

Review Articles



Review Articles

Appendix One presents review articles of spontaneous regression of cancer that have appeared in the medical literature over the last 100 years.

The chapter is divided into two sections. The first section contains 30 annotated references from medical journals, 5 reviews of books or monographs in which spontaneous regression is the primary topic, and 8 supplemental references.

The second section presents abstracts of the proceedings of the first and only world conference devoted solely to spontaneous regression held at Johns Hopkins Medical School on May 9 and 10, 1974.

The first reference in this section is a summary of the only critique of the conference which was published in *Medical World News* in 1974.

The opening address at the conference was given by Dr. Warren Cole, co-author with Tilden Everson of the monograph of 176 cases of spontaneous regression of cancer published in 1966.*

Papers were presented at the conference in four sessions. At the first session, clinical documentation, 13 papers presented case histories and clinical information on spontaneous regression of different kinds of cancer, among them malignant melanoma, lung, breast, and colorectal cancers. At session two, clinical and experimental mechanisms, four papers were presented. Three papers were presented at the third session, host defense mechanisms. At the last session, speculations, hypotheses and theoretical considerations, 6 papers were presented.

* Tilden C. Everson and Warren H. Cole, *Spontaneous Regression of Cancer* [W. B. Saunders Company 1966, 560 pages].

Review Articles

On Spontaneous Cure of Cancer

GAYLORD HR; CLOWES GHA
Surgery, Gynecology and Obstetrics 2: 1906; 633-658

Extracted Summary

As a result of studies conducted in the author's laboratory that suggest that there may be immune responses that are antagonistic to cancer, the authors present a detailed review of the data regarding the spontaneous cure of cancer in mice, both laboratory experiments and case studies.

The authors then evaluate fourteen cases of spontaneous recovery from cancer found in the medical literature. They include two epitheliomata, one scirrhus cancer of the breast, one malignant adenoma of the rectum, seven cases of choriocarcinoma, one endothelioma, and two sarcomata. Full text of several case reports is presented and critically reviewed by the authors. The authors conclude from their analysis that spontaneous recoveries do certainly occur, that cancer is not always incurable, and that further research should be initiated.

The Natural Cure of Cancer

HANDLEY WS
British Medical Journal 1: Mar 6 1909; 582-589

Extracted Summary

In the literature of carcinoma there are embedded a number of scattered observations, usually referring to single cases, which show that under certain circumstances the disappearance of cancerous masses of macroscopic size may occur spontaneously. In a few cases all clinical evidence of the disease has in this way disappeared, and a natural cure seems to have been brought about.

Occurring in what is usually regarded as a steadily progressive malady pursuing its undeviating course to a fatal event, these facts have appeared strange and anomalous to most of the authors who have recorded them. Their possible significance in respect to the cure of cancer, a significance which it would be difficult to overestimate, has been referred to by Mr. Pearce Gould, who, in a lecture on "Cases Illustrating Repair in Cancer of the Breast," pointed out that "we are justified in speaking of repair in cancer, even in its advanced stages"; a conclusion which "justifies, nay, compels, a belief in the possibility of the cure of cancer, and gives us an indication of the direction in which a cure is to be sought."

In this lecture I propose to consider, as fully as time and a difficult and elusive subject will allow, the facts which bear on the natural cure of cancer.

I hope to show that, as I have stated elsewhere, "the progress of a cancer is normally accompanied by retrogressive or curative processes"; that the recorded cases of natural repair in cancer, far from being anomalous and exceptional, merely illustrate more strikingly than usual the natural laws which govern every case of the disease. The order of Nature admits of no real anomalies, and is often best brought to light by the close study of apparent exceptions.

The Spontaneous Cure of Cancer

MCCONNELL G
International Clinics 20: 1910; 98-108

Extracted Summary

A literature review of animal studies and case histories of spontaneous regression of malignant growths is presented. In the cases that are mentioned, both those in human beings and in mice,

there has been a tumor present which for a while has undergone growth and in some instances given rise to metastases. Then for some unknown reason the carcinoma has undergone regressive changes with partial or complete disappearance.

Fluctuations in the Growth Energy of Malignant Tumors in Man with Especial Reference to Spontaneous Recession

ROHDENBURG GL

Journal of Cancer Research 3(2): 1918; 193-225

Extracted Summary

It is a generally accepted fact that transplanted animal tumors may fluctuate widely in their growth energy, the fluctuations varying from a temporary cessation of growth followed by renewed cellular activity to recession and complete disappearance of the tumor. This process also occurs in the spontaneous tumors of man. Handley has well expressed the situation as follows: "The progress of a cancer is normally accompanied by regressive or curative processes. The recorded cases of natural repair of cancer, far from being anomalous and exceptional, merely illustrate more strikingly than usual the natural laws which govern every case of the disease."

The general body reactions noted in man during tumor recession are of several different types. The greatest number of spontaneous regressions have occurred following incomplete surgical removal of the tumor; next in order of frequency during some acute febrile process; and least frequently, in connection with some profound alteration in the metabolic processes of the organism such as extreme cachexia, artificial menopause, or the puerperium.

When recession occurs after incomplete operation, search for a possible explanation becomes very confusing. The cases coming under this heading can best be explained by classifying them according to what has actually been done at the operation, and then considering the various possibilities under each subdivision.

In the first subdivision of this broad group come the cases in which neoplasms have partly or completely receded after a simple exploratory laparotomy, the only tumor removed having been a small piece for histological diagnosis. In some of the histories of this group a high temperature developed after operation and continued without remission for several days.

In the second subdivision come the cases in which complete extirpation was impossible, though a large portion of the tumor was removed. The author speculates that it is possible that, since precancerous inflammation may extend for some considerable distance outside the tumor, and that it is often impossible to distinguish this tissue from the tumor, complete extirpation of the tumor at surgery may have occurred, and that the precancerous inflammation was mistaken for tumor tissue. Another possibility is that after incomplete removal the surgery may have interfered with the blood supply of the remaining malignant tissue thus causing death of the remaining tumor from malnutrition.

In the third subdivision, the question of heat externally applied is considered. Practically all these cases are uterine carcinomata which, being surgically inoperable, were curetted and cauterized to ease the symptoms of discharge and hemorrhage.

The observation that a neoplasm may be absorbed subsequent to, or during, an acute infection, opens a most interesting field for speculation. The greater number of cases in this group have occurred after an attack of erysipelas, an observation which has led to the use of toxins of the causative organism as a therapeutic measure. However, further observation shows that recession has also occurred after smallpox, pneumonia, malaria, and acute tuberculosis. No one organism is, therefore, specific in causing regression. In the histories of those cases that are given in detail, there is a common symptom, namely, high temperature, sustained without remission for several

days. It is well to emphasize here that not every case of erysipelas, acute tuberculosis, or smallpox has a temperature as high as 104°F continuously for from three to five days. Injections of bacterial toxins, while they do give rise to violent febrile reactions, are not characterized by the continuance of fever in full violence and without remission over a period of forty-eight hours. The author reports a series of cases in which concurrent infection seemed to have some effect on the recession of the cancer.

With the idea of emphasizing the frequency of variations in the growth energy of human tumors, and at the same time of seeking further facts bearing upon these variations in proliferative activity, the cases of marked recession or spontaneous cure recorded in the literature have been summarized, additional cases added, and the entire material subjected to analysis from the standpoint of our present knowledge of experimental cancer. Including those recorded in this paper (3 cases), the author has been able to collect a total of 302 cases in which recession, either temporary or permanent, has occurred in a malignant growth. These have been divided into three main groups: Group I consists of those reports which stand a most rigid scrutiny (70 cases abstracted, 3 cases summarized); group II contains those cases in which some slight question may be raised regarding the adequate control of all possible diagnostic errors (28 cases abstracted); the cases included in group III comprise those open to more or less grave doubt as to the correct diagnosis (34 cases abstracted). Each of these main groups has been subdivided into (a) the group of complete recession, and (b) that of partial recession.

