A HISTORY OF CANCER BACTERIA RESEARCH

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Overview

Since the 1920s, researchers have consistently isolated and cultured bacterial forms from cancer patients. Among the first investigators to have made the discovery was the Canadian physician Thomas Glover. Glover claimed that his organism displayed different forms including a filter-passing one closely resembling viruses. In what was perhaps the first long-term clinical trial involving a cancer therapy, two of Glover's colleagues---Dr.'s Clark and White---claimed favorable results for a variety of cancers using an anti-sera originally developed by Glover. The trial, however, was not controlled or randomized and the actual results would be difficult to determine by today's standards or protocols.

The Glover anti-sera was made from horse antibodies derived from inoculation of human cancer bacteria (see how Glover's anti-sera was prepared).

While Glover, White, Clark and Scott were among the first to document and
then use as an anti-bacterial cancer vaccine, a New-Jersey physician named Virginia Livingston advanced Glover's controversial theories starting in the late 1940's.

**Livingston's Findings**

After conducting a number of experiments which included the darkfield and electron microscope, Livingston and several colleagues said they had corroborated Glover's bacteria theory via the established tenets of Robert Koch (i.e. "Koch's Postulates")[1]. Livingston named her cancer bacterium *Progenitor cryptocides* and she described it as a highly pleomorphic entity that behaved, in many ways, like *Mycobacteria*. *Mycobacteria* are responsible for certain forms of pneumonia, leprosy, TB and other infectious diseases. These microorganisms possess somewhat permeable cell walls that can be stained with a special laboratory dye for identification purposes; further identification is made based on the fact that *Myocbacteria* are generally resistant to removal of the stain once it's been applied (a phenomena referred to as "acid-fastness"). Later, scientists began identifying yet another type of bacterium known as *Mycoplasma*. The latter are considered among the smallest organisms and belong to a different family of bacteria than *Mycobacteria*. *Mycoplasma* lack true cell walls, display virus like properties, and are also acid-fast.

[NOTE: Throughout this article you will see various references to "Mycobacteria" as well as "Mycoplasma." Please bear in mind that a number of different investigators have reported different species of organisms in their studies of cancer. Current research is suggesting that different bacteria may play different, or possibly combined roles in cancer. Further, new research is also finding various microbial species might share similar genes or characteristics which make them hard to absolutely quantify or fully identify--an idea that is a departure from classical microbiology].

Regarding Livingston's study of *Mycobacteria*, she ascribed atypical qualities such as filter-passing virus phases (similar to *Mycoplasma*) and also intermittent acid-fastness depending on the life cycle being observed ('intermittent' meaning acid and non-acid fast phases). Livingston and her longstanding colleague Eleanor-Alexander Jackson also claimed to isolate filter passing bacterial forms from cultures of pure *Rous sarcoma virus* (RSV)[2]. The RSV was the first cancer-causing virus ever discovered.

Like bacteria, some viruses have been implicated in cancer. But unlike bacteria, the primary focus of mainstream research for the past half century has largely been on cancer viruses, much smaller organisms that are capable of infecting their host and causing damage sometimes years before cellular
changes occur, resulting in cancer. Currently, preventive vaccines are being used for some forms of cervical cancer, much in the vein that anti-bacterial vaccines are used to prevent bacterial diseases.

Livingston's Rous research was potentially significant because RSV can only be isolated using extremely small laboratory filters designed to allow extremely small organisms to pass through. Yet, Livingston claimed that after filtering pure virus cultures, she was able to "regrow" bacteria from them. This was anathema to mainstream research which held that bacteria are not large enough to pass through filters, suggesting a virus-phase to bacteria as yet unknown. Thus, the implications of Livingston's research were that a bacterium might somehow be associated with cancer in poultry and that they might also mimic, or simulate viruses. For this reason, Livingston urged patients---as well as the general public---to avoid poultry. Despite Livingston's claims, however, RSV is the only entity that has been associated with cancer in poultry; further, science has not demonstrated that RSV is capable of infecting humans, or causing cancer. To date, we know of no other studies used to corroborate, or dispute Livingston's and Jackson's claim of an RSV-related bacterium.

