

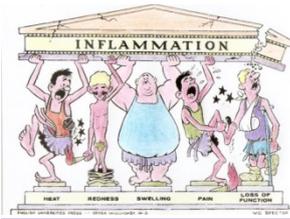


A Science of Medicine  
The Art of Care

# Overview and historical significance of inflammation

Dr Linda Mayer and Prof Rashid Bhikha

November 2013



## General overview of Inflammation

The phenomenon of inflammation has become more important over the last few years, as we realize its extensive involvement in more and more disorders. Bronchial asthma was identified as an inflammatory disorder about 20 years ago, followed by various other allergies. Since then many others, such as diabetes I, Alzheimer's, various cancers, some heart diseases and even ageing have been identified as either acute or chronic inflammatory disorders (Glynn, 2013).

Tibb is very much central to this, as the normal inflammatory response, Physis and inflammation are closely meshed with lifestyle, especially diet. One of the most prevalent underlying beliefs about health in the Western world is that illness is a mistake, and that symptoms of a disease must be eradicated on order to restore health. What is defined negatively as 'pathology' by western medicine is often the body's attempt to reach for health.

Mistrusting the body's ability to self-heal, results in a deep and widespread fear of illness. In order to change the paradigm of a disease-based approach to a person-centred one, a conscious shift is needed, from fearing symptoms to understanding and embracing the innate healing ability of **Physis** to restore internal balance.

The source of the inflammation needs to be found by identifying the trigger factors which cause the inflammation, which includes physical, environmental, emotional, chemical, and most important nutritional factors.

Understanding the important role and stages of inflammation in the process of healing is fundamental to prevent chronic and debilitating diseases from occurring. The prevailing signs and symptoms of an acute inflammatory response are both warning and protective

mechanisms of the body, which enables the immune system to respond accordingly. Any attempts to impede this natural process will interfere with the innate healing ability of Physis.

Inflammation is an important manifestation of the natural body's response to injury, which is a necessary requisite to healing. Various approaches to managing inflammation vary according to the conventional allopathic or other complimentary health disciplines. Interfering with the natural inflammatory response can result in pathology and chronic inflammation.

The underlying causes for many diseases have their origins in poor lifestyle choices, which may result in chronic systemic inflammation, such as obesity, diabetes, high blood pressure, and gout. Hidden inflammation is not as easily detected as an acute inflammatory response, and it is a lot harder to control and manage, especially because of the increasing propensity of lifestyle-induced diseases. Chronic systemic inflammation is an underlying cause of many seemingly unrelated, age-related diseases. However, they are all related by an imbalance of the internal environment in the body.

The conventional approach to inflammation facilitates healing by introducing treatment methods which controls and even inhibits the inflammatory process, mainly with medication. The Tibb's approach to inflammation is to maintain the human body in a state of balance, harmony and vigour, by allowing Physis to go through the various stages of the inflammatory stages and process in order to facilitate healing. The physical, mental, emotional and spiritual forces of human life need to be respected, as they are all contributory factors to the outcomes of health and disease.

The Temperament of an individual determines the specific eliminative therapy which will be adopted to maintain and restore health, and in the prevention and management of inflammation and any other disease. Tibb also understand that the lifestyle factors play a pivotal role in this process. This includes environmental air and breathing, food and drink, movement and rest, sleep and wakefulness, emotions and elimination and retention.

In Tibb the relationship of heat, moistness, coldness and dryness has a direct bearing on the health status of an individual. Heat is generally more favourable than cold for maintaining the proper balance and general health of the body. Health will only be maintained as long as the overall quality of the humours is in harmony with the overall quality of the individual's temperament.

### **Definitions of Inflammation**

Inflammation is associated with heat via the symbol of a flame. The word inflammation comes from the Latin "inflammo", meaning "I set alight, I ignite" or "inflammare (to set

alight). The ancient Greeks referred to inflammation as a “hot thing.” The Greek word, “phlegmon” was used to describe internal inflammatory lesions (Nordqvist, 2012).

The definition of inflammation depends on whether one views this from a clinical, cellular or molecular perspective, but is clear that it embraces a great variety of biological processes, which is modulated by many factors in the cell’s environment (Scott et al, 2004). The definition of inflammation has changed dramatically since it was first used by Celsus nearly 2000 years ago.