The author presents a table of his conclusions based on 192 cases from the literature with tumor type, organ of incidence and assigned cause of the absorption as the categories. Tumor types are divided into carcinoma and epithelioma, 158 cases, chorioepithelioma, 7 cases, endothelioma, 2 cases, hypernephroma, 1 case, and sarcomas, 24 cases. The causes of recession, as given by the various authors, or as determined by the history of the case, include acute general infection (also included in heat category), 27 cases, fibrosis or calcification, 7 cases, heat, whether the result of some general acute infection such as erysipelas, tuberculosis, or pneumonia, or heat applied externally, 64 cases, incomplete operation, 69 cases, nutritional causes, 15 cases, and no cause given, 36 cases. If all cases are considered collectively, without regard to the probable accuracy of the various reports, it is noted that malignant epithelial tumors are present in the largest number, with malignant connective tissue tumors second in order of frequency. In the complete series of cases, regardless of tumor type or site of incidence, there is almost an equal number of cases where the cause was attributed to heat or incomplete operation.

The author concludes that occasionally, perhaps with greater frequency than is ordinarily imagined, a malignant tumor will spontaneously recede. That such a regression does ever occur suggests that there may be found some method of bringing it about at will, even though this cannot be accomplished at the present time.

Tissue Resistance in Malignant Disease

BOYD W

Surgery, Gynecology and Obstetrics 32: 1921; 306-310

Extracted Summary

The author discusses the concept of tissue immunity to malignant growths and presents case reports to substantiate his theories of tumor growth and proliferation.

One report presented describes a case of complete disappearance of widespread metastases; another, the apparent ability of a patient to continue a normal existence while metastatic growth is occurring throughout his body. No conclusions about the reasons for this apparent resistance are given.

The Spontaneous Regression of Cancer

DECOURCY JL

Journal of Medicine (Clinical, Experimental and Theoretical) 14: May 1933; 141-146

Extracted Summary

The human organism possesses powers of defense that enable it to resist in greater or less degree the development of malignant tumors. These powers of defense are expressed under some conditions in the complete regression of microscopically demonstrable cancer. The existence of signs of regression in biopsy specimens is to be regarded as improving the prognosis in cases where complete surgical extirpation is impracticable.

The Simultaneous Disappearance of Treated and Untreated Tumors After Irradiation

DELARIO AJ

American Journal of Roentgenology 60(2): Aug 1948; 207-212

Extracted Summary

The author discusses the phenomena of disappearance of tumors, both treated and untreated, and relates biochemical and physiological information about the growth and functional aspects of cancerous tissue. In some cases of multiple tumors, treatment of one lesion is followed by the simultaneous disappearance of others. Occasionally a tumor may disappear without treatment. The human body can, through some physical or chemical change, occasionally cause the disappearance of tumors. There are reported in the literature at least 400 hopeless cases of malignant new growths in which cures resulted after such inadequate procedures as a biopsy, an incomplete operation, after some secondary infection, or some unexplained fever.

Some Observations on the Natural Behavior of Cancer in Man

DUNPHY JE

New England Journal of Medicine 242(5): Feb 2 1950; 167-172

Extracted Summary

Evidence is presented to show that cancer is not invariably a steadily progressive process. It may undergo spontaneous regression and is often subject to temporary arrests, and when it metastasizes the rate of growth of the same tumor varies widely in different locations. The theoretical and practical significance of these observations is discussed.

Duration of Life in Untreated Cancer

SHIMKIN MB

Cancer 4: Jan 1951; 1-8

Extracted Summary

Data from the literature is reviewed relative to the duration of life in untreated patients with cancer of ten sites or types (breast, rectum, cervix, oral cavity, stomach, larynx, esophagus, prostate, bladder, leukemias and lymphomas), using as the criterion the onset of clinical symptoms or signs to death.

Long-term survivals are occasionally encountered in untreated patients with cancer, particularly in cancer of the breast and in leukemia and lymphoma. Spontaneous fluctuations in growth and regressions of cancer also may rarely occur.

The data emphasizes the extreme care that must be exercised in the evaluation of the effect of therapy in individual cases with cancer. The statistical analysis of final results on sufficiently large groups consisting of adequately controlled cases is the only method by which cure or prolongation of life can be acceptably substantiated.

Experiences in Spontaneous Regression of Neoplastic Disease in Man

STEWART FW

Texas Reports on Biology and Medicine 10: 1952; 239-253

Extracted Summary

To establish a definition for cancer requires the condensation and simplification of the many attributes of cancer. Ewing, in the first edition of *Neoplastic Diseases* published in 1918, defines a tumor as "an autonomous new growth of tissue." A more recent definition in a major textbook of pathology defines a neoplasm as "an uncontrolled new growth of tissue."

The author argues that either of these definitions, implying uncontrolled or autonomous behavior of neoplasms is unacceptable for, even though biology has yet discovered the laws of tumor control, it cannot be assumed that these laws do not exist. The author suggests that rather than the terms autonomous and uncontrolled as terms applied to cancer growth, heterotrophic might be a better adjective. Heterotrophic as applied to cancer is defined as the ability acquired by the tumor cell to exist outside of its locus of origin.

With this in mind, the author reviews possible biological mechanisms of tumor control including evidence from studies of spontaneous or induced control, from the possible influence of hormones on the course of some cancers, from embryonic controls, and from reported cases of spontaneous regression.

In closing, the author emphasizes "that the cancer cell, though superficially anarchical, is not, and cannot be, unbiological...there are differences in the patterns of the host acceptance amounting to evidence for host control. Therefore, one may not be too far out of line in suggesting that great profit may ensue by redirecting some of the efforts at destruction of tumor cells or their radical removal toward an understanding of host-tumor interrelation..."

Striking evidence of biological control of the cancer process can be seen from reports of spontaneous regression of established cancers. To that end, the author reports cases of spontaneous regression from his personal experience.

Cancer as a Chronic Disease

MORTON JJ JR; MORTON JH

Annals of Surgery 137(6): May 1953; 683-703

Extracted Summary

Scattered through the literature a series of remarkable cases indicates how unpredictable cancer is as a disease. In any series of untreated cases there will be certain ones with much longer survival than the average. Some apparently show spontaneous disappearance either of the primary tumor or of secondary implants. Some seem to grow in cycles with times of rapid growth alternating with stationary periods or actual recessions. And there is the phenomenon of delayed recurrence where the tumor reappears years later in the scar of the previous operation or in its immediate neighborhood.

A series of 17 cases of cancers originating in various organs is presented by the author which show the unpredictable nature of cancer. These cases are unusual in that the patients had long periods of useful survival, although the malignant disease had not been completely eradicated. Because of the differing response of individuals to cancer, the physician should be cautious in estimating the survival of any patient suffering from carcinoma.

Unexplained Disappearance and Changes in Malignancy of Cancer Cells

COWDRY EV

Cancer Cells [Philadelphia: W B Saunders Company 1955, Chapter 19, 534-545]

Extracted Summary

Some very small primary cancers occasionally appear in large numbers in the breast, prostate and uterus. Many of these do not develop, remain latent for years or spontaneously regress completely. Alterations, usually temporary, in the size of well-developed cancers are not infrequently seen. These may be brought about by the operation of many factors affecting the volume of the malignant cells and of the stroma. Unexplained alterations in the type of malignant tumors occasionally occur for no evident reason. There are several examples on record of the disappearance of neuroblastomas in children. In some of them this is correlated with progressive differentiation of the malignant cells for reasons unknown. A few verified cases of the complete regression of cancers have been described which cannot be attributed to the treatment given. Evidently some kinds of malignant cells are in extremely rare cases controlled by physiological mechanisms.

Spontaneous Regression of Cancer: Preliminary Report

EVERSON TC; COLE WH

Annals of Surgery 144(3): Sep 1956; 366-382

Extracted Summary

A study of the incidence and nature of spontaneous regression of cancer has been initiated. Of over 600 cases published or obtained by personal communication, to date we have considered only 47 cases to have adequate documentation to be accepted as possible examples of spontaneous regression. It is barely possible that if we had more clinical data a large number of cases studied but not included would meet our prerequisites. In 11 of the 47 collected cases regression was complete and verified by microscopic examination of the tissues after regression. One of the main purposes of this study is to see if we can identify a significant factor or factors responsible for the regression. Several factors have been mentioned by various authors (particularly Rohdenburg), and noted by us in case histories kindly submitted by our friends. Important among these are endocrine factors, unusual sensitivity to inadequate irradiation or other therapy, fever and/or infection, allergic reactions, interference with nutrition of the tumor, and removal of the carcinogenic agent.

