Leukemia Research Vol. 15, No. 6, pp. 407–408, 1991.
Printed in Great Britain.

0145–2126/91 $3.00 + .00
Pergamon Press plc

EDITORIAL

TO TREAT OR NOT TO TREAT, THIS IS THE REAL QUESTION

Our third editorial in the series *"Our hematologic heritage"* is by Jan Waldenström, one of the first to describe the clinical syndromes of macroglobulinemia, porphyria, and carcinoid tumors. Waldenström, Emeritus Professor of Medicine at the University of Lund in Sweden, is a member of the Academies of Science in Sweden, France, and the U.S.A., the French Academy of Medicine and the Academy of Arts and Sciences in Boston. He has been awarded an honorary doctorate at eight universities, including London, Paris and Oxford. Among the many meetings organized in his honor is one published by the journal *Medical Oncology and Tumor Pharmacology* (Vol. 3, no. 3/4, 1986).

PETER REIZENSTEIN
Editor

FOR ABOUT 50 years I have been especially interested in problems regarding myeloma, macroglobulinemia and also lymphatic leukemia. The clinical picture in these B-cell malignancies is very variable. This also means that the prognosis, both untreated and after competent treatment, may vary very much. One of the most important lessons that we have to learn is to understand the natural history of disease.

It is evident that great advances in treatment could make the medical profession what I call "treatment-happy". For a young doctor the temptation to start treatment and to continue until the parameters measuring disease become normal is very strong.

One of the greatest changes in hematology during my career has been the advent of effective therapy. I guess that the treatment of pernicious anemia with liver that has now developed our understanding of B-12 deficiency in a general meaning is the greatest achievement. It is a pleasing fact that you cannot overtreat and also obtain results that are 100% effective. As I see it, the advent of erythropoietin in such quantities that it can be used freely is another great advance, even if we have to look out for possible evil effects. It is interesting to realize that B-12 is a vitamin and erythropoietin a hormone. Overdosage with true vitamins (D is an exception, being really a hormone) never occurs. On the contrary all hormones may cause trouble if overdosed. The same is evidently true of the third great advance in hematological therapy, i.e. cytostatic drugs.

The therapeutic results that have been obtained in the treatment of leukemia are of course impressive, sometimes almost incredible. The use of cytostatics, above all alkylating agents, has shown that malignant cells may be killed by using the right drug. Every physician agrees that eradication of the last malignant cell is the ideal result of treatment. Acute leukemia has been an excellent example of this program. On the other hand, I feel convinced that it is exceptional with such a battle of annihilation, as the military strategists call it when they speak of Hannibal's victory at Cannae, as the ideal. In many instances, for example myeloma, macroglobulinemia and chronic lymphatic leukemia, it is much more profitable for the patient with a slow but steady and sure defence against the disease. We have an excellent principle for measuring the therapeutic results in all these diseases numerically. There is an old Swedish proverb: "the best may be an enemy of the good". If we try to obtain normality, the result will sometimes be disastrous for the patient because of damage to the normal bone marrow.

I have a feeling that the enthusiasm that characterized early radiology, with severe damage to normal tissues, may also characterize some of our present-day pharmacological treatment programs. For many years I have quoted to the medical students an inscription on a tombstone: "I felt well, but wanted to feel better—therefore I am here". The careful adjustment of therapy in order to obtain slow but steady improvement is often superior to the dramatic results that seem more striking to the young and inexperienced doctor.

The real problem, however, may perhaps be condensed into the three words: "let well alone". For more than 30 years I have been especially interested in patients who have a monoclonal increase of immunoglobulins (Ig) in the plasma without showing any progression towards a malignant state. In principle the same is also true of patients who are and remain

well for decades with a slight increase in lymphocyte numbers and even with some moderate lymphadenopathy. It may seem tempting to start cytostatic treatment in order to obtain "normal values". This should be avoided for two reasons. First, we must remember that cytostatic drugs are always toxic; second, if treatment has been started, it is difficult to stop and the result may be that the patients have to be supervised closely for the rest of their lives. In order to be sure that the patients do not suffer from a progressive disease their status should be followed for 2–3 years. Regarding monoclonal Ig, I have called this condition "benign monoclonal gammapathy" and a similar condition also exists regarding lymphocytosis.

I have been asked to give three pieces of advice to a young colleague in hematology. This is in itself impossible because there are so many pitfalls in diagnosis and treatment. I feel convinced, however, that it is still of paramount importance to listen to the patient and to perform a close physical examination. This may be a guarantee that you are not drowning in the sea of detailed laboratory results. Another important rule is to avoid treating one special symptom. Rather, one should try to improve the patient's general state of health. The third would perhaps be to avoid gunshot therapy hoping that something will hit the target. A well organized diagnostic program should always precede therapy.

Overtreating may mean different things. The most important is of course what I have discussed here. Another question, however, is overtreating in order to be sure that nothing has been missed. In recent years there has been much discussion about starting treatment for the benefit of the doctor's feeling safe and not for the best of the patient's health. Economic developments are of course responsible for this deplorable situation.

Most discussions regarding treatment nowadays contain a pious phrase about quality of life. This is of course the essence of medicine, and still it is so difficult to define. *"Per aspera ad astra"* may mean two things, if you are a little cynical. *Per aspera ad astra* = through hardships to the stars, either to heaven or to health and good luck. The same is true of therapy. Modern cytostatics, as most effective drugs, certainly cause hardships that may lead to death, although the purpose is improvement of health. The dividing line may, however, be difficult to find and the quality of life may be suffering severely.

If your patient follows the example of the great Swedish poet Stiernhielm and may write on his tombstone: *"Vixit, dum vixit, laetus"* (he lived happily as long as he lived), you have certainly succeeded to improve his quality of life.

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