Short Commentary

Immune System's Role in Cancer

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It has been known for many years that the immune system plays a major role in neoplastic development and control, since patients who are immunosuppressed have a higher risk of cancer, and spontaneous regression of many types of malignant tumors is a rare but well-recognized phenomenon-occurring in approximately 1 in every 60,000 to 100,000 cancer cases

Throughout history there are multiple accounts about tumorous growths regressing or disappearing after an infectious and/or high febrile episode, having been reported from ancient Egypt up to the early 18th century in Europe, but the scientific basis for attempts at modulating the immune system to treat cancer can find its modern roots only in the second half of the 18th century, when histologic confirmation of a malignancy became possible. More than 135 years ago the German physicians Busch and Fehleisen independently noticed regression of tumors in cancer patients after accidental infections by erysipelas. In 1868, Busch was the first to intentionally infect a cancer patient with erysipelas and he noticed shrinkage of the malignancy. Fehleisen repeated this treatment in 1882 and he also eventually identified Streptococcus pyogenes as the causative agent of erysipelas. In 1891, an American surgeon, William Coley, of the Bone Tumor Service at Memorial Hospital in New York, followed up on his own independent observation of a long-term regression of a sarcoma after an erysipelas infection by starting a 43-year-old project involving the injection of heat-inactivated bacteria ("Coley's toxins") into patients with inoperable cancers. He reported a significant number of regressions and cures in more than 1,000 patients, many or most with sarcomas, and the method started gaining wide acceptance and

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ARTICLE HISTORY Received: June 05, 2021 Accepted: June 20, 2021 Published: June 26, 2021

notoriety. His toxins gradually disappeared from use because of several factors, including his failure to follow good scientific protocols and inability to consistently obtain reproducible results. The development of radiation therapy and chemotherapy also contributed to the loss of interest in using this type of therapy to treat cancer. Nonetheless, after no fewer than five marked shifts in attitude toward CI since the 1890 Coley's principles have been shown to be correct, and the use of bacteria finally found sound justification in 1976 when Morales established the effectiveness of the bacterium Bacillus Calmette-Guérin (BCG) in the treatment of superficial bladder cancer. The underpinnings for this clinical trial include a 1959 study by old showing the anti-tumor effects of BCG in a mouse model. Besides his work on BCG, Old also performed extensive research on other CIrelated topics, and were a discoverer of tumor necrosis factor in 1975. Due to their foundational discoveries and lifelong dedication to the field, Coley and Old have each been referred to as the "Father of Immunotherapy", a title which is perhaps best shared.

Cancer immunotherapy (CI) is rapidly advancing and can now be considered to be the "fifth pillar" of cancer therapy, joining the ranks of surgery, cytotoxic chemotherapy, radiation, and targeted therapy. The CI which has sparked the most interest antibodies involves to inhibitory immune Although checkpoint molecules. thev have produced dramatic results in only a subset of some malignancies to date, it is difficult to not be very excited about their potential.

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Citation: Dennis P (2021) Immune System's Role In Cancer. Am J Prev Med Public Health, Volume: 7, Issue: 6

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