The Problem of Spontaneous Regressions of Malignant Tumors

SIRTORI C; PIZZETTI R

Giornale Italiano di Chemioterapia 3: 1956; 176-199

Extracted Summary

A critical review is made of the cases of spontaneous regression of malignant tumors referred in the literature. Three personal cases are described, concerning: a) a 2-year-old baby with large laterocervical metastases of mediastinal neuroblastoma, spontaneously regressed for five years; b) a baby of few months, with laterocervical metastases of neuroblastoma (the site of the primary tumor not discovered) spontaneously regressed for 4 years; c) a 26-year-old woman, hysterectomized for chorioepithelioma, with pulmonary, vaginal and subcutaneous metastases, regressed for 7 years.

Spontaneous regressions may be related to ischemic necrosis, to cellular differentiation or to a defensive action of the stroma. A comparison is made between the cytohistological features of the spontaneous and therapeutical regressions: the former show cytolysis, differentiation and connectional reactions; in the latter the mitotic alterations are more typical.

Spontaneous healing may be biologically related to endocrine or neurohormonal factors, to general or local immunity phenomena, to sudden variations of the biological balance of the soma, and to other yet-unknown stimulations.

False regressions concern the cases of erroneous diagnosis, some tumors of biologically doubtful malignancy (Smith's multiple cutaneous epithelioma, papillary tumors of the ovary), and finally tumors that easily undergo noticeable clinical regressions (hypernephroma).

A regression may be simulated also in the cases in which metastases or relapses appear after a very long period of latency. Two interesting personal observations are referred, concerning: a) a lymphogranuloma which remained clinically completely silent during 6 years in a young woman, allowing marriage and a normal delivery; b) an ovarian adenocarcinoma, which gave clinical evidence of pulmonary metastases (operated) 26 years after the ovariectomy.

Further studies of the spontaneous regressions of cancer will be useful to understand the great differences of malignancy existing in the same type of tumor, the intrinsic defense powers of some organisms, the biochemical and morphological features of such a defense, and the exact mechanism of action of some anticancer substances. (Noetic Sciences translation)

Cures, Regressions and Spontaneous Remissions of Cancer

FAUVET J; CAMPAGNE J; CHAVY A; PIET G
La Revue du Praticien 10: 1960; 2349-2384

Extracted Summary

Even if it remains mysterious, the spontaneous healing of cancer, after having been the subject of many controversies, is now accepted as an indisputable fact. With the addition of two cases personally seen by the authors, the authors have attempted to update this issue by assembling the maximum number of published instances with sufficient documentation to confirm the diagnosis of cancer and its recovery. Observations tend to multiply since the authors have found 64 cases since 1950.

What is the percentage of spontaneous recoveries? Following calculations which might be subject to criticism, the authors quote the following figures: 1 in 80,000 cancers (Boyers); 1 in 100,000 cancers (Bashford). These numbers seem negligible. Let us say, simply, that the chance of a cancer patient recovering is 8 to 10 times greater than that of winning at the National Lottery! The number of cases, though negligible according to the estimates of Bashford or Boyers, are very important in that they prove that cancer is not an irreversible process.

(Noetic Sciences translation)

Spontaneous Regression of Tumors

SMITHERS DW
Clinical Radiology 13: 1962; 132-137

Extracted Summary

"Spontaneous" tumour regression is a well-authenticated natural phenomenon. Its study may lead us to a better understanding of the natural history of neoplastic disease which so commonly progresses but rarely regresses. Some reasons why regression may occur in the eight groups of tumours (embryonal tumours in children, carcinoma of the female breast, chorionepithelioma, adenocarcinoma of the kidney, malignant melanoma, soft tissue sarcoma, carcinoma of the bladder, carcinoma of the skin) in which it has been most frequently observed are put forward.

Dr. Smithers suggests that "it is possible that the adoption of too strict criteria for the acceptance of spontaneous regression as a phenomenon to consider may have delayed our progress in understanding the wider issue of balance in tissue growth which may play such an important part in the neoplastic process."

Spontaneous Regression of Cancer

BRUNSCHWIG A

Surgery 53(4): Apr 1963; 423-431

Extracted Summary

Three documented cases of spontaneous regression of malignant neoplastic disease are presented. In two instances postregression biopsies to confirm regression were possible. In one case of cancer of the bladder, hepatic metastases became apparent 5 years after the original tumor was removed, regressed spontaneously, and a year later another cancer of the bladder developed. This is evidence that factors of host resistance to cancer and etiologic factors are not necessarily closely related. Furthermore, in this patient, the presence of some factors that lead to regression of hepatic metastases from bladder cancer did not impede the inception of a colon cancer that metastasized locally.

Certain criteria for the reporting and acceptance of instances of spontaneous regression of cancer in man are presented and discussed. These criteria include: 1) The presence of macroscopic and microscopic evidence of a malignant neoplasm and/or its spread from site of origin; 2) A period of observation during which macroscopic evidence of malignant neoplasm and/or its spread have disappeared and, if possible, biopsy of the sites of primary or secondary spread have shown no evidence of persistent malignant neoplasm; 3) a record of all treatment during the period of observed regression; and 4) roentgenographic evidence alone of pulmonary spread is acceptable only with major reservations and should be accompanied by reports of repeated cytologic study of sputum and/or bronchial aspirations.

The presence of severe infection is also to be recorded. While the possible effect of this on the course of malignant neoplastic disease is still a moot question, with general opinion that it is of little or no importance, its influence cannot be categorically disregarded. There is abundant laboratory evidence that it may in some instances impair, at least temporarily, the progress of neoplastic disease. The author further suggests that a registry of living patients whose histories are acceptable as examples of spontaneous regression be established.

Spontaneous Regression of Cancer

EVERSON TC

Annals of the New York Academy of Sciences 114(2): April 2 1964; 721-735

Extracted Summary

An evaluation of more than 1000 cases of spontaneous regression of cancer published in the world medical literature or obtained by personal communication has been made. To date only 130 cases have been considered by us to have adequate documentation including histologic confirmation of the diagnosis of malignancy, to accept as probable examples of spontaneous regression of cancer. The 130 cases of probable spontaneous regression of cancer are tabulated according to type or location of tumors.

Clinical evidence of spontaneous regression of cancer may be divided into several categories: (1) regression of primary tumor; (2) regression of metastatic tumor (histological confirmation of the malignancy of the metastatic tumor); (3) regression of metastatic tumor (no histologic confirmation of the malignancy of the metastatic tumor); (4) regression of presumptive metastases as diagnosed by roentgenograms.

Spontaneous regression of cancer was most commonly noted in neuroblastoma, hyperneph-

roma, choriocarcinoma, and malignant melanoma. Possible factors which may be responsible for spontaneous regression of cancer include endocrine influences, unusual sensitivity to usually inadequate therapy, fever and/or infection, allergic or immune reactions, interference with nutrition of the tumor, and removal of the carcinogenic agent.

Cancer Cures and Spontaneous Regressions

FAUVET J; ROUJEAU J; PIET G
La Revue du Praticien 14(17): 1964; 2177-2180

Extracted Summary

This article is a continuation of a previous article by the same authors (*Revue Praticien* 10: 1960; 2349). Additional cases of spontaneous recoveries from cancer are reported. After reviewing 26 cases of spontaneous regression of cancer published in the literature from 1958 to 1963, the authors describe two personal cases. In one a 19-year-old woman was discharged with ascites and in terminal condition approximately 1.5 months after bilateral oophorectomy for an ovarian myxosarcoma, but improved rapidly and was in good condition 8 years later. In a second case, a 7-year-old boy with Hodgkin's disease had a short episode of icterus with fever which was followed by the complete disappearance of peripheral and mediastinal adenopathies (otherwise resistant to prednisone) and the remission lasted 3 years. (Noetic Sciences translation)

Spontaneous Regression of Cancer

A Study and Abstract of Reports in the World Medical Literature and of Personal Communications Concerning Spontaneous Regression of Malignant Disease

EVERSON TC; COLE WH
W. B. Saunders Company, Philadelphia, 1966; 560 pages

Extracted Summary

From a study of the world medical literature since 1900 and from cases obtained by personal communication, 176 cases of cancer have been considered to have adequate documentation (including histologic confirmation of the malignancy) to be accepted as possible examples of spontaneous regression of cancer.

