1, 12 Feb 1944
5. Natelson EA, Lynch EC, Hettig RA and Alfrey CB: Histiocytic medullary reticulosis. *Arch Intern Med* 122:223-9, Sept 1963
6. Kalderon AE: Histiocytic medullary reticulosis associated with inclusion cytomegalic disease. *Cancer* 27:659-66, March 1971
7. Liao KT, Rosai J, Daneshbod K: Malignant histiocytosis with cutaneous involvement and eosinophilia. *Amer J Clin Path* 57:438-48, April 1972
8. Friedman RM and Steigbigel NH: Histiocytic medullary reticulosis. *Amer J Med* 38:130-3, Jan 1965
9. Lynch EC and Alfrey CP Jr: Histiocytic medullary reticulosis. *Ann Intern Med* 63:666-71, Oct 1965
10. Rappaport H: Tumors of the Hematopoietic System. In *Atlas of Tumor Pathology*. Washington, DC, Armed Forces Institute of Pathology, Sec 3 - Fascicle 8, 1966, pp 49-63
11. Willcox DRC: Haemolytic anaemia and reticuloses. *BR Med J* 1:1322-5, 21 June 1952
12. Selegram BR, Rosner F, Lee SL and Kagan MD: Histiocytic medullary reticulosis. *Arch Intern Med* 129:109-113, Jan 1972