Defining inflammation according to clinical signs and symptoms has major limitations, as in most cases the cellular processes and signals that underlie the cardinal signs occur at a subclinical level and do not give rise to any heat, redness, swelling, or pain. For example, the inflammation of delayed onset muscular soreness may cause tenderness on palpation or mild discomfort, but no redness or swelling. The definition also depends on the particular perspective one is viewing inflammation - whether it be clinical, cellular, or molecular (Scott et al, 2004).

Inflammation is a localised protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off both the injurious agent and the injured tissue (Saunders, 2007). It is a normal response to disturbed homeostasis caused by infection, injury, and trauma. The host responds with a complex series of immune reactions to neutralize invading pathogens, repair injured tissues, and promote wound healing (Pavlov, et al, 2003). It is a physiological, protective response to injury or tissue destruction, which is self-limiting; however, pathology may develop if the natural healing response of Physis is tampered with.

Inflammation is a complex process involving the circulatory system and blood-born cells. It is a natural body response to an injury, be it of physical, chemical or infectious origin, and it is a necessary process for healing (Merck Animal Health, 2013).

The common sore throat, rashes or a sprained ankle are protective responses of the body to inflammation, which communicates distress in the body. The problem arises when:

- There is an **overreaction** of the immune response, in conditions such as allergies, asthma, autoimmune diseases or rheumatoid arthritis.
- There is **no overt or visible sign** of inflammation, which is at the root of all chronic diseases, such in diabetes, heart disease, cancer, dementia and depression. This inevitably results in a chronic, smouldering inflammation that slowly interferes with optimal functioning by destroying the organs, leading to rapid ageing (Hyman, 2012).

The natural anti-inflammatory response that ensues after acute inflammation tends to reverse tissue homeostasis towards normality, and should therefore be regarded as a true

defensive reaction of the affected tissue. Inflammation is now recognized as a type of nonspecific immune response.” “Inflammation is the basic process whereby tissues of the body respond to injury.” All signs have been regarded as secondary to one primary pathophysiological event – enhancement of vascular permeability as a direct consequence of tissue injury (Stankov, 2012).

### **Incidence and Prevalence of Inflammatory Diseases**

Immune-mediated inflammatory diseases are a group of common and highly disabling chronic conditions that share inflammatory pathways. Its estimated prevalence in Western society is 5%-7% (Gabalawy et al, 2010). Inflammatory disorders are increasing due to poor lifestyle choices, especially diet, and include allergy-related disorders, such as asthma, diabetes, heart diseases, certain cancers, Alzheimer’s disease and even ageing, amongst a host of other conditions.

According to the Marshall Protocol Knowledge Base for Autoimmunity Research Foundation, in 2004 133 million people (half of all Americans) live with chronic conditions. This accounts for 83% of the health care spending, and those with 5 or more chronic conditions have an average of 15 physician visits per year, with more than 50 prescriptions per year (Wood, 2004). The Journal of the American Medical Association published a paper in 2010, highlighting the rate at which chronic health conditions among children in the United States increased from 12,8% in 1994 to 26,6% in 2006 (Van Cleave et al, 2010).

According to the International Journal of Endocrinology the global emergence of obesity increases the risk of developing chronic metabolic disorders, which is associated with chronic systemic inflammation. From 2005-2006 it has shown that 33.3% of men and 35.3% of women were obese (Hernandez et al, 2013).

The incidence and prevalence of Inflammatory bowel disease re increasing with time and in different regions around the world (Molodecky et al, 2012). In one of the largest studies, based upon nine million health insurance claims, the prevalence of ulcerative colitis in adults in the United Sates was 238 per 100,000 population, and the prevalence of Crohn's disease was 201 per 100,000 population.

Rheumatoid arthritis (RA) and osteoarthritis (OAO) are the two most common rheumatic diseases, accounting for a large percentage of disability worldwide, creating huge health, social and economic burdens (Sanga, 2000).

Gout is the most prevalent form of inflammatory arthritis. The American College of Rheumatology has shown that the prevalence of gout in the U.S. has risen over the last twenty years which currently affects 8.3 million (4%) Americans. This may be associated with a higher increase in obesity and hypertension (Wiley-Blackwell, 2011)

### **A Historical overview of inflammation**

Infections caused by Group A Streptococcus (GAS) is a human pathogen which is responsible for many diseases, ranging from streptococcal pharyngitis to impetigo. Infections which were caused by GAS have been documented as far back as 6500 BC. In the late 17<sup>th</sup> century, **Thomas Sydenham** clinically distinguished scarlet fever from measles (Leday, 2006).