To the four categories of clinical evidence of spontaneous regression of cancer previously enumerated by Everson and Cole (T. C. Everson, 1964) the authors add two additional categories: (5) prolonged arrest of cancer and (6) delayed metastases or recurrence of cancer. The authors comment that although these last two categories do not represent evidence of spontaneous regression in its strictest definition, they indicate possible biologic control which may be closely related to spontaneous regression.

In this collected series, spontaneous regression of cancer was noted most frequently in adenocarcinoma of the kidney (31 cases), neuroblastoma (29 cases), malignant melanoma (19 cases), choriocarcinoma (19 cases), cancer of the bladder (13 cases), soft-tissue sarcoma (11 cases), and sarcoma of the bone (8 cases). Spontaneous regression of cancer was found less frequently in cancer of colon and rectum (7 cases), cancer of the ovary (7 cases), cancer of the testis (7 cases), cancer of the breast (6 cases), metastatic cancer with primary unknown (4 cases), cancer of the uterus (4 cases), cancer of the stomach (4 cases), cancer of the liver (2 cases), and one case each of cancer of the larynx, lung, pancreas, thyroid, and tongue.

Spontaneous regression of cancer is defined by the authors as the partial or complete disappearance of malignant tumor in the absence of all treatment or in the presence of therapy which is considered inadequate to exert a significant influence on neoplastic disease. It is not implied that spontaneous regression need progress to complete disappearance of tumors, nor that spontaneous regression is synonymous with cure. Possible mechanisms of spontaneous regression and case reports are presented.

The Spontaneous Regression of Cancer

BOYD W

Charles C. Thomas Publisher, Springfield, Illinois, 1966; 99 pages

Extracted Summary

In the preface the author states that "Down through the centuries we read accounts of miraculous cures of this deadliest of diseases, but we reject them because of insufficient proof, for miracles no longer occupy the enviable position in happy therapeutic results that they used to do. It was only when biopsy with histological confirmation of the clinical diagnosis became general that 'miraculous cures' could be accepted, and even then there was always the possibility that the pathologist might have been in error."

The author reviews case reports of spontaneous regression from the medical literature and from personal communications with a view toward the concept of tissue resistance to cancerous invasion. A historical overview of cancer regression and a discussion of the theoretical aspects of regression are also presented.

Spontaneous Regression of Cancer and Long-Term Recrudescences

WEAVER JO

Journal of the Medical Association of Georgia 55(8): Aug 1966; 351; 354-356

Extracted Summary

The author discusses the phenomenon of spontaneous regression of cancer and reviews the pertinent literature on the subject. He urges that patients who present spontaneous regression be intensely studied in order to elucidate possible mechanisms underlying this phenomenon.

Spontaneous Regression of Cancer

EVERSON TC

Progress in Clinical Cancer 3: 1967; 79-95

Extracted Summary

In an evaluation of cases of spontaneous regression of cancer published in the world medical literature since 1900 or obtained by personal communication to date, we have considered 176 cases to have adequate documentation, including histologic confirmation of the malignancy, for acceptance as probable examples of spontaneous regression of cancer.

The 176 cases of probable spontaneous regression of cancer are tabulated according to type or location of tumors. Spontaneous regression of cancer was most commonly noted in hypernephroma, neuroblastoma, choriocarcinoma and malignant melanoma. Possible factors which may be responsible for spontaneous regression of cancer include endocrine influences, unusual sensitivity to usually inadequate therapy, complete surgical removal of cancer, fever and/or infection, allergic or immune reactions, interference with nutrition of the cancer, removal of the carcinogenic agent, and incorrect histologic diagnosis of malignancy.

Evidence of spontaneous regression of cancer may be significant from several standpoints. The existence of spontaneous regression of cancer, in at least some cases, supports the concept of biologic control of cancer and reinforces the hope that a more satisfactory method of treating cancer, other than surgery and/or irradiation, may be found in future years. The occurrence of spontaneous regression of cancer demonstrates the need for caution in the assessment of the value of chemotherapeutic and unorthodox therapeutic measures in isolated 'cures' of cancer. The possibility of spontaneous regression must be considered in the evaluation of the prognosis of certain cancers. The remote possibility of spontaneous regression may be of some psychotherapeutic value in the patient with cancer which is not amenable to surgical and/or radiation treatment.

Spontaneous Regression of Cancer

SHAPIRO SL

Eye Ear Nose Throat Monthly 46(10): Oct 1967; 1306-1310

Extracted Summary

The author begins his investigation of spontaneous regression of cancer with the story of St. Peregrinus (See page 46.), and then presents brief synopses of cases that he has personally observed as well as those reported by others. He presents the case of Sister Gertrude who, it is reported, was cured of pancreatic cancer after the sisters of her order interceded with Mother Seton, deceased founder of the order. In a series of novenas, the sisters asked Mother Seton to spare the life of Sister Gertrude and she began to improve in health. She lived 7 1/2 years and died of a pulmonary embolism. At autopsy, no evidence of pancreatic cancer was found.

The author reviews Drs. Everson and Cole's, Spontaneous Regression of Cancer. Possible factors that may influence spontaneous regression are discussed. Some of the tantalizing reports regarding the successful use of immunology in cancer are also presented.

Life Expectancy and Unusual Course in Untreated Malignant Tumors

KAUFER C; WULFING D; FRIEDRICH E

Burns Beitrage für Klinischen Chirurgie 217: 1969; 141-154

Extracted Summary

Spontaneous regression or spontaneous healing of carcinomatous diseases are described once in a while, but these single observations do not allow any conclusions as to the frequency of such occurrences. Among 4,900 patients with carcinoma seen at the Surgical Department of the University of Bonn, there were 1214 cases which did not receive causal treatment.

Life expectancy was determined of the various carcinoma, and the cases which showed an unusually long survival time were followed. Six patients survived two or more years after confirmation of the diagnosis; they did not receive any treatment which, to our knowledge, could be considered sufficient for the cure of carcinoma. Only 3 cases remain after a critical evaluation.

Thus, the frequency of unusually long survival times (0.06%) is in the range of the figures reported by other authors. In relation to the total number of patients this percentage is so low that spontaneous healing in the course of a carcinomatous disease practically does not occur.

Spontaneous Regression of Malignant Tumors

GARZIA L

Fracastoro 64(5): Sep-Oct 1971; 370-384

Extracted Summary

A study of the literature about spontaneous regression of cancer has been done and significant cases are summarized. The views of the more important authors, who have treated the incidence and nature of this phenomenon are reported. Different hypotheses on the possible etiology of spontaneous regression are pointed out.

Spontaneous Regression of Malignant Tumors

BRINCKER H; ANDERSEN AP

Ugeskrift for Læger 134(12): Mar 20 1972; 597-601

Extracted Summary

Three cases of spontaneous regression of malignant tumours are presented. These were represented by two malignant melanomata and one reticulosarcoma. In one of the cases, some evidence is available that immunological factors may have played a role in the spontaneous regression. It is emphasized that it is always difficult to establish the prognosis in individual cases, even in so-called "hopeless" cases of cancer. Recognition of the possibility of spontaneous regression should be borne in mind when considering the prognosis in malignant disease.

Healing and Recurrence of Cancer from a Point of View of Surgery

JINNAI D; MORI T

Japanese Journal of Cancer Clinics (Gan No Rinsho) 19(4): 1973; 275-284

Extracted Summary

The cases of spontaneous regression, delayed recurrence and prolonged arrest of cancer in Japan were collected. The "spontaneous regression of cancer," defined as the disappearance of a histologically diagnosed cancer without any effective treatment, was observed in seven cases, including five cases of gastric cancer, one case each of cancer of the pancreas and of the uterus. In all but one case in which the patient refused operation, cancer was so advanced that the removal of the tumor was impossible. In order to reveal the biological factors which may influence tumor growth, 109 cases of gastric cancer with extremely unusual prognosis were studied, with regard to histological differentiation, mucin production, carcinoembryonic antigen, stromal reaction, serum globulin level, lymphocyte count, T-cell count, skin reaction, etc.

Spontaneous Regression of Cancer: The Metabolic Triumph of the Host?

