Therapeutic Timidity in Dermatology*

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Nec temere, nec timide

"Never rash, never timid" was the motto of a Danish naval hero from the 17th century, admiral Niels Juel. I would meet these words every morning, when entering the front hall of the Naval Academy, during my years as midshipman in the Royal Danish Navy in 1940s. Later as a medical student, another motto was presented to me by one of my professors. On the front page of his textbook he had printed: "In primum nihil nocere", first of all do no harm. These were the days when medical students were supposed to have some knowledge of Latin. Today, many years later, I often wonder if I carried too much of the motto from my first profession with me to the latter, disregarding the wisdom from the textbook. But this essay on "therapeutic timidity" is not meant to promote the abolition of timidity within our speciality. The intent is to point out examples, from those I have encountered over the years, where I believe therapeutic timidity may have led to inadequate treatment or to a poorer quality of life than necessary among patients.

Should we start with the high or the low dose?

It is generally accepted by dermatologists in most cases that when starting therapy with topical corticosteroids, we should use potent steroids in the beginning and then gradually reduce to the strength necessary to control the disease. However, it is unfortunate that at the same time as we have been so successful in making GPs and the general public aware of the hazards of topical steroids, this has often led to some patients, whose dermatoses require potent steroids, being denied effective therapy and left only to the aid of hydrocortisone or emollients.

Meanwhile, the same principle of starting with the higher dose is often abstained from in systemic therapy. Timidity has made it not uncommon to recommend slow proceeding, to reach the right maintenance dose from below, thereby delaying clearing for weeks or months and often losing the patient's confidence and compliance. An example can be found in the revised guidelines for the use of cyclosporin A (CsA) (1) , for which this practice was introduced in 1992 to reduce toxicity, even though early dose-finding studies (2) indicated the superiority of the opposite procedure. Short-term toxicity of CsA is normally a smaller problem to deal with than long-term, which is related to the length of therapy and cumulative dose and not to the initial dose, when given within recommended levels.

Using an introductory extremely low "test dose" is recommended in the guidelines for methotrexate (MTX) (3), although to my knowledge no data have been presented showing that "hypersensitivity" to the drug exists when starting therapy, unless the patient belongs to a risk group. The latter should be ruled out before therapy is given. I admit, however, that no harm has been caused by this prudence, as the delay in this case is minimal. As with CsA, however, the delay is longer if the same principle of working one's way up from a low dose to the appropriate maintenance dose is used. This is important, since MTX does not work as fast as CsA, and before the right dose has been reached and accomplished its result, the patient and occasionally even the physician may have reached the wrong conclusion that the drug does not work.

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The controversy regarding whether to use aggressive therapy at an early or late stage in cutaneous T-cell lymphoma has not been solved, although there is a trend towards more aggressive therapy aimed at cure in North America versus the more palliative approach in many European centres (4). Advocates of the palliative approach justify their position with the lack of studies showing any prolongation of life expectancy. They often forget, however, to mention the number of complete or partial remissions, which the more aggressive therapies, topical as well as systemic, may lead to, thereby increasing quality of life. Certainly the potential side effects of over-enthusiastic aggressive therapy in elderly frail patients should be taken into consideration.

Which drugs should we use?

It is well known that in severe cases of acne, the natural cause persists in excess of 10 to 15 years, and that in the meantime, the disease may lead to intractable scarring, while therapy with oral isotretinoin is an almost guaranteed success. Still many patients with a severe case of the disease initially receive a variety of other oral and topical therapies due to timidity and a threshold set too high for introducing systemic isotretinoin.

For years "the liver scare" (5) was responsible for a significant drop in the use of MTX for severe psoriasis. Timidity combined with the fear of recommending a liver biopsy contributed to the decline in popularity of this valuable drug. In the space of time before other systemic agents appeared on the market, this must have led to both a significantly lowered quality of life for many patients and to an unnecessary progression in many cases of psoriatic arthritis.

The knowledge that CsA may introduce not only reversible functional renal toxicity, but also cause irreversible morphological renal damage (6), probably contributed to a similar hesitation to prescribe this drug in a number of cases, where it definitely could have contributed to a higher quality of life for patients with severe psoriasis or atopic dermatitis. Our knowledge should instead be used to register how long the drug can be used safely, and it should be included in appropriate rotation therapy for the relevant diseases. We all accept that upper dose levels exist for the various types of phototherapy as well as for radiotherapy. There is no reason not to accept similar cumulative dose levels for drugs in systemic use and deal with them appropriately, instead of discarding the therapy. Naturally a risk benefit analysis should be made. This is not "timidity", but proper clinical practice.

When handling patients suffering from autoimmune bullous diseases, dermatologists are prepared to deal promptly and sufficiently, while there is a tendency to "wait and see" in many cases of other autoimmune diseases and to rely on symptomatic therapy instead of the use of disease-moderating drugs. In a number of cases this may cause unnecessary organ damage. Examples can be found among the systemic disorders of connective tissue.

Surgical procedures

For many reasons, including almost certainly timidity, dermatological surgery was reduced for many years to minor procedures such as curettage, minor cryosurgery and electrosurgery. Judging, however, from the programs of recent AAD meetings in this "age of lasers", dermatological timidity seems to have nearly vanished within this particular area. None the less, there are still several developed countries where dermatological surgery has such low priority that many dermatologists of the younger generation keep away from surgery as far as possible.

General considerations

I have taken CsA and MTX only as examples; other drugs could have been used as well. The question is: Is there therapeutic timidity in dermatology and is there any reason to fear that dermatologists are more counterproductively timid than other specialists are? I believe that the answer to both parts of this question is yes. But does such timidity influence the outcome of dermatological therapy? It has been suggested that sometimes, timidity does lead to inadequate, inefficient, even incorrect therapy, while in other cases, the outcome may only be delayed improvement. But in still other cases, it may lead to a failure to recognize that an adequate dosage of the correct drug would help when a lower one did not, to the erosion of

patient confidence and failure to comply. In the worst cases, therapeutic timidity may lead to unnecessarily prolonged misery from disease, or to disease progression that could have been stopped. This article is being written to ask dermatologists to be aware of the problem. Naturally, the dictum "nihil nocere" should not be forgotten. Sometimes, for example, starting with a high dose when dealing with drugs like hydroxyurea or dapsone, where the difference between the therapeutic and the toxic dose is small, is not good clinical practice. Nor is it good clinical practice to neglect performing the relevant risk benefit analyses before choosing the drug or combination of drugs.

In the last analysis, appropriate care of patients means using the best available evidence combined with the best clinical judgement. A laser should not be used to scratch an itch, but powerful drugs in adequate dosages must be used when called for to relieve misery and prevent disease progression.

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Photodynamic Therapy

Photodynamic therapy, PDT, is becoming increasingly more common as the standard therapy for a number of skin diseases, mainly precancerous or cancerous. During the 29th Nordic Congress on Dermatology in Gothenburg recently, a group of Nordic dermatologists with an interest in PDT met to form a "Nordic Working Group on PDT". The idea is to exchange knowledge and experience and to discuss guidelines and clinical research among dermatologists interested in PDT. We will try to work cooperatively with other groups, especially the European Society for Photodynamic Therapy in Dermatology, the "Euro-PDT". At the founding meeting in Gothenburg I was asked to proceed with organising the group. An executive committee will be established during the autumn, with our first larger meeting to be organized in the winter, hopefully in close cooperation with the Euro-PDT. Since I am aware that many colleagues were not able to participate at the founding meeting in Gothenburg, I use this opportunity to inform all Nordic Dermatologists. If you are interested and have not yet been contacted, please do not hesitate to contact me.

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