

## Monocytic and Monomyelocytic Leukaemia with Increased Serum and Urine Lysozyme as a Late Complication in Plasma Cell Myeloma

ELLIOTT F. OSSERMAN

Monocytic or monomyelocytic leukaemia has developed as a late and terminal complication in three of our cases of multiple myeloma after the prolonged chemotherapeutic suppression of the multiple myeloma (see Table).

Case and Sex	Age at Onset of Multiple Myeloma	M-Protein	Duration of Multiple Myeloma Before the Leukaemia (years)	Therapy
1 M	41	Bence Jones	4	Radiotherapy, urethane, and melphalan
2 F	35	IgG	6	Melphalan, androgen
3 M	21	Bence Jones	7	Melphalan, cyclophosphamide androgen

The relatively young age of onset of multiple myeloma in all three cases is noteworthy. Case 3 was in fact the youngest patient in our experience with over 400 cases of multiple myeloma. In all three cases the clinical and haematological features of the leukaemia appeared abruptly and terminated fatally within one to two months. Nevertheless, in Cases 2 and 3 there were transient episodes of fever and leucocytosis with relative monocytosis for several months preceding the final florid leukaemic phase. Increasing proportions of monocytes and monoblasts were also recorded in the bone marrows of these cases during the pre-leukaemic periods.

In all three cases the multiple myeloma had been exceptionally well suppressed by continuous chemotherapy for the periods shown in the Table. Chemotherapy for the multiple myeloma had been discontinued 2, 10, and 18 months, respectively, in the three cases before the emergence of the monomyelocytic leukaemic phase because of evidence of bone marrow failure. There was no evidence of recrudescence of the multiple myeloma in any of these cases during the later preleukaemic and leukaemic phases. Moreover, the myelomonocytic leukaemia was consistently associated with appreciable increases in serum and urine lysozyme (muramidase) levels. There was also evidence of renal tubular dysfunction secondary to lysozyme overloading ("lysozyme nephropathy")—that is, hypokalaemia, hyperkalemia, and "tubular" proteinuria.

It is postulated that the development of monomyelocytic leukaemia in these cases of multiple myeloma is related to the functional interrelationship between monocytes (histiocytes) and plasma cell in the processing of antigen and in the formation of antibody. The possibility that the preceding myeloma chemotherapy may have contributed to the ultimate development of a monocytic dyscrasia cannot be excluded, but if the chemotherapy did, in fact, contribute to the development of leukaemia it was a "reasonable price" to pay for the prior benefits derived.

Institute of Cancer Research and Department of Pathology, College of Physicians and Surgeons, Columbia University, New York, N.Y. 10032

ELLIOTT F. OSSERMAN

## Extramedullary Plasmacytoma

E. WILTSHAW

Despite the widespread distribution of plasma cells throughout the body, plasma-cell tumours most commonly occur within the bone marrow and only rarely present in extramedullary sites. A study of 266 cases of extramedullary plasmacytoma has shown that 75% present in the submucosa of the upper air passages and that many are apparently multifocal. The mode of spread resembles that of reticulum-cell sarcoma and is characterized by early invasion of lymph nodes draining the primary site, followed by blood borne metastases to bones, subcutaneous tissues, and other organs.

Even when the disease is widespread, the bone marrow is rarely affected and as a result large doses of chemotherapy with alkylating agents may be given safely. In most cases this treatment is followed by dramatic and sometimes prolonged remissions, and in two instances complete healing of bone metastases has been seen.

On the other hand, the findings in a study of 77 cases of solitary myeloma of bone confirm that in regard to age at presentation, mode of spread within skeletal bone marrow, and the lack of extramedullary lesions—even in advanced disease—solitary myeloma of bone is a rare form of presentation of myelomatosis and not a separate entity.

	Extramedullary Plasmacytoma	Solitary Myeloma of Bone
Age at presentation (years) range and median	8—52 51—60	14—72 51—60
Presenting site	Upper air passages in 75% of cases	A vertebra 20%; pelvis 20%; femur 20% (40% showed a trabeculated lesion)
Dissemination	By metastases Bone deposits 40.5% Bone and soft tissue deposits 40.5%. Soft tissue deposits only 19%	By widespread involvement of areas of active haemopoiesis. Bone deposits only 100%
Myeloma cells found on marrow aspiration	10% of cases with disseminated disease	All cases with disseminated disease

Royal Marsden Hospital, Fulham Road, London S.E.3  
E. WILTSHAW

## Prognostic Factors in Myelomatosis

BO JOHANSSON

Since 1930 a total of 271 patients with myeloma have been seen at the Radiumhemmet in Stockholm. Of these, 142 were seen before 1960 and were treated with palliative radiotherapy; the remaining 129 were treated mainly with cytotoxic drugs, and their survival rate was about three times higher than in the earlier group. As well as the later treatment being more effective there may be other explanations for this improvement in survival—such as earlier and more frequent diagnosis and differences in the types of patients referred to the hospital during different periods of time.