COLE WH

Annals of the New York Academy of Sciences 230: 1974; 111-141

Extracted Summary

A summary of the 176 cases collected by Everson and Cole and reported in their monograph (Spontaneous Regression of Cancer, 1966) is presented. In this monograph, cases reported in the literature from 1960 to 1966 were included, in addition to cases referred to the authors by friends during this period. The leukemias, lymphomas, and squamous cell epitheliomas were excluded because many examples of these lesions varied greatly in their rate of growth. The types or locations and the number of cases of each type or location were as follows: Hypernephroma-31 cases; Neuroblastoma-29 cases; Malignant melanoma-19 cases; Choriocarcinoma-19 cases; Bladder-13 cases; Soft-tissue sarcoma-11 cases; Colon and rectum-7 cases; Ovary-7 cases; Testis-7 cases; Breast-6 cases; Metastatic cancer, primary unknown-4 cases; Uterus-4 cases; Stomach-4 cases; Liver-2 cases; Larynx-1 case; Lung-1 case; Pancreas-1 case; Thyroid-1 case; Tongue-1 case.

The monograph also discusses factors that may be the causes of these regressions. Among those factors discussed are: (1) Immunological factors; (2) Hormonal factors; (3) Chemotherapy; (4) Elimination of a carcinogen; (5) Miscellaneous factors.

A third subject covered in this monograph is possible factors that affect the growth and spread of cancer. The factors discussed include: (1) Immunologic factors; (2) Cellular elements

involved in the immune process; (3) The role of immunoglobulins; (4) Blocking and unblocking agents; (5) The significance of immunosuppression; (6) Hormones; (7) Enzymes; (8) Elimination of carcinogen; (9) The possible role of interferons; (10) Theoretical factors possibly responsible for spontaneous regression; (11) Alteration of the tumor-host relationship; (12) Elimination of the carcinogen; (13) Effect of excision of primary tumor on metastases; (14) Viral interference or viral antagonism; (15) Hormones; (16) Miscellaneous factors.

Restraint of Growth and Spontaneous Regression of Cancer

STOLL BA

*Mind and Cancer Prognosis, BA Stoll (ed.), Chichester, England,
John Wiley & Sons Ltd., 1979; Chapter 3, 19-29*

Extracted Summary

Spontaneous regression of human cancer is well authenticated and when cases of temporary and partial shrinkage of cancer are included, the incidence is probably many hundred times its reported frequency. Evidence is provided that the phenomenon is related to that of dormant cancer which involves a much smaller tumour burden and is much more common. To quote Weiss (1976) in this respect, "The dissemination of tumour cells and their long persistence in the tissues of surgically cured patients are perhaps more the rule than the exception; also the presence (especially in older individuals) of islands of neoplastic tissue that remain sufficiently insular to permit what we consider a normal life span and normal health." The phenomena of spontaneous regression and dormant cancer may arise from stimulation of immunological or endocrine defence factors in the host. These in their turn may be triggered either by a physical stimulus or even by a psychophysiological stimulus. On a similar basis, sudden activation of cancer activity could be explained by changes in defence factors, and here again, psychophysiological stimuli might play a part.

Spontaneous Regression in Cancer

FRANKLIN CIV

*Prolonged Arrest of Cancer, BA Stoll (ed.), John Wiley & Sons Ltd :
1982; Chapter 5, 103-116*

Extracted Summary

The author reviews cases of spontaneous regression reported in the medical literature using the definition of spontaneous regression of Everson and Cole (1966). The author remarks that "In the review of 176 cases in the literature by Everson and Cole (1966), 60% of the regressions lasted more than two years, with many over ten years. If the same criteria were applied to regression following hormonal or cytotoxic chemotherapy, response rates may not be much greater than the reported incidence of spontaneous regression!"

The review is organized under the following headings: Regression in adult cancer (kidney cancer, melanoma, testicular cancer, choriocarcinoma, bladder cancer, bone tumours, other tumors); regression in childhood cancer (neuroblastoma, Wilm's tumor, retinoblastoma); leukemia and lymphoma; in situ cancer of the cervix uteri; possible mechanisms in regression (infections, endocrine factors, psychological factors); and incomplete regression.

The author comments that perhaps the criteria applied to spontaneous regression is too stringent and, therefore, advocates the study of those cases in which there is an unexpected fluctuation or arrest of growth, whether temporary or partial.

Spontaneous Regression of Tumours. Cancer! Disease Without Hope?

THEISS E

Zeitschrift für Allgemeinmedizin 58(23): 1982; 1218-1224

Extracted Summary

Various articles in the medical literature state that some spontaneous regressions, the disappearance of tumours (primary or even metastatic), have been firmly established. This general survey is based on the publication by Cole and Everson which reviews 176 cases of spontaneous regression of cancer, and on some other more recent articles. So this survey covers more than 200 cases. Many factors have been put forward to explain these regressions. A particular place must be given to immunity mechanisms.

This report is largely intended for medical practitioners, to help them, in conjunction with their own observations, to elucidate in time the factors still unknown which play a major role in the mechanism of regression. It should also convince doctors that they must never abandon hope for a cure, even in the most desperate cases.

Unexpected Recoveries: Spontaneous Remission and Immune Functioning

KENT J; COATES TJ; PELLETIER KR; O'REGAN B

Advances 6(2): Summer 1989; 66-72

Extracted Summary

The authors speculate that at least some of the reported instances of spontaneous remission may be a result of the interplay of physical and psychological factors. The miracle cures of Lourdes are one collection of medically documented cases in which spiritual or religious faith is considered the cause of the remissions. Another area of investigation, psychoneuroimmunology (PNI), is based on the premise that multiple factors, psychological, emotional, genetic, endocrine, nervous and immune, affect immune functioning and hence resistance to disease. Research on the effect of positive emotions on health and immune functioning may lead to a further understanding of spontaneous remission.

The authors conclude that spontaneous remission appears to be a natural phenomenon whose causes remain unknown. This paper suggests that beliefs, coping style, and emotions may play a role in spontaneous remission and that further research into this area should be initiated.

The Spontaneous Regression of Cancer

A Review of Cases from 1900 to 1987

CHALLIS GB; STAM HJ

Acta Oncologica 29(5): 1990; 545-550

Extracted Summary

The literature on the spontaneous regression of cancer is reviewed from 1966 to 1987 to update reviews by Everson & Cole and by Boyd. These authors reviewed all cases of spontaneous regression from 1900 to 1965. We then report the entire series from 1900 to 1987. We also attempt to determine what attributions for spontaneous regressions have been reported. Although almost half of the authors failed to speculate or specify a possible cause for the spontaneous regression, the remainder postulated responsible factors such as immunological or endocrine, surgical, necrosis, infection, or operative trauma. The only unorthodox treatment to appear in the literature

was the psychological. We conclude that the literature on the spontaneous regression of cancer is still unable to provide unambiguous accounts of the mechanisms operating to affect these regressions.

Spontaneous Regression of Cancer

PAPAC RJ

Connecticut Medicine 54(4): Apr 1990; 179-182

Extracted Summary

The medical literature includes reports of spontaneous regression of cancer with reasonable documentation since the early 19th century, although many would not meet criteria which have evolved for spontaneous regression. Osler reported two cases of carcinoma of the breast with disappearance of metastases in 1901. Rohdenburg collected 300 patients reported by 1918. Boyd, Everson, and Cole later reviewed published cases, and concluded that many were poorly documented. In Everson and Cole's review of cases from 1900 to 1964, only 176 fulfilled the following criteria: documented histologic regression of biopsy-proven metastases; radiologic regression of presumptive neoplastic disease; and regression of metastatic tumor following therapy generally deemed ineffective. In this review, cases of leukemia, lymphoma, and squamous cell carcinoma were excluded. These, however, were included in a subsequent conference monograph from the National Cancer Institute.

Over half of the reported cases of spontaneous regression of cancer reviewed by Everson and Cole developed in four tumor types—renal cell carcinoma, neuroblastoma, malignant melanoma, and choriocarcinoma. The circumstances and undoubtedly the mechanisms of regression differ. Clinical features of these tumor types are presented. We have observed eight patients who have experienced spontaneous regression of cancer and two patients in whom the possibility seems likely, although the role of therapy cannot be entirely excluded.

We have observed two additional cases considered to be spontaneous regressions, although we have not been directly involved in the management of these cases. One patient presented at a tumor conference had gastric carcinoma with hepatic metastases found at surgery. Without any additional therapy, the liver metastases resolved, documented by reexploration a year later. The second patient, seen only in consultation, had chronic lymphocytic leukemia with underwent remission for a four-year period following a bout of pneumococcal pneumonia.