Whatever the true nature of Livingston's bacterium, she made what some consider her most important discovery in 1974. In 1974, the physician found that cancer bacteria could produce the fetal growth hormone hCG[3]. Adding to this discovery were the findings of other independent researchers who discovered that cancer cells are also capable of producing or synthesizing hCG. Livingston summed up her research findings this way:

- Cancer bacteria display intracellular parasitism during certain life-cycle phases and can invade healthy cells. They can also secrete toxic chemical fractions such as actinomycin-D which may result in karyotypic changes, resulting in malignancy.

- After cancer begins, bacteria act in concert with cancer cells, and in a way that is not fully understood, help cancer cells synthesize hCG.

- hCG is a universal cancer marker which also acts as a protective hormone for the cancer cell. Paradoxically, hCG protects the growing fetus from host immunity.

- Vaccines which can attack hCG-producing and cancer/promoting bacteria are able to deprive cancer cells of a key source of hCG; as the levels of hCG are lowered, the immune-system's ability to launch an assault on cancer cells increases.
In 1969, Livingston established a cancer treatment clinic in San Diego, and began administering an autogenous anti-bacterial vaccine (made from urine-derived bacterial isolates). Livingston prepared the vaccines by first screening individual bacterial cultures via darkfield microscopy and examining the organisms for acid-fastness. She also conducted growth inhibition studies to determine antibiotic sensitivity. After Livingston noted that a dark, reddish-brown material growing in her bacterial cultures yielded the hormone hCG, she began assaying her cultures for that hormone and incorporated this additional test in her vaccine preparation. In fact, the entire cornerstone of her therapy was dependent on the ability to neutralize hCG—a factor which is now being investigated in mainstream research and via clinical trials (see Virginia Livingston's background).

The NCI Investigation

A centerpiece of the National Cancer Institute's long standing rejection of a bacterial cause of cancer was due to an investigation it conducted between 1963 and 1974 [4].

Prior to 1963, a number of researchers were reporting "virus" type bodies as well as bacteria in the blood of leukemia patients. Preliminary reports suggested the bacteria to be Mycoplasma. Thus the NCI launched its investigation and predominantly focused on Mycoplasma, and not Mycobacteria [5,6,7] as playing a possible role in cancer causation. However, they didn't perform darkfield, or hanging-drop examinations of live blood or fresh cancer tissue sections using Livingston's protocols, and did not employ the specific culture media or triple-staining techniques as described by Jackson in her published papers. The peer-reviewed studies performed by Livingston and Jackson were not referenced once in any of the NCI papers reviewed by this author.

A review of all Journal of the National Cancer Institute (JNCI) indexes for the years 1963-1974 revealed seven primary studies specifically focusing on Mycoplasma and cancer, with the primary focus being on leukemia[8]. The brunt of cancer bacteria research by Glover, von Brehmer, Villesquez, L'Esperance, Fonti, and Livingston involved non-leukemic cancers.

NCI investigators later concluded that Mycoplasma didn't appear to be a causative agent of cancer or leukemia based on the low percentage of these isolates found in humans. For example in one study involving 1,950 leukemia blood cultures, only 71 were positive for Mycoplasma[9]. Yet in other studies, conflicting results were noted, with as many as 40% of cultures testing positive. Overall, the 1963-1974 investigations centered on a number of Mycoplasma species including M. neurolyticum, M. pneumonia, M. orales and M. pneumoniae. Very little attention was made regarding M. fermentans or M.
hyorhinis---organisms which today are the focus of cancer causation.

Several of the NCI studies proved that cancer could be caused in the absence of bacteria. For example, an experimental tumor was grown in animals that were declared "germ free" after exposure to radiation.