Records of holistic medicine go back to the Egyptian god of medicine, **Imhotep**, who lived in 2980 BC. The origins of Egyptian medicine lie in religion and spirituality, and it was believed that the gods intervened in matters of health and disease. At that time it was recognised that blood was the nutritive and regulatory substance and the heart was the centre of the circulatory system. It was widely recognised that respiratory patterns influenced blood circulation.

Early concepts about inflammation were largely derived from intuition rather than careful scientific investigation, but which provided the framework for critical experimentation in the later centuries. The history of inflammation dates back to the ancient Egyptian and Greek cultures. In 1650 the ancient Egyptians recorded the earliest transcripts on **papyrus** (Nordqvist, 2012).

**Hippocrates** (460-370 BC) introduced the term, 'wound putrefaction' ('sipsi' – make rotten), meaning enzyme decomposition, especially by proteins, with the production of foul-smelling compounds (Saunders, 2007).

**Galen** (130-201 AD) viewed inflammation, particularly pus, as part of the beneficial reactive response to injury (Phlogosis), rather than a superimposed pathology (Scott et al, 2004; Silva, 1978).

**Avicenna** (979-1037 BC) observed that the coincidence of blood putrefaction, namely, septicaemia was usually accompanied by fever.

The doctrine of the four cardinal signs of inflammation, namely: redness (rubor), swelling (tumor), heat (calor) and pain (dolor), was originally termed by **Aulus Cornelius Celsus** in the 1st century AD (Rather, 2012).

The French chemist, **Louis Pasteur** (1822-1895) discovered that tiny single cell organisms caused putrefaction. He called them bacteria or microbes and correctly deduced that these microbes could be causing disease (German Sepsis Society, 2013). Louis Pasteur linked the decay of organic substances to the presence of bacteria and microorganisms, which were killed by heating.

**Rudolph Virchow** (1821-1902) was a German physician, anthropologist, politician and founder of the field of cellular pathology. He viewed inflammation as inherently pathological. He stressed that most of the diseases of mankind could be understood in terms of the dysfunction of cells (Edwards (2013). His theory of cellular pathology became a basis for the understanding and fight against pathological processes in living organisms.

Virchow described the inflammatory process as having been derived from the increased activity (nutritive irritability) of the cell to find the appropriate source of food in the surrounding tissues. He concluded that 'the inflammatory reaction is a consequence of an excessive intake by interstitial cells of food from the liquid part of the blood, filtering through the vessel wall', which would result in hypertrophy, or degeneration of the cells, which would multiply to form an inflammatory tumour (Silva, 1978).

Virchow created the new paradigm of cellular pathology when he critically analysed the meaning of the four key symptoms of inflammation and proposed that inflammation constitutes various inflammatory processes. He is also said to be accredited to have introduced the fifth cardinal sign – "*function laesa*", or loss of function, whereby he viewed inflammation as inherently pathological. He highlighted the importance of the inflammatory stimulus (Heidland et al, 2006). In contrast with Galen, Virchow viewed inflammation as inherently pathological (Scott et al, 2004).

**Elie Metchnikoff** (1845-1916) is considered to be the father of natural immunity, and, together with Paul Ehrlich, they were the pioneers of cellular and humoral immunology. Metchnikoff is recognised for the biological significance of leukocyte recruitment and phagocytosis of microbes in host defence against infection, inflammation and immunity (Gordon, 2008). He observed that neutrophil granulocytes (microphages) were removed from the inflamed site by being ingested by macrophages while still intact (Savill, 1997).

**Sir Joseph Lister** (1827-1912), the Father of modern surgery, introduced the antiseptic method by disinfecting with carbolic acid, which was also used during this period as an effective disinfectant in sewers. He also sprayed the air with carbolic acid to kill airborne germs. Lister is quoted to have said: 'Anyone trying to wire the broken pieces together without the antiseptic technique would be faced with an infected knee and hospital gangrene' (Lamont, 1992). He also introduced sterilised catgut for internal sutures.

**Friedrich Daniel von Recklinghausen** (1833-1910) characterized the pus cells in acute inflammation, and he showed that pus cells could migrate from the places of their origin in the interstitium to other tissues and epithelial cells. He also contributed to the concept of phagocytosis (Heidland et al, 2009).