SUPPLEMENTAL REFERENCES REVIEW ARTICLES

Disappearing Tumors

WARTHIN AS; SPITZLEY WA

Medical News 79: Sept 21 1901; 443-447

The Arrest of Cancerous Growths

CLARKE WB

Clinical Journal 29: 1907; 264-267

Zur Lehre von der Spontanen Heilung der Myome und Carcinome

THEILHABER A; EDELBERG H

Zeitschrift für Krebsforschung und Klinische Onkologie 13: 1913; 461-499

Spontaneous Regression of Cancer [letter]

NELSON DH

British Medical Journal 2: 1960; 670

Spontaneous Regression and Inhibition of the Growth of Histologically Proven Malignant Tumors Without Any or Adequate Causal Therapy

DERRA E; VON ELMENDORFF HF

Langenbecks Archiv für Chirurgie 311(2): Aug 9 1965; 89-99

Fluctuations in the Growth Rate of Cancer

DEVITT JE

Mind and Cancer Prognosis, BA Stoll(ed), John Wiley & Sons Ltd : 1979; chapter 2, 9-17

When Cancer Vanishes
HOCHMAN G
Science Digest: Summer 1980; 94-96, 110

Spontaneous Regression and Cytodifferentiation of
Cancer in Early Life: The Oncogenic Grace Period
BOLANDE RP
*Survey and Synthetics of Pathology Research 4(4): 1985;
296-311*

Conference on Spontaneous Regression

*Held at the Johns Hopkins Medical Institutions, Baltimore, Maryland,
May 9 and 10, 1974*

REVIEW OF THE CONFERENCE

Spontaneous Cancer Regression—First World Conference Asks: How Does It Work?

Medical World News : June 7 1974; 13-15

Extracted Summary

Rare but apparently indisputable cases of spontaneous regression of cancer were the subject of the first conference on spontaneous regression. The purpose of the conference held at Johns Hopkins was to determine whether spontaneous regression occurs at all; if so, what is its mechanism of action, and does that mechanism suggest any new therapeutic approach?

The most substantial body of information presented at the meeting was a survey of 176 cases culled from published and unpublished sources by surgeons Warren H. Cole and Tilden C. Everson of the University of Illinois. They could assemble this series only by defining regression very loosely: "a partial or complete disappearance of a tumor in the absence of treatment which ordinarily is considered capable of producing a regression." Dr. Cole mentioned seven possible causes: immunological response, elimination of a carcinogen, body response to operative trauma, hormonal factors, the effects of irradiation, of infection or fever, and of noncancer drugs. He also suggested that some cases might be explained by interference of the blood supply to the tumor or severe malnutrition in the patient—either could starve the tumor. Immunological response was the explanation clearly favored by attendees.

One attendee, Dr. Rene Mastrovito of the neuropsychiatric service at Memorial Sloan-Kettering Cancer Center, alluded to historical references to cures following religious conversion or prayer. Although a number of theories were proposed regarding the mechanism of spontaneous regression, no decisive conclusions could be extrapolated from the evidence reported.

Opening Address: Spontaneous Regression of Cancer and the Importance of Finding Its Cause

COLE WH

National Cancer Institute Monographs 44: 1976; 5-9

Extracted Summary

A few years ago Everson and I assembled all the examples of spontaneous regression in the world medical literature from 1900 to 1960 and added numerous cases from experiences of our friends. Our figure was 176. We excluded squamous cell carcinoma of the skin, leukemia, Hodgkin's disease, and a large number of cases that did not fulfill the prerequisites of confirmed diagnosis and no significant treatment. The four most common examples of regression were carcinoma of the kidney (31), neuroblastoma (29), malignant melanoma (19), and choriocarcinoma (19); these constituted more than half the group. We did not require that the regression be permanent because it appeared that the explanation of temporary regression would be just as important as the cause of permanent regression. There was no proven specific cause of the regression, but the following mechanisms had a possible relationship: immunologic action, elimination of carcinogens, trauma (altering the antigen-antibody relationship), hormones, irradiation, infection and/or fever, and drugs or chemicals. The most applicable of these is elimination of the carcinogen. Immunologic reactions seem to offer the best explanation, and the potential of humoral immunity is more impressive than that of cellular immunity.

I. CLINICAL DOCUMENTATION OF SPONTANEOUS REGRESSION OF CANCER

A Pathologist Looks at Spontaneous Regression of Cancer

FIRMINGER HI

National Cancer Institute Monographs 44: 1976; 15-18

Extracted Summary

We are all subjected to varying amounts of mutating, potential cancer-inducing events, which are cumulative. In most instances, the accumulations are repaired or are lethal. If a viable clone survives, it must proliferate in order to become manifest and eventually to overpower the host's normal regulatory and defense mechanisms. The proliferation may be incited and sustained by cocarcinogens, hormone excess, chronic infections such as schistosomiasis, and, in the case of lymphoid cells, by immune incompetence.

On the other side are the protective repairing enzymes, which serve to cut out the damaged segments of DNA and repair them as fast as they can. The normal homeostatic mechanisms tend to keep cell proliferation and activity within the beneficial bounds of need. The controlling forces that cause cells to stop reproducing themselves and differentiate to perform a useful function also tend to slow or even stop the useless proliferation if all the cells can undergo maturation to a post-mitotic state. There are also the protective mechanisms of immunity: Sensitized B lymphocytes tag the antigenic sites of tumor cells and activate the T-cell macrophages to destroy the tagged cells.

Spontaneous Regression of Genitourinary Cancers

SCHIRMER HKA

National Cancer Institute Monographs 44: 1976; 19

Extracted Summary

In genitourinary cancers, spontaneous regression has occurred in few instances and for reasons unknown. Although it cannot be denied that nephrectomy may have promoted regression of distant metastases in some cases, this is an unproved relationship and, in any event, an extremely rare sequence.

Spontaneous Regression of Colon Carcinoma

SERPICK AA

National Cancer Institute Monographs 44: 1976; 21

Extracted Summary

Apparent spontaneous regression of advanced colon carcinoma has been reported in 7 patients. (Everson and Cole, 1966) This is a very rare event, and the circumstances accounting for this are elusive. All 7 patients with spontaneous regression were alive at a median period of 9 years after diagnosis. It is attractive to postulate that most patients were cured.

Spontaneous Regression of Breast Cancer

LEWISON EF

National Cancer Institute Monographs 44: 1976; 23-26

Extracted Summary

The dramatic but rare regression of a verified case of breast cancer in the absence of adequate, accepted, or conventional treatment has been observed and documented by clinicians over the course of many years. In my practice limited to diseases of the breast over the past 25 years, I have observed 12 patients with a unique and unusual clinical course valid enough to be regarded as spontaneous regression of breast cancer. These 12 patients, with clinically confirmed breast cancer, had temporary arrest or partial remission of their disease in the absence of complete or adequate treatment. In most of these cases, spontaneous regression could not be equated ultimately with permanent cure. Three of these case histories are summarized, and patient characteristics of pertinent clinical interest in the remaining case histories are presented and discussed. Despite widespread doubt and skepticism, there is ample clinical evidence to confirm the fact that spontaneous regression of breast cancer is a rare phenomenon but is real and does occur.

Spontaneous Regression in Gynecologic Neoplasia

JULIAN CG

National Cancer Institute Monographs 44: 1976; 27-30

Extracted Summary

As I have tried to tabulate and evaluate the cases of spontaneous regression of gynecologic malignancy, several facts stand out: (1) They were infrequent. (2) The tumors most commonly undergoing spontaneous regression were the germinal epithelial tumors of the ovary; there was no case of spontaneous regression of any other variety of ovarian neoplasm. (3) There was not one legitimate case of spontaneous regression of an invasive epidermoid carcinoma of the vulva, vagina, or uterus.

Spontaneous Regression of Bronchogenic Carcinoma

BAKER RR

National Cancer Institute Monographs 44: 1976; 31-33

Extracted Summary

Two cases of spontaneous regression of bronchogenic carcinoma were discovered in the literature, and the pertinent findings are described. Six equivocal cases of spontaneous regression are also presented. The reasons for the scarcity of spontaneous regression of bronchogenic carcinoma are discussed; no apparent reasons for spontaneous regression in these two cases could be determined.