In a 1972 appraisal, IM Spence, reporting in the South Africa Journal of Medical Sciences wrote that while Mycoplasma may be "unable to induce malignancy on their own, the possibility exists that their presence on the surfaces of tissues, together with the presence of...other cancer agents might act...to trigger a carcinogenic response"[10]. Spence also urged future investigators to study cancer cultures taken from "biopsy and fresh necroscopy material" as a means of providing "confirmatory evidence for Mycoplasma infection" and for ruling out the long debated issue of Mycoplasma contamination---long considered a problem, especially before the days of direct genetic sequencing and analysis of organisms.

**ACS Disputes Bacterium**

The long standing schism between mainstream medicine and a bacterial cancer theory reached a head in 1990, when the American Cancer Society found "gross errors" in Virginia Livingston's research[11]. Up until that time, Livingston had arguably become the most controversial and outspoken of the theory's proponents.

The primary argument cited by the ACS was that Livingston had missclassified her organism with unrelated species of bacteria. According to the ACS, "immunohistochemical techniques....used to analyze P.Cryptocides cultures supplied by Livingston.....were identified as Staphylococcus epidermidis and not Mycobacteria". Thus, Livingston's credibility in isolating a specific bacterium of malignancy was in question. It is noteworthy, however, that Livingston and her colleagues had specifically and consistently described acid-fast microorganisms in their three decades or research; Mycobacteria are among the few species that are acid-fast (while Staphylococcus are not). Acid-fastness describes the ability of certain organisms to retain a pink or red stain because of idiosyncracies in their cells walls. By contrast, non acid-fast entities can't retain such a stain and will typically exhibit a blue color. From a common sense standpoint, it seems almost comprehensible that Livingston and particularly Eleanor Jackson---an acclaimed professor of microbiology at Cornell and a lifelong authority on Tuberculosis---could conceivably confuse an acid-fast with non-acid fast organism for thirty years. A more likely explanation appears to be sloppy research and/or contaminated samples which may very well have been 'misclassified'. Unfortunately because of this single issue, Livintgston's entire body of research has been permanently tainted.
Dr. Alva Johnson, a former professor of microbiology at the University of Virginia Medical School explained in a 1992 interview with this author, that Livingston had stopped performing necessary laboratory analyses of live blood and fresh tissue cultures obtained from her cancer patients[12]. Instead, she largely focused on treating patients via the use of an autogenous vaccine made from urine. Because these urine cultures showed the presence of hCG, Livingston assumed they must be proof that Progenitor cryptocides (or a Mycobacterium) was the culprit. Later, when asked to provide samples for independent review by the ACS, Livingston submitted bacteria derived from the so-called Progenitor-infected urine cultures. However, the cultures were found to consist of Staphylococcus epidermidis a common skin contaminant.

Despite Livingston's errors, attempts to repeat or corroborate her earlier experiments as chronicled in her work Compendium were not undertaken.

Ironically, staphylococci have been corroborated as playing a possible role in some cancers. For example, Cantwell reported the isolation of Staphylococcus epidermidis from breast cancer patients and researchers at Lund University, University Hospital, Malmo, Sweden recently noted a "strong association" between Squamous cell carcinoma (SCC) of the skin, and the presence of Staphylococcus aureus[13]. In addition, Hernan Acevedo of the Allegheny-Singer Research Institute in Pittsburgh found that a number of different bacterial strains---including Staphylococcus haemolyticus and Staphylococcus epidermidis---could be isolated from cancer patients. Perhaps more importantly, these bacteria were also found to manufacture hCG [14].

