

# **In medicine, as in politics, it is sometimes difficult to disentangle the effects of what we are doing**

Every cloud, it is said, has its silver lining: but does every silver lining have its cloud? So it often seems in daily life, and there is no situation so favorable that men are incapable of extracting disaster from it. But medicine is one field in which progress seems almost unalloyed: setbacks are at worst temporary. After all, there had to be antibiotics before there was resistance to antibiotics.

Until the 1960s, Hodgkin's lymphoma was essentially untreatable and invariably fatal. A combination of radiotherapy and chemotherapy improved the prognosis dramatically to the point of cure, though the treatment was very unpleasant and it gradually emerged that those who survived their Hodgkin's were more than usually susceptible to developing a second cancer.

By the time a cure became available, medicine had entered the era when anecdotal evidence, until then the mainstay of the science, was no longer deemed sufficient, and it was necessary to prove the effects of treatment, good and bad, more rigorously. This is difficult to do where, as in the case of Hodgkin's lymphoma, it is *a)* necessary to follow up patients for a long time, and *b)* the treatment of the disease changes all the time.

A paper by Dutch researchers in a recent edition of the *New England Journal of Medicine* tries to answer the question of whether changes in the way in which Hodgkin's lymphoma is treated – reductions in the dose of radiotherapy and the

employment of less toxic anti-cancer drugs – has resulted in a lower incidence of subsequent second cancers. As an accompanying editorial in the journal puts it, “Long-term survival after a diagnosis of Hodgkin’s lymphoma depends on two interrelated factors – successful elimination of disease and the avoidance of treatment-related second cancers.” The trick is to eliminate the disease without increasing the chances of a second cancer, and it was assumed that newer treatments did this better than old.

The researchers followed up 3905 patients treated in Holland for the disease between 1965 and 2000. They estimated the rates of secondary cancer after the patients had been cured, that is to say once they had remained free of Hodgkin’s lymphoma for five years after treatment. It was expected that, with newer and ‘gentler’ forms of treatment, the incidence of such cancers had fallen.

This, however, was not the case, at least for what are known as solid cancers (the incidence of blood cancers had indeed fallen, but they accounted only for a small proportion of the total). Overall, the patients had a risk of developing secondary cancer four times greater than if they had not had Hodgkin’s lymphoma treated by radio- and chemotherapy, but the rate had not fallen.

However, the difficulty of hitting a moving target was illustrated by the example of cancer of the breast, which accounted for 40 per cent of the secondary cancers in women. The incidence had remained the same over the years, but such cancer was detected earlier in cases treated more recently. This was because, more recently, women underwent screening more frequently, and therefore detection rates may have risen. In other word, the *meaning* of the finding that rates of breast cancer had remained the same was uncertain.

Moreover, treatment of Hodgkin’s lymphoma has changed further since 2000, so that it is impossible to apply the paper to

current practice. To find the comparative effects of current practice, we shall have to wait another fifteen years.

The paper makes no mention of death rates among the treated patients: whether they have risen, fallen or remained the same. Survival after secondary cancer may have increased, so that overall survival would have increased. What the paper does make clear, however, is that, as in politics, it is sometimes difficult to disentangle the effects of what we are doing.

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