Spontaneous Regression of Hematologic Cancers

WIERNIK PH

National Cancer Institute Monographs 44: 1976; 35-38

Extracted Summary

Spontaneous regression of hematologic cancer is extremely rare. Data gleaned from the literature and from previously unreported cases allow certain interesting general conclusions. Spontaneous remission of acute leukemia is associated with bacterial infection and is of short duration, weeks to months. Spontaneous regression of lymphoma or plasma cell dyscrasia is often of substantial duration, months or years, and frequently is associated with viral infections. Spontaneous regression of chronic lymphocytic leukemia is also of significant duration and has been associated with the occurrence of a new primary carcinoma in one-third of the cases.

Spontaneous Regression of Cancer Evaluated by Computerized Data

STEPHENSON HE

National Cancer Institute Monographs 44: 1976; 43-47

Extracted Summary

Where immunologic integrity wanes, clinicians observe a greatly increased incidence of neoplasia. Factors in this phenomenon are reviewed. With complete and detailed recorded data on patients who have exhibited spontaneous regression of cancer, a systematic data-reduction approach becomes a practical reality, without the inherent handicaps of missing details in patient histories or anecdotal and often conjectural observations. Presented here is the plea for detailed recording of complete histories of all carcinoma patients who exhibit the phenomenon of spontaneous regression. Physicians of several decades ago generally considered as unrelated much data deemed important to us today.

Spontaneous Regression of Neuroblastoma

EVANS AE; GERSON J; SCHNAUFER L

National Cancer Institute Monographs 44: 1976; 49-54

Extracted Summary

Cases of spontaneous regression of neuroblastoma continue to occur in the present multimodal therapy era at institutions where physicians are prepared to withhold treatment on certain patients with residual primary or metastatic disease. From a survey of the 22 member institutions of Children's Cancer Study Group, seven hospitals submitted data on 24 neuroblastoma patients

whose disease underwent regression after minimal, unusual, or no treatment. An analysis of these patients and of 33 patients from two large series in the literature shows that the majority of patients are infants with Stage II or Stage IVS disease. The spontaneous regression usually consists of complete disappearance of the disease, but in some neuroblastomas, maturation to ganglioneuroma takes place. The various factors that may influence regression are discussed.

Spontaneous Regression of Sarcoma

BLUMING AZ

National Cancer Institute Monographs 44: 1976; 55-57

Extracted Summary

Three pathologic processes generally regarded as non-neoplastic conditions are presented and discussed as examples of poorly controlled proliferations of lymphoid tissue. A study of these three disorders (infectious mononucleosis, hyperthyroidism, and Dilantin-induced lymphadenopathy) provides clues to an understanding of the pathogenesis and occasional spontaneous regression of the malignant lymphomas.

Spontaneous Regression in Choriocarcinoma and Related Gestational Trophoblastic Neoplasms

HERTZ R

National Cancer Institute Monographs 44: 1976; 59-60

Extracted Summary

Gestational trophoblastic neoplasia represents a biologic spectrum of tumors progressing from the hydatid mole, to invasive mole, and to choriocarcinoma. This progression is reflected in increasing degrees of aneuploidy in the respective lesions. Just as there is a natural tendency for the rejection of the trophoblast of a normal pregnancy culminating either in parturition or in spontaneous abortion, rejection of tumors of trophoblast occurs at any point in the progression of the disease spectrum. The unusual effectiveness of chemotherapy in trophoblastic disease may be related to this natural tendency to rejection. This tendency, in turn, is thought to derive from the genetic disparity between the maternal host and the tumor tissue of fetal origin, since the fetus possesses both maternal and fetal antigens.

Spontaneous Remission in Burkitt's Lymphoma

ZIEGLER JL

National Cancer Institute Monographs 44: 1976; 61-65

Extracted Summary

Three cases of spontaneous regression of Burkitt's lymphoma are reviewed and additional clinical and laboratory observations relevant to the role of host defences are summarized. Spontaneous regression of Burkitt's lymphoma provides compelling evidence for antitumor immunity.

Spontaneous Regression of Malignant Melanoma: A Review of the Literature on Incidence, Clinical Features, and Possible Mechanisms

NATHANSON L

National Cancer Institute Monographs 44: 1976; 67-76

Extracted Summary

A review of the clinical features of spontaneous regression of malignant melanoma was undertaken. Thirty-three patients with total regression of primary melanoma ("primary regressors") and 40 (13 of whom were somewhat doubtful) with regression of metastatic disease were reviewed in detail. These patients appeared to represent a typical age incidence of melanoma but the primary regressors showed an unexpected predominance of male over female patients. A variety of unique clinical features of the histories of the patients were noted, but none appeared to explain the regression with any degree of predictability. Cutaneous metastases constituted the most common site of regression, followed, in order, by lymphatic, pulmonary, and hepatic metastases. About 40% of patients with spontaneous regressions appeared to have "spontaneous cure," which implies that the disease had not relapsed either during a long period of follow-up or until death from some other cause.

Mechanisms that possibly relate to spontaneous regression of melanoma fall into the following general categories: immunologic, endocrine, pigment metabolic, intracellular, nutritional, and carcinogenic. Further quantitative studies of patients actually undergoing spontaneous regression or the development of a model of spontaneous regression may be a key to our understanding of this interesting "experiment of nature."

II. CLINICAL AND EXPERIMENTAL MECHANISMS OF ACTION

Regression of Cancer Following Surgery

SINDELAR WF; KETCHAM AS

National Cancer Institute Monographs 44: 1976; 81-84

Extracted Summary

Postsurgical tumor regressions are rare but well-recognized entities. The causes of such phenomena are unknown but probably are multiple. Regression of any tumor must ultimately come about by changes in the host-tumor interaction which suddenly becomes unfavorable for tumor growth. This is likely a manifestation of changes in the immunocompetence of the host. There are many variables influencing the host-tumor interaction, and the study of tumor immunology is still in its infancy. It is through the exploration and investigation of basic mechanisms of the immunology of cancer that the most potentially fruitful associations between tumor growth or regression and surgical manipulations may be made and applied to the treatment of cancer patients.

Immunotherapy in Malignant Melanoma

HOLMES EC; MORTON DL; EILBER FR; GOLUB SE; SULIT HL

National Cancer Institute Monographs 44: 1976; 85-86

Extracted Summary

Accumulated evidence suggests that human neoplasms contain antigens that elicit humoral and cellular immunity in the immunocompetent host. A recent summary report showed that Stage II

melanoma patients with metastases to regional lymph nodes had a lowered incidence of recurrence and a higher incidence of survival following surgery and postoperative BCG immunotherapy. To verify these findings, clinical trials are now under way in which we randomized melanoma patients into groups to compare treatment by surgery alone with surgery and BCG only, or surgery and BCG in combination with allogeneic melanoma cell vaccine. Serum samples from each patient are monitored by in-vitro techniques to define those methods which best correlate to clinical course. Hopefully, such correlations can be used to monitor response to immunotherapy before disease is clinically apparent. Although immunotherapy does not cause regression of far-advanced disease, it undoubtedly will be beneficial against subclinical, microscopic tumor.

Nonspecific Antigen Reactions

KLEIN E; ROSNER D; HOLTERMANN OA; STOLL HL JR; SONG SY
National Cancer Institute Monographs 44: 1976; 87-97

Extracted Summary

Cell-mediated immune challenge reactions to a number of antigens at tumor sites resulted in regressions of various types of benign, premalignant, and malignant lesions in man. Regressions varied from partial to complete and lasted from several months to more than 10 years. Increased levels of cell-mediated immunocompetence were attained by several means, including reduction of tumor burden, immunopotentiality, or transfer of immunity. Antitumor activities of immune challenge reactions are selective for tumor cells and appear to be independent of the nature of the antigens used or the type of neoplasm. Combinations of immunotherapy with other treatment modalities resulted in augmentation of antitumor effects. Preliminary studies indicate that cellular and noncellular mediators of delayed hypersensitivity induce antitumor activities that may be significant in the regressions of neoplasms induced by cell-mediated immune challenge reactions. Since cell-mediated immune reactions are frequent occurrences, they may be a factor in apparently spontaneous regressions of neoplasms.