Acevedo also agreed with Livingston's premise that such bacteria have "revertant" forms, lack true cell walls, are filter passing (able to simulate viruses) and also intermittently acid fast---characteristics indicating pleomorphism and one espoused by Livingston throughout her career[15]. Such findings might conceivably hurt or help Livingston. For example, while the ACS cites Acevedo's work as proving that a "unique" species of bacteria are not responsible for cancer---thus undermining the basic thrust of Livingston's theories---others argue an affirmation of Livingston's thesis (i.e., that cancer-associated bacteria are capable of producing hCG). In this regard, some see 'remarkable errors' while others, a semantical mistake.

It has long been argued that Livingston ascribed cancer-causing characteristics to a species of bacteria (Mycobacteria) that are alleged not to exist. However, recent studies challenge that assumption. For example, scientists reported in one of the world's leading peer reviewed journals Oncogene, that the species Mycobacterium tuberculosis caused malignant changes in lung tissues. The researchers stated that these bacteria "play a pivotal role in TB-induced (cancer).....by inducing DNA damage" and concluded "our experimental
findings showed a causal link between pulmonary TB and lung tumorigenesis"[16].

**Compelling New Evidence**

Several years after the refutation of Livingston's hypothesis, scientists had finally established that a bacterium---*H. pylori*---was capable of causing cancer. However, while the currently accepted consensus focuses primarily on this entity, a number of other species are being implicated.

In 1995, Shy-Ching Lo substantiated a link between *Mycoplasma fermentans* and oncogenesis[17]. Lo's research confirmed the multistage, malignant transformation of embryo cell lines persistently exposed to *Mycoplasma* infection as well as animal models so exposed. Recall the NCI's negative studies did not focus on *fermentans*. Chan and colleagues also report the prevalence of *Mycoplasma* DNA in ovarian cancer[18]. Additional studies conducted in Switzerland by Schmidhauser show that the p37 gene associated with mouse sarcoma cells originates from *M. hyorhinis*[19]. Schmidhauser added that "p37 is part of a....high-affinity transport system in *M. hyorhinis*, a Gram-positive bacterium." The investigators also found that when they infected various cancer cells with *M. hyorhinis*, there was a proportionate increase in malignant invasiveness. The study authors concluded that "a cellular protein..." (deriving from *M. hyorhinis*) ...structurally related to P37 apparently influence invasive behavior (of cancer cells).

Another intriguing finding involved the isolation of cancer-related markers which are specific to various organs in the body. These markers are called "organ-specific neoantigens" or OSNs, and they elicit specific immune responses. After analyzing OSNs from human colon adenocarcinomas, researchers found the OSNs proteins to originate from *Mycoplasma*.

Yet in another study conducted at the Fujisaki Institute, Ushio found that "*Mycoplasma* infected cells have a higher ability to metastasize in vivo than non-infected cells"[20]. The researchers isolated a cancer-promoting molecule known as "Ag 243-5" from *Mycoplasma hyorhinis*.

Evidence collected by Bogoch demonstrated that a polysaccharide-like substance is able to mask certain cancer antigens, thereby helping cancer cells avoid immune-system recognition. In addition, *Mycoplasma* also secrete polysaccharides such as galactan and may therefore be directly involved in the prevention of immune responses against malignant cells.

How *Mycoplasma* and other cancer bacteria may further be involved in
suppressing host immunity and cancer lies in an understanding of the pregnancy hormone hCG.

While it has been generally asserted that hCG is not a unique product of cancer bacteria and that it is produced both in healthy and diseased tissues, there may exist differences in hCG concentration between healthy people and those with cancer. For example in an earlier study published in 1995, researchers noted "...a statistically significant difference" in levels of an hCG sub-unit molecule known as sialic acid[21]. Crook also reported "a highly significant difference between...serum sialic acid in....myeloma patients compared to (controls)...."[22]. P.B. Macomber, writing in the British journal Medical Hypothesis also posited that hCG subunit residues adhere to cell surfaces on cancer controls, trophoblast and sperm cells; these residues then create an electrostatic repulsion between white blood cells and cancer cells [23]. This discovery was also supported in the early research of Van Beek[24]. White and Loke also reported that sialic acid protects human tissues from immune system targeting[25].

