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Vital Longevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

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INFECTIONS and 'UNRELATED' DISEASES

Who would think that having the common Epstein-Barr Virus (EBV) infection known as 'mono' could set you up for later Hodgkin's Disease? It does: 40% of persons with Hodgkin's show clear evidence of previous EBV infection. Disquieting, to say the least.

Researchers and others interested in such phenomena are fascinated by well-documented, peer-reviewed findings linking infections with subsequent, seemingly unrelated disease. (Serum antibody levels in the body provide a history—and concrete evidence—of previous exposure/infection.) Recent groundbreaking research has uncovered links between an astonishing variety of infectious agents and subsequent diseases, from reactive arthritis being linked to *Salmonella*, *Shigella*, *Yersinia*, and *Campylobacter* (all food-borne infections) to obesity being linked to Adenovirus 36.

Meanwhile, neuro-psychiatric disorders have been linked to several types of infection: the parasite *Borrelia burgdorferi* (Lyme disease); the spirochete *Treponema pallidum* (syphilis); the transplacental sporozoan *Toxoplasma gondii*; and the viruses Borna, transplacental Influenza, and Human Endogenous RetroViruses in combination with Cytomegalovirus.

Using the powerful research resource of the OFAS Serum Treasury and the related Kaiser Permanente databank, OFAS and its collaborators have published their research correlating infections and subsequent disease, including:

- links between Epstein-Barr Virus and: Hodgkin's disease (1989); nasopharyngeal carcinoma (ambiguous) (1991); non-Hodgkin's lymphoma (1991)
- links between *Helicobacter pylori* and: gastric carcinoma (1991); gastric adenocarcinoma (1993); non-Hodgkin's gastric lymphoma (1994, 1997); esophageal adenocarcinoma (negative, possibly protective) (2005)

- links between Multiple Sclerosis and: *Chlamydia pneumoniae* (2004); EBV (2006)
- Nine of the eleven correlations were positive, *i.e.*, the infection acted as precursor to, not inhibitor of, disease.

Covert Infections: The Invisible Threat

The microbes we are constantly exposed to do not become a problem until they are inhaled, ingested, or allowed to enter our bodies through an open wound. Though most microbial infections are promptly noted by the presence of pus, mucous, fever, etc. (signs that the body's immune system is on the job), lingering infections often have no perceptible symptoms.

Then there are 'covert infections', the term for certain microbes—particularly viruses such as the Human Papilloma Virus (HPV)—that invade with great stealth from the beginning. Silently and cumulatively, these microbes affect tissues until they (just like covert, chronic non-viral infections) eventually produce disease—in some, but not all, cases.

Lung cancer statistics provide a good illustration of this 'sometimes, but not always' precept; all smokers are exposed to the cell-transforming chemical mutagens in tobacco, yet only 30% develop lung cancer. What protects the other 70%? This is the essence of the conundrum facing scientists today; the challenge is to discover the

unknown factors that determine whether we incur or avoid certain diseases.

Infections and Cancer

Infectious agents, ranging in size from sub-cellular viruses to multi-cellular parasites, can turn a cell cancerous either through years of chronic inflammation/irritation (the usual non-viral *modus operandi*) or by direct cell transformation (the viral approach). A covert infection's potential to cause cancer is determined by the strength and specificity of both the microbe and the individual's immune system. For example, only an adequate dose of some Human

Malignancies Linked to Specific Infections.

Note well: A malignancy is a relatively rare response to an infection that is usually present in persistent form and requires co-factors.

Site or Type of Cancer	Infective Agent
Primary liver cancer	HBV
Primary liver cancer	HCV
Burkitt's lymphoma	EBV
Cervix cancer	HPV 16/18
Penis cancer	HPV
Adult T-cell leukemia	HTLV 1
Kaposi's sarcoma	HHV8
Nasopharynx cancer	EBV
Stomach cancer	<i>H. pylori</i>
Hodgkin's disease	EBV
Post-transplant lymphoma	EBV
Oro-pharynx cancer	HPV 16/18

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Table 1.