Latent Carcinoma and Carcinoma in Situ

PIERCE GB; FENNELL RH JR
National Cancer Institute Monographs 44: 1976; 99-102

Extracted Summary

Lesions exist in the cervix that are diagnosed as carcinoma in situ; some may progress to invasive carcinoma and some may regress. Many are probably over diagnosed, may represent effects of promoting agents rather than initiating agents, and may entail risk for the patient in that the lesion may be an unusually good target in carcinogenesis. Latent carcinomas are small foci of initiated cells unable to express their malignant phenotype because of environmental controls. Latent cells are produced in experimental carcinogenesis and occur in spontaneous tumors as G-O stem cells.

Some Immunologically Based Reactions That Can Cause the Regression of Large Tumor Masses

ALEXANDER P

National Cancer Institute Monographs 44: 1976; 105-108

Extracted Summary

A widely held view is that the immune reactions of the host directed against tumor-specific membrane antigens can only eliminate a relatively small number of tumor cells. There are, however, some therapeutic maneuvers that, under some conditions, can cause the regression of large tumor masses to which immune factors make a critical contribution. Among these are the injection of complement, administration of double-stranded RNA and endotoxin, and the induction of inflammation.

Immune Surveillance: A Powerful Mechanism with a Limited Range

KLEIN G

National Cancer Institute Monographs 44: 1976; 109-113

Extracted Summary

There is excellent evidence for the belief that immune surveillance mechanisms prevent the outgrowth of potentially neoplastic cells induced by horizontally transmitted, ubiquitous, potentially oncogenic viruses, indigenous to natural populations. Polyoma virus in mice, Marek's disease in the chicken, Herpesvirus saimiri in the squirrel monkey, and the Epstein-Barr virus in man are examples. There is much less evidence for immune surveillance against chemically induced tumors. It is argued that surveillance against the virus-induced tumors may have evolved by the selective fixation of appropriate immune responsiveness (IR) genes. It is important to distinguish between the breakdown of an existing surveillance mechanism, e.g., by immunosuppression, and the lack of immune recognition, due to the deficiency of the IR gene equipment. Presently available in-vitro lymphocytotoxicity tests are not yet developed to the point where they can reliably distinguish between these alternatives.

Neoplastic Disease and Tumor Immunology from the Perspective of Host-Parasite Relationships

WEISS DW

National Cancer Institute Monographs 44: 1976; 115-122

Extracted Summary

Neoplasia is considered within the biologic framework of host-parasite relationships, and the arguments favoring this perspective are discussed. By viewing neoplastic processes as dynamic interactions between transformed clones, host defense mechanisms, and the environmental circumstances impinging directly on the neoplastic event, the experimentalist and clinician are better prepared conceptually for a balanced assessment of all factors determining the development and outcome of confrontations with neoplastic clones. The frame of reference placing progressive neoplasia into the category of host-parasite associations also prepares the ground for technical approaches to the study and observation of oncologic phenomena appropriate to their essential

nature. The correct evaluation and most promising future development of the current emphasis on immunologic parameters of neoplasia demands, especially, an awareness of the role of immunologic variables in other host-parasite relationships.

IV. SPECULATIONS, HYPOTHESES, AND THEORETICAL CONSIDERATIONS

Metastatic Spread and “Escape” from the Immune Defenses of the Host

ALEXANDER P

National Cancer Institute Monographs 44: 1976; 125-129

Extracted Summary

The effectiveness of the host's immune reaction against primary and disseminated tumors depends not only on the magnitude of the host's immune response, such as the number of cytotoxic cells and antibody molecules produced, but also on the capacity of tumor cells to evade destruction. The latter process which has been termed “escape” depends on several factors including intrinsic properties of the tumor cell. In some experimental systems, it was shown that the capacity of disseminated tumor cells to give rise to distant metastases is in part determined by the efficiency of escape. Tumors which in-vivo appear to be nonimmunogenic may still carry tumor-specific antigens to which the host responds by making cytotoxic mononuclear cells, but these fail to kill because escape is effective.

Spontaneous Tumor Regression: Possible Relationship to In-Vitro Parameters of Tumor Immunity

HELLSTRÖM KE; HELLSTRÖM I

National Cancer Institute Monographs 44: 1976; 131-134

Extracted Summary

Evidence is discussed from three animal systems (Shope papillomas in rabbits, Moloney sarcomas in mice, Schmidt-Ruppin-Rous sarcomas in Japanese quail) that immune reactions can be important in spontaneous tumor regression. In-vitro studies performed in these systems indicate that blocking serum factors can thwart cell-mediated immune responses and that “unblocking” antibodies are often found in animals whose tumors have regressed. To what extent spontaneous regressions of human neoplasms are due to immunologic mechanisms is unknown; in 2 patients who had undergone spontaneous tumor regression, tumor cell cytotoxic lymphocytes and unblocking serum factors were detected. Better animal models and better knowledge about the mechanisms of tumor immune reactions are needed before tumor regression can be more successfully induced by immunologic manipulations (to what extent that will even be feasible in man is unknown).

Mechanisms of Escape from Immune Surveillance

KLEIN G

National Cancer Institute Monographs 44: 1976; 135-136

Extracted Summary

The escape from immune rejection is, like the development of drug resistance in microorganisms, a multi-pathway process. Selection favors the phenotype, i.e., the cell that can grow in spite of the immune rejection process, not the underlying mechanism. Experimental evidence documents the roles of host immunosuppression (genetic or environmental), immunoresistance at the cellular level, "sneaking through" (i.e., growth of a tumor to irreversible size prior to the mobilization of an appropriate immune response), lack of antigenic recognition, and blocking enhancement type reactions.

Possible Mechanisms in Regression

THOMAS L

National Cancer Institute Monographs 44: 1976; 137-139

Extracted Summary

The mechanisms responsible for spontaneous regression of cancer may be nonimmunologic. The author suggests two models other than immunologic that could be related to underlying mechanisms of spontaneous regression. One model, using the effects of endotoxin on the horseshoe crab, suggests that the necrotizing properties of endotoxin may offer an open approach to the problem. Another model, based upon the observations of the behavior of syncytial trophoblasts in pregnancy, is postulated. In pregnancy, trophoblastic cells are shed by the placenta and enter the maternal blood supply. The author speculates that this shedding which may act to desensitize the maternal host against any antigens possessed by the fetal tissue could also be applied to the shedding of cancer cells into the blood from neoplastic tissue. The underlying purpose of the shedding process may be the same in both situations.

Summary of Our Recent Studies on the Assessment of Cell-Mediated Cytotoxicity in Vitro

WEISS DW

National Cancer Institute Monographs 44: 1976; 141

Extracted Summary

Experiments employing two new methods for the in-vitro assessment of cell-mediated immunity against neoplastic target cells are indicated. Both methods offer the advantage of rapid and quantifiable determination of very early events in cell-cell confrontations. One technique measures the incorporation of precursors of protein, RNA, and DNA synthesis by neoplastic cells incubated with effector cells during the first hours of contact. It was found that exposure of BALB/c plasmacytoma (PCT) cells to splenocytes from PCT-sensitized donors failed to bring about inactivation of the target cells or their release of ^{51}Cr during several hours of interaction. However, inhibition of ^3H -thymidine incorporation was almost instantaneous and pronounced. This observation suggests that cytostatic events may transpire in cell-cell interactions in the absence, or before the onset, of lethal changes. The second method assays the specific adherence of ^{51}Cr -labeled lymphoid cells from Rous sarcoma (RS)-bearing chickens to RS target cells. This immuno-adherence test revealed preferential, specific reactivity in autochthonous as compared with allogeneic interactions, which indicated recognition of individual-specific tumor-associated antigens against a background of strongly expressed group antigenicities.

Spontaneous Regression of Cancer: Summary and Profile for the Future

NOSSAL GJV

National Cancer Institute Monographs 44: 1976; 145-148

Extracted Summary

The proceedings of the Conference on Spontaneous Regression of Cancer, held at The Johns Hopkins Medical Institutions, Baltimore, MD, on May 9 and 10, 1974, are summarized. Spontaneous regression of advanced cancer is extremely rare, occurring in $< 1/1,000$ cases. Furthermore, 60% of all regressions occur in only four cases: hypernephroma, neuroblastoma, malignant melanoma, and chorionic cancer. The following points relating to spontaneous regression are discussed: clinical documentation, surgery, radiotherapy, and psychological factors; established facts in immune responses to tumors; immunological events during tumor progression; and the future of tumor immunology.