An attempt was made to see whether the heterogenous group of patients with multiple myeloma treated with cytotoxic drugs could be subdivided into subgroups with different prognosis.

We confirmed the long-recognized fact that patients with Bence Jones proteinuria and patients with renal failure have a poor prognosis. As far as the radiological appearances were concerned those patients with well-circumscribed osteolytic lesions were found to have a worse prognosis than those in whom the only finding was a more or less pronounced generalized osteoporosis. Different patterns of response of the immunoglobulin levels were observed in the first six months of treatment. In most patients these levels fell, either slowly or very rapidly. Those patients with a slow fall or no change in the immunoglobulin level had a better survival time than those in whom the level fell rapidly. Ten of the patients had very poorly differentiated plasma cells in the bone marrow as the predominant cell type, and only one of them has survived for more than three years. Thus a small group of patients can be distinguished who

have a poorly differentiated tumour and a very bad prognosis.

When the clinical findings in the groups of patients treated before and after 1960 were compared a striking difference was found only in the frequency of different radiological appearances, the other clinical features being very similar in the two groups. Hence part of the improved survival rate in the past decade is probably due to differences in the types of multiple myeloma treated during the different time periods. Nevertheless, this is not the only explanation and some of the improvement must be due to the cytotoxic drug therapy.

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Radiumhemmet, Stockholm, Sweden  
BO JOHANSSON

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## Gynaecology in General Practice

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### Venereal Disease in Women—I

C. S. NICOL

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#### Sexually Transmitted Diseases

A number of infectious diseases are usually transmitted between individuals by close bodily contact during the sex act. These are most commonly found in the lower genitourinary area, but are sometimes capable of spreading to the upper genitourinary tract as well. They may also involve other parts of the body by genito-oral or genitoanal contact and may infect the conjunctival sac or sometimes spread via the blood stream. Small girls may get similar genital conditions by chance infection from either parent; the eyes of newborn children may be infected from the mother's genital tract, and in the case of syphilis transplacental infection affects the fetus. Only very rarely are these infections transmitted by other forms of contact between individuals or indirectly via some inanimate object.

In every patient with suspected sexually transmitted disease the general practitioner must get an accurate history of all recent incidents of sexual intercourse or of any other type of contact, either heterosexual or homosexual. It is surprisingly easy to get this information from patients nowadays, as long as they appreciate the reason for this type of question. In many cases of sexually transmitted disease the patient has been promiscuous. If possible the identity of both the primary (source) contact and of all secondary (infected) contacts must be established. Quite often the only secondary contact will be the patient's wife, whose exposure has been entirely intramarital.

The general practitioner then has to decide whether he has the facilities for accurate diagnosis, contact tracing, and

follow-up before he gives the appropriate treatment. He must also remember that in the presence of any one sexually transmitted disease, however minor, he should do the appropriate examination and tests to exclude all the other sexually transmitted conditions. If he decides he has not the necessary facilities he should refer the patient (preferably untreated) as soon as possible to a special clinic. If some antibiotic has already been given this should be mentioned in his referring letter to the venereologist.

This article is in four parts: the first two deal with the venereal diseases as legally defined, the others with the other sexually transmitted diseases.

#### Legal Definition

The venereal diseases, as defined in an Act of Parliament in 1917, include syphilis, gonorrhoea, and chancroid (soft chancre). New cases of these diseases comprise about 25% of total new cases seen in clinics. Patients can attend these clinics without referral from their general practitioner and without an appointment; treatment is free (no prescription charge) and confidential. In the past ten years new cases in most clinics have doubled; the ratio of men to women has changed from about 3 to 1 to 1.5 to 1.

#### Syphilis

Syphilis is caused by *Treponema pallidum* and has an incubation period of from 9 to 90 days. The early phase lasts for two years—during most of which time the patient is contagious—and consists of a primary stage, a secondary stage, and a latent stage; sometimes primary or secondary type lesions reappear in a recurrent stage. The late phase is divided into a latent stage, a tertiary stage (gummatous), and

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St. Bartholomew's and St. Thomas's Hospitals, London  
C. S. NICOL, M.D., F.R.C.P., Physician in Charge of Venereal Diseases Clinic