**Julius Friedrich Cohnheim** (1839-1884) observed the dilatation of the arteries and veins, adhesion of colourless cells to the endothelial cells, and the subsequent transmigration from the capillaries and venules into the interstitial space (Heidland et al, 2009). Cohnheim was Virchow's pupil, produced many observations which are the antecedents of modern concepts in inflammation. He showed that the origins of pus cells are from the blood and not from local tissue elements, as Virchow believed (Prichard, 1961).

**Ignaz Semmelweis** (1818-1865) deduced that childbed fever was caused by "decomposed animal matter that entered the blood system". He introduced hand washing with a

chlorinated lime solution before every gynaecological examination, but the hygienic measures were not accepted at that time (German Sepsis Society). Semmelweis observed the significant effect of hygienic measures on decreasing the mortality of women during childbirth (Rittirsch et al, 2008; Kubendiran, 2011).

**Hugo Schottmüller** (1867-1936) explained: "Sepsis is present if a focus has developed from which pathogenic bacteria, constantly or periodically, invade the blood stream in such a way that this causes subjective and objective symptoms." He also maintained that: "A therapy should not be directed against bacteria in the blood but against the released bacterial toxins' (German Sepsis Society).

**Roger C. Bone** (1941-1997) defined sepsis as "an invasion of microorganisms and/or their toxins into the bloodstream, along with the organism's reaction against this invasion." He influenced the development of new therapeutic strategies by having elucidated the various stages or physiologic alterations that occur in the septic patient (Balk, 2011).

About a century ago Paul Ehrlich proposed "horror autotoxicus" as immune reactivity against self, which is now called autoimmunity. In 1957 Burnet and others demonstrated the presence of autoantibodies and provided a theoretical basis for auto reactivity (Amagai & Matsushima, 2010).

Advances in **microscopy** and cell biology in the 19th century gave rise to cell based definitions of inflammation. Researchers began to question whether inflammation was a single process. In the middle of the 19<sup>th</sup> century scientific methods were vigorously applied to ascertain the causes of many infections by germs and viruses. By the end of the 19th century it was acknowledged that changing cell populations arising from both the blood and local proliferation were a key feature of many models of inflammation (Scott et al, 2004).

## **Summary**

The pioneers of individuals who recognised and understood the processes and mechanisms of inflammation have led to many advances in the field of inflammatory diseases. However, the global increase of disorders associated with poor eating habits, smoking, lack of exercise and sleep, are just a few examples of increasing incidences and prevalence of chronic inflammatory diseases.

The role of lifestyle factors plays a pivotal role in the overall health and wellbeing of an individual. This includes sensible choices for living life as healthy as possible within the parameters of each person's ideal Temperament, which considers: environmental air and breathing, food and drink, movement and rest, sleep and wakefulness, emotions and elimination and retention. Other interventions to live a healthy anti-inflammatory lifestyle, or to assist the body to restore it back to health, include Tibb herbal medication, herbal stimulants, vitamins, as well as tissue salts.

In order to change the paradigm of a disease-based approach to a person-centred one, a conscious shift from fearing symptoms to understanding the innate healing ability of Pheis to restore internal balance is needed. The aim is to assist Pheis in the healing process and not to stop or interrupt its progress.

## **References**

Nordqvist, C. (2012). *What Is Inflammation? What Causes Inflammation*. [Online]. Available <http://www.medicalnewstoday.com/articles/248423.php>

Scott, A., Khan, K.M., Cook, J.L., Duronio, V. (2004). *What is "inflammation"? Are we ready to move beyond Celsus?* An International peer-reviewed journal of sport and exercise medicine. *Br J Sports Med* 2004; 38:248-249 doi:10.1136/bjsm.2003.011221. [Online]. Available <http://bjsm.bmj.com/content/38/3/248.full>

Saunders. (2007). *Dorland's Illustrated Medical Dictionary*. USA: Elsevier.

Merck Animal Health (2013). *Pyrexia and Inflammation*. [Online]. Available <http://www.banamine.com/research/pyrexiaandinflammation.asp>

Hyman, M. (2012). *UltraWellness Lesson 2: Inflammation & Immune Balance*. [Online]. Available <http://drhyman.com/blog/2010/04/28/ultrawellness-lesson-2-inflammation-immune-balance/>

Stankov, S.V. (2012). *Definition of Inflammation, Causes of Inflammation and Possible Anti-inflammatory Strategies*. *The Open Inflammation