Papilloma Viruses, HPV 16/18 specifically, combined with an inadequate immuno-recognition of them seems to permit cervical cancer to develop.

The element of time is also part of the equation, though its precise role is elusive. Take *H. pylori*, for example. Does this infection need decades to generate gastric cancer, or simply an aged immune system—or some combination of the two? To further muddy the waters, recent research seems to indicate that *H. pylori* might actually offer protection...against esophageal cancer.

Approximately 18% of new cancer cases are linked to viral infections, some 1.8 million worldwide each year. Table 1 lists the most common and highest probability links between microbes and cancers. (Antibody testing is generally available for the infections listed, and in some cases preventive vaccines exist or are being tested.)

While 1.8 million annual cases of infection-related cancer may seem alarming, the fact is that the vast majority of people with viral infections do not develop the cancers linked to them. Again scientists confront an enigma brimming with tantalizing questions. What protects the majority? Predisposes the minority? Can that protection be transferred or replicated? These subjects are the focus of prevention-oriented public health research.

Infections and Autoimmune Diseases

When immune system cells mistakenly attack the body's own cells as invaders, the result is autoimmune disease. It occurs when a genetically predisposed immune system confronts a relevant environmental trigger or risk factor, in many cases a common infection. Ordinarily, the immune system's B and T cells recognize an invading microbe primarily by detecting its "foreign" protein. But microbe proteins can resemble the body's normal proteins through molecular mimicry, and some immune systems—unable to recognize (for reasons still not understood) the difference between the two—attack the body's proteins as well as the invaders. This process continues long after the infection resolves and can be very destructive, resulting in chronic inflammation, tissue destruction, and disabilities.

Remnants of ancient viral infections in the human genome seem to be the source of Human Endogenous RetroViruses (HERVs). HERVs have been linked to several autoimmune diseases, including Sjögren's

syndrome, rheumatoid arthritis, type I diabetes, MS, systemic sclerosis, lupus erythematosus, and even alopecia areata and its variants. But, while antibodies to one or more HERV protein particles are the common factor shared by individuals with links to autoimmune disease, it has yet to be proven that any HERV is the agent responsible for the onset of the disease.

More is known, however, about the childhood-onset disease PANDAS (Pediatric Autoimmune Neuropsychiatric Diseases Associated with *Streptococcus*). Extensive research has uncovered new information about the obsessive-compulsive behavior and tics that characterize PANDAS. It appears that the cycles and severity of these symptoms parallel the body's Strep A antibody levels and are often preceded by Strep A infections. PANDAS is currently the subject of intense investigation.

Current Research: Points to Remember

When appraising the research on links between common infections and subsequent diseases, it is important to be aware of the following factors: 1. Studies are usually epidemiologic or observational. 2. They establish correlations of statistical probability. 3. Correlations represent coincidence or causality. 4. Co-factors still undiscovered are probably essential to the processes expediting (or inhibiting) disease development.

Awareness and Prevention

Until this complex subject is more thoroughly understood, staying informed and taking sensible precautions are your best bet.

- Take heart from the Hygiene Hypothesis: exposure to common benign microbes can be preventive exercise for the immune system.
- Avoid (especially repeated) infections: use protective gloves; wash hands thoroughly; use repellents against nature's dirty needles (ticks, mosquitoes); practice safer sex; encourage respiratory etiquette.
- Strengthen your protective shield: get vaccinated (Tetanus boosters, annual flu shots, HPV, Hepatitis B).
- Know what antibodies you have and keep track of their levels.

A wide selection of supplementary reading and reference material on this subject is available at our website: www.orentreich.org/vital.

Information for Donors

The Orentreich Foundation for the Advancement of Science, Inc., was founded in 1961. OFAS is a non-profit institution dedicated to biomedical research to prevent, halt, or reverse those disorders that decrease the quality or length of life. It is duly registered with the US Internal Revenue Service as an Operating Private Foundation under Section 4942(j)(3).

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