

THE PRESENCE OF DELAYED HYPERSENSITIVITY REACTIONS IN PATIENTS TOWARD CELLULAR EXTRACTS OF THEIR MALIGNANT TUMORS

1. *The role of tissue antigen, nonspecific reactions of nuclear material, and bacterial antigen as a cause for this phenomenon*

T. H. M. STEWART, MB, ChB, FRCP (C)

Patients have a delayed hypersensitivity reaction toward extracts of cells of their malignant tumors in 26% of cases. This is not due to a nonspecific reaction to nuclear material in the majority of cases. It is unlikely to be due to tissue specific antigen. In carcinoma of the breast, bacterial antigen can be excluded as a cause of this phenomenon. In carcinoma of the gastrointestinal tract, it is shown that bacteria may not be a cause, although the natural termination of these tumors makes it impossible to be dogmatic. The greatest reaction is seen toward the extract derived from centrifugation of tumor homogenate at 14,000 g. a fraction that probably contains external cellular membranes. No correlation can be made between the presence of the D.H.R. to tumor extracts and the reactivity shown by the patient to Varidase, a test agent toward which a high percentage of healthy adults react in a delayed fashion when tested intradermally.

IN RECENT YEARS THERE HAS BEEN GREAT INTEREST in the possibility that there may exist an immunologic defense mechanism against malignant tumors in man. In 1964, Hughes and Lytton¹ published their results on a study of 50 patients. Their approach was based on the work of Brent, Brown, and Medawar² who in 1958 demonstrated that guinea pigs, actively rejecting foreign skin grafts, showed a delayed hypersensitivity reaction (D.H.R.) to an acellular extract prepared from the graft cells. This tuberculin-like reaction correlated well with the presence

of a satisfactory graft rejection mechanism. These workers were able to transfer sensitized lymphocytes from these guinea pigs that had rejected such a graft, and these cells gave protection to other animals subsequently challenged with grafts from similar donors. Hughes and Lytton used a similar approach and extracted an acellular pellet from tumor cells taken from the patient. All tumors were demonstrably sterile after 48 hours of bacterial culture, and 27% of the patients showed a positive delayed hypersensitivity reaction to this material. No correlation was found between the presence of such a skin reaction and the histology of the tumor, in terms of cellular differentiation and metastases. Because of the limited number of patients, survival studies could not be correlated with the presence or absence of such reactions. Since January 1966, patients at the Ottawa General Hospital coming to surgery for malignant tumor have been studied in a similar fashion. This report is the result of such skin testing on 142 patients.

MATERIALS AND METHODS

1. Selection of patients. They were taken from the group in the Ottawa General Hos-

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Address for reprints: T. H. M. Stewart, MB, Ottawa General Hospital, 45 Bruyere Street, Ottawa, Ont.

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Table of Contents Tissue Reactions Supplement To Volume 12

1. Understanding the eBook Tissue Reactions Supplement To Volume 12
 - The Rise of Digital Reading Tissue Reactions Supplement To Volume 12
 - Advantages of eBooks Over Traditional Books
2. Identifying Tissue Reactions Supplement To Volume 12
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Tissue Reactions Supplement To Volume 12
 - User-Friendly Interface
4. Exploring eBook Recommendations from Tissue Reactions Supplement To Volume 12
 - Personalized Recommendations
 - Tissue Reactions Supplement To Volume 12 User Reviews and Ratings
 - Tissue Reactions Supplement To Volume 12 and Bestseller Lists
5. Accessing Tissue Reactions Supplement To Volume 12 Free and Paid eBooks
 - Tissue Reactions Supplement To Volume 12 Public Domain eBooks
 - Tissue Reactions Supplement To Volume 12 eBook Subscription Services
 - Tissue Reactions Supplement To Volume 12 Budget-Friendly Options

6. Navigating Tissue Reactions Supplement To Volume 12 eBook Formats
 - ePub, PDF, MOBI, and More
 - Tissue Reactions Supplement To Volume 12 Compatibility with Devices
 - Tissue Reactions Supplement To Volume 12 Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Tissue Reactions Supplement To Volume 12
 - Highlighting and Note-Taking Tissue Reactions Supplement To Volume 12
 - Interactive Elements Tissue Reactions Supplement To Volume 12
8. Staying Engaged with Tissue Reactions Supplement To Volume 12
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Tissue Reactions Supplement To Volume 12
9. Balancing eBooks and Physical Books Tissue Reactions Supplement To Volume 12
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Tissue Reactions Supplement To Volume 12
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine Tissue Reactions Supplement To Volume 12
 - Setting Reading Goals Tissue Reactions Supplement To Volume 12
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Tissue Reactions Supplement To Volume 12
 - Fact-Checking eBook Content of Tissue Reactions Supplement To Volume 12
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
 - Integration of Multimedia Elements

- Interactive and Gamified eBooks

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