Newer research, both in cancer and reproductive medicine also corroborates hCG as a modulator of immunity, both in cancer and fetal development. For example when cells become malignant, their surfaces change and become charged with such carbohydrate residues as oligosaccharides. These, in turn, combine with the amino acid carbohydrate sialic acid, a key molecule of hCG[26]. Beside making malignant cells less prone to host immunity, sialic acid has been shown to make them more invasive (ibid). One of the pathways by which sialic acid/hCG can mediate immune system attack is due to the net negative charge of hCG[27].

More currently, the link between cancer cells, bacteria and hCG has been intently studied and reported on by Acevedo who believes that hCG is a common denominator of cancer and is also associated with some bacteria. In one of his key papers, he notes that 6 of 9 bacterial strains showed "...bizarre forms of reproduction" and also expressed "hCG- like material"[28]. This confirms Livingston's initial claim of an hCG-bacteria relationship. Acevedo has also found that human cancer cells, "irrespective of type and origin" expressed hCG proteins---a "common...characteristic of cancer." Despite the fact that the ACS has understated the hCG/cancer relationship arguing that hCG is commonly found in both healthy and some cancer tissues, Acevedo is careful to point out that benign tumors don't express hCG. It appears that hCG is only a byproduct of fetal, embryonic and malignant cells. Thus, Acevedo explains that "cancer is a problem of development and differentiation, and, to the authors' knowledge, prove(s) definitively for the first time that synthesis and expression of hCG, its subunits, and its fragments, is a common biochemical denominator of cancer,*

* providing the scientific basis
for studies of its prevention and/or control by active and/or passive immunization against (hcg)[29]. [bold highlight, ours.]

While Acevedo distanced himself from the Livingston controversy by stating that his isolation of multiple strains of hCG-producing bacteria proves there isn’t one cancer bacterium— an obvious reference to Livingston and one that was cited by the ACS in its condemnation of the embattled physician— his claim of being the first to identify hCG as a common denominator of cancer is not accurate. It was Livingston who made such a claim in 1974, calling hCG "the hormone of life and the hormone of death" due to its dual role in fetal life and in malignancy. And like Acevedo, Livingston believed that the 'prevention and/or control by active and/or passive immunization against hCG' should be a predominant cornerstone of cancer treatment.

**Toward A New Paradigm**

The stringent conclusions of Virginia Livingston regarding *Progenitor cryptocides* as well as the American Cancer Society's contrary finding of *staphylococci* in her cultures likely requires further investigation and revision considering the multiplicity of bacteria now being studied in cancer, and the difficulty of isolating cell wall deficient forms from cultures. For example, *Salmonella typhi* was recently found associated with gallbladder cancer[30][31] *Streptococcus bovis* with colorectal cancer[32] and *Chlamydia pneumoniae* in lung cancer[33]. In fact, new research is supporting the multiple cancer bacteria concept— an idea that will undoubtedly stir intense debate among microbiologists trained in the one species/one disease paradigm.

In one of a series of recent studies, investigators commented on the numerous organisms they had isolated from oral cavity cancers. They wrote:

Despite increasing interest in the possible relationships between bacteria and the different stages of cancer development, the association of bacteria with cancer of the oral cavity has yet to be adequately examined...Surface contamination was eliminated by immersion in Betadine and washing with phosphate-buffered saline....Isolates were identified by 16S rRNA gene sequencing. Twenty deep-tissue specimens, 19 with corresponding superficial tissues and 12 with control tissues, were successfully processed. A diversity of bacterial taxa were isolated and identified, including several putatively novel species. Most isolates were found to be...acid-tolerant species. Notably, some species were isolated only from either the tumorous or nontumorous tissue type, indicating a degree of restriction. Successful surface decontamination of the specimens indicates that the bacteria detected were from within the tissue. A diversity of bacterial groups have been isolated from within oral squamous cell carcinoma tissue. The significance of these bacteria within the tumor warrants further study" [34].

Careful attention was paid to eliminate contamination---an oft cited problem
with cancer bacteria isolates; further, the organisms were identified using genetic sequencing. Hooper noted a 'degree of restriction' meaning that certain species seemed exclusive to cancerous, as opposed to non-cancerous tissues. All of which underscores the complexity of cancer bacteria and the urgent need for scientists to remain open about rethinking traditional concepts.

Careful consideration must now be given to the possibility of a diverse group of organisms playing critical roles in cancer, albeit in many human diseases as well. And it is quite possible that the time honored tenets of Robert Koch---the gold standard for isolating a bacterium and linking it to a specific disease---may have to be viewed in an entirely new light. Consider, for example, recent research which has found that the vast majority of microorganisms now categorized had previously gone unnoticed via traditional culture methods. In addition, analyses of ribosomal RNA taken directly from the environment has revealed that traditional cultivation methods find less than 1% of the bacteria and archaea species in a given sample[35]. Further complicating these findings is the current field of metagenomics which has found a large amount of bacterial DNA existing in the human body, the ratio being 10 bacterial genes to 1 human[36]. Human bacteria have also been shown to swap genes at rapid horizontal transfer rates, possibly making conventional categorization of some bacteria not always feasible[37]. It is possible that genetic transfer may occur between cancer cells and bacteria of different genera resulting in an as yet, not fully elucidated symbioses. For example, Robinson found that mammalian derived tumor bacteria identified via ribosomal RNA gene sequencing as gram-positive Staphylococcus epidermidis were capable of self-organization in a process he calls "prokaryote to eukaryote transformation"[38]. Robinson found that such transformed bacteria grew into complex tissues, complete with vascular blood networks, mammalian characteristics not associated with normal bacteria. According to Robinson, this symbiosis might occur through "vertical" gene transfer between cancer cells and bacteria, and results in multicellular tissue-like sheets (not biofilms), and vascular networks that may be involved in tumor neo-angiogenesis [39].

Such new findings may someday explain the inconsistent and highly variable results obtained throughout the years by Livingston and other proponents of a bacterial cause of human cancer.

**Conclusion**

The existence of a number of possible bacterial species or genetically altered bacteria whether directly responsible for cancer or existing as opportunistic infections, as well as the capability of cancer bacteria to synthesize hCG and related substances---likely significant factors in a number of cancers---presents a view of cancer that centers on a microbiologic/infectious component. In addition, a growing understanding about hCG and the riddle of
Immune-system suppression may open the door to a revolutionary way of approaching cancer treatment.

Attacking the underlying infectious component via antibiotics specific to individual bacteria cultures, and also the concurrent use of anti-hCG vaccines used in a multi-pronged attack against cancer is a hypothesis that should be investigated. Such a therapeutic model need not interfere with any of the established therapies available currently or about to become available, and the relatively low toxicity of such a protocol should present no moral or ethical problems in cancer treatment (see here for a review of anti-HCG clinical trials). At the present time, laboratories are now capable of synthesizing purified anti-hCG vaccines capable of targeting highly specific hCG subunits found on cancer cells.

In conclusion, a therapeutic model involving vaccines and immunological methods might possibly serve to undermine both hCG, its constituents, and the underlying bacteria which may play key roles in cancer. Based on this hypothesis, we feel this is an area that should be actively and intensely investigated.

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NOTES


4. Personal communication from: Carol Case, Chief, Public Inquiries section, Office of Cancer Communications, National Cancer Institute, (October, 1986).

5. Ebbesen P, Lind K. "Lack of evidence for oncogenic or amyloid inducing qualities of


12. Personal communication from: Dr. Alva Johnson, Dept of Microbiology and Immunology, Eastern Virginia Medical School, May 27, 1992.


29. ibid.


39. ibid.