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

Vignettes: Press Relations

To anyone who writes about science or medicine for a living, the word *breakthrough* has a kind of transcendent power. The procedure or molecule or discovery under discussion may or may not in fact be a breakthrough, but if anyone in a position of expertise or authority utters the word, the writer possesses a ticket to journalism's most precious real estate: the front page of the newspaper, the magazine cover, prominent play on the evening news.

—*Stephen S. Hall*, in *A Commotion in the Blood: Life, Death, and the Immune System* (Holt)

The sheer lack of *nous* demonstrated by scientists in their relations with the press is perpetually astonishing. Tom Wilkie, former science editor of *The Independent*, recalls a memorable example from 1988, when the British computer firm Inmos was sold off to a Franco-Italian company. "The sale raised a host of issues concerning short-termism and the national commitment—or otherwise—to research and development. I wrote an op-ed piece about these issues and the response consisted of a single letter, where an academic pointed out that I had given the wrong number of megaflops for one of Inmos's transputers."

—*Graham Farmelo*, in *Science Today: Problem or Crisis?* (Ralph Levinson and Jeff Thomas, Eds.; Routledge)

diploid and polyploid levels. *Natural Hybridization and Evolution* is an exposition on these themes. Through a discussion of numerous intriguing studies, this book makes a multifaceted case for the importance of hybridization. It also highlights the biases, misconceptions, and misinterpretations that might lead to an underestimate of the evolutionary importance of hybridization.

Arnold observes that interspecific hybridization is antithetic to the major mechanistic and historical species concepts. He advocates the study of hybridization free of the shackles of species concepts. He might also have said that we may need a species concept that allows hybridization. Indeed, species could be recognized on the basis of their unique relationship to the physical and biological environment. Hybrids between population systems that differ substantially in these respects are also likely to display genomic disharmony that will reduce, but not necessarily preclude, gene flow between these systems. As post-mating barriers are incidental by-products of selective and stochastic divergence, the issue of hybridization need not be brought into the species equation.

Arnold's discussion of gametic recognition and gametic competition is one of the highlights of the book. The relative performance of conspecific and heterospecific sperm (in animals) and microgametophytes (in plants) often has been inferred by comparing the independent outcomes of conspecific crosses on the one hand and heterospecific crosses on the other. We want to know what happens when sperm of two species are present in the female reproductive track and when pollen tubes of two species are growing in the same pistils. This is what often occurs in nature. Gametic competition leads to a pronounced decrease or exclusion of hybrid formation, but hybrids are formed nevertheless.

It long has been held that hybrids are usually less fit than the parental species. Arnold effectively challenges this dogma. Indeed, hybrids often may be more fit than their parents, even in parental environments. He argues that most hybrid zones are shaped in part by selection favoring certain hybrid genotypes and that alien genes may spread from sites of species contact.

The long-term impact of hybridization lies in the stabilization of hybrid derivatives. This is revealed in phylogenetic reconstructions from discordance between phylogenetic hypotheses based on different approaches. Arnold discusses several well-chosen cases of such discordance from a rapidly growing list. Of particular interest is the fascinating work by Rieseberg and associates on *Helianthus*, which shows how the genomes of *H. annuus* and *H. petiolaris* are combined on the chromosomes of *H. anomalous*.

Although this book covers a broad scope, there are some topics central to hybridization that are not included or are only mentioned in passing. These include impediments to hybridization other than gametic competition, character expressions and character correlations in first- and later-generation hybrids, reproductive character displacement, and experiments demonstrating the origin of new species through hybridization. Nevertheless, *Natural Hybridization and Evolution* is a convincing and well-crafted testament to the importance of hybridization in evolution. The reader will be enlightened.

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Browsings

Defeating Darwinism by Opening Minds. Philip E. Johnson. InterVarsity Press, Downers Grove, IL, 1997. 131 pp. Paper, $15.99. ISBN 0-8308-1360-8.

The author of *Darwin on Trial* tries again, this time aiming at an audience of "late teens."

History of Physical Anthropology. An Encyclopedia. Frank Spencer, Ed. Garland, New York, 1997. In two volumes. xxvi, 1195 pp., illus. $175. ISBN 0-8153-0490-0. Garland Reference Library of Social Science, vol. 677.

The development of "human natural history" traced by way of entries by 169 contributors discussing particular researchers, organizations, and institutions, various subdisciplines, concepts, and theoretical issues, and sites and geographic areas on which work has focused, with selective bibliographies and name and subject indexes.

Menachem's Seed. A Novel. Carl Djerassi. University of Georgia Press, Athens, 1997. xii, 198 pp. $21.95. ISBN 0-8203-1925-2.

A third entry in the author's "science-in-fiction" series (see *Science* **246**, 829 [1989] and **269**, 109 [1995]), this one featuring Middle East politics and advanced techniques of insemination.

Questioning the Millennium. A Rationalist's Guide to a Precisely Arbitrary Countdown. Stephen Jay Gould. Harmony (Crown), New York, 1997. 190 pp., illus. $17.95 or C$24.95.

The prolific paleontologist and popularizer takes up calendrics and associated apocalyptic beliefs.

Sex on the Brain. The Biological Differences Between Men and Women. Deborah Blum. Viking, New York, 1997. xxii, 329 pp. $24.95. ISBN 0-670-86888-4.

A journalist gives the relevant research, including evolution and endocrinology, a sometimes ironic once-over-lightly.