Intravenous injection of killed Corynebacterium parvum 2 days before, or 8-10 days after, subcutaneous injection of viable cells of two isogenic mouse tumours (a spontaneous mammary carcinoma and a chemically induced fibrosarcoma) delayed the appearance of palpable tumours. Once palpable, tumours grew at the same rate in treated and control mice. [The SCI® indicates that this paper has been cited in over 295 publications.]

Immunotherapy for Cancer
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May 24, 1989

When I learned of B.N. Halpern’s work1 showing that injection of killed Corynebacterium parvum powerfully stimulated reticuloendothelial function, I resolved to study the effect of this agent on tumours if Halpern would let me have some of this material, which he generously did. My research assistant (Dr. J.L. Boak) and I showed that intravenous injection of C. parvum inhibited the growth of two isogenic mouse tumours. This was soon confirmed with other mouse tumours in my laboratory and elsewhere; subcutaneous or intramuscular injection, however, was ineffective.

Many morphologically similar organisms have since been tested; the active ones are either propionobacteria or corynebacteria, but the label “C. parvum” is commonly applied to them all. It was shown later in various laboratories2 that intratumour injection of C. parvum could cause regression of various established tumours; this effect, however, unlike that of systemic administration, proved to be T-cell dependent.

This work was followed by clinical trials of C. parvum in patients with advanced cancer.3 Subcutaneous or intramuscular injection proved innocuous but, with a few reported exceptions, therapeutically ineffective. Intravenous infusion by slow drip was more effective but resulted in severe pyrexial reactions that were only partially controlled by aspirin. Intrapleural injection of C. parvum in patients with malignant pleural effusions often dried up the effusion,4 but did not significantly prolong survival.

A phase-II randomized trial of a single intravenous infusion of C. parvum as an adjuvant to surgery in 49 patients with operable lung cancer was not decisive but suggested that the treatment may have prolonged survival.5 An attempt to set up a larger trial failed because many patients and doctors were understandably deterred by the pyrexial reactions.

In another randomized trial6 in patients with non-small cell operable lung cancer, there was no difference in the length of survival or the disease-free interval between those treated by surgery plus a placebo and those treated by surgery plus combined intrapleural and intravenous infusion of C. parvum. Since an earlier trial6 had shown that combining intravenous infusion of C. parvum alone with surgery actually shortened survival in similar patients, the authors accepted that intravenous injection alone might conceivably be beneficial, but no trial of this was reported.

Can the severe pyrexial reactions that follow intravenous injection of C. parvum somehow be prevented without loss of therapeutic effect? The development of “second generation” biological response modifiers has diverted attention from this question, but it merits serious study.