BOOK REVIEWS

Heroic Therapies

A Commotion in the Blood. Life, Death, and the Immune System. STEPHEN S. HALL. Holt, New York, 1997. xiv, 544 pp. + plates. $30 or C$41.95. ISBN 0-8050-3796-9.

Immunotherapy, a treatment for cancer that acquired high visibility in the media in the early 1980s and that continues to be viewed as a promising approach to the cure of malignant tumors, has been presented by its advocates as proof that a better scientific understanding of mechanisms of malignant transformation and of immune responses can lead to the development of an efficient anti-tumor therapy. Stephen Hall's lively and readable book tells the story of the development of cancer immunotherapies. It traces their origins to studies made in the late 19th century by the New York surgeon William Coley and then follows out recent developments in this area.

A Commotion in the Blood is a well-documented study that makes complicated scientific issues accessible to a non-specialized public and provides fascinating descriptions of medical science in the making. The book starts with a detailed history of Coley's cancer therapy. In 1891 Coley became acquainted with a case of long-term regression of an advanced sarcoma (a soft-tissue cancer) in a patient who simultaneously developed erysipelas—a severe infection induced by the bacterium *Streptococcus pyogenes*. Encouraged by a description of similar cases in the medical literature, Coley decided to deliberately infect sarcoma patients with erysipelas. The artificial infection was seldom successful, and Coley turned to the administration of a mixture of substances secreted by the bacteria *Streptococcus pyogenes* and *Serratia marcescens* ("Coley's toxins"). These substances induced high fever and other side effects, and the therapeutic results were unpredictable. However, in selected cases Coley was able to demonstrate an impressive, long-term regression of sarcomas.

Coley's therapy was controversial from the beginning, because of its side effects, its numerous failures, and the absence of a convincing scientific explanation why the toxins occasionally worked. The advent of radiotherapy—the first non-surgical treatment of malignant tumors—accelerated its demise. In the 1970s, however, new developments in immunology led to a (partial) return to the principles developed by Coley—first through attempts to stimulate anti-tumor immune mechanisms with bacteria such as bacillus Calmette-Guérin, then by the use of molecules (interleukins, interferons, growth factors) that activate immunocompetent cells. At first sight, recent immunotherapies that employ highly purified recombinant molecules have little in common with the administration of Coley's toxins, a crude "soup" of molecules secreted by bacteria in culture. Hall points, however, to two similarities between early and late immunotherapies: the "heroic" aspect of both (a paradoxical characteristic of therapies based on the physiological principle of the activation of natural defenses of the body) and their low overall efficacy, combined, nevertheless, with an ability to occasionally induce long-term regressions of otherwise incurable tumors. On both these counts, Hall reports, Coley's toxins fared rather better than the new immunotherapies: their side effects seemed to be less severe and the number of apparent cures higher. The juxtaposition of the histories of old and new immunotherapies raises numerous questions concerning progress in the development of cancer therapies.

Hall's book, well written, carefully documented, and thought-provoking, may be seen as an example of scientific journalism at its best, while its weak points reflect the limitations of the genre. The journalist's focus on the singular experience of individuals tends to obscure the extent of transformation in medicine and biomedical research. The medicine of the late 20th century is quite different from that of the late 19th century, but the personal experience of the Italian immigrant Zola, the first patient cured through administration of Coley's toxins in 1891, was not very different from that of Phil Karr, cured in 1981 through the application of anti-tumor monoclonal antibodies, or of Linda Taylor, successfully treated in 1985 with interleukin-2/LAK therapy. Similarly, accounts focused on the personalities of medical researchers do not forward understanding of the professional and institutional environment in which they worked: we learn about conflicts between William Coley and his hierarchic superior, James Ewing, but not about the organization of cancer treatment in the early 20th century; about the tendency of National Cancer Institute surgeons to have inflated egos and to practice interventionist "macho" medicine, but not about NCI's research policies.

The insistence on "human interest stories" also tends to weaken the book's overall message. Thus while Hall indirectly criticizes expensive and painful therapies that at best are buying a little time for the sick person, when he is following a patient's story he affirms that the value of additional time on Earth, gained through a high-tech experimental therapy is "so incalculable that it is far beyond the reach of scientific discussion." He ends the book with the affirmation that, thanks to investigations made in the 1990s, tumor immunology has entered into "the realm of hard-core science" and therefore that "unlike in earlier eras, there is good reason—good *scientific* reason—to be optimistic" (an argument repeatedly attached to each new development in tumor immunology in the last 30 years). This conclusion contradicts the implicit message of the book: the persistent difficulty of translating scientific understanding of cancer and of immune mechanisms into efficient cures. One of the main merits of Hall's book is the presentation of this difficulty to a non-specialized public. The awareness that the present science-based, high-tech, interventionist cancer medicine is not an unmixed blessing should stimulate studies that investigate the scientific, sociological, historical, cultural, and economic background of the development of new anti-tumor therapies, but also a political debate on the priorities in cancer research and cancer treatment.

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Crosses in Nature

Natural Hybridization and Evolution. MICHAEL L. ARNOLD. Oxford University Press, New York, 1997. xiv, 215 pp., illus. $60 or £45, ISBN 0-19-509974-5; paper, $29.95 or £22.50, ISBN 0-19-509775-3. Oxford Series in Ecology and Evolution.

As elaborated by G. L. Stebbins decades ago, hybridization can enrich local gene pools and lead to new adaptations, and hybrid derivatives can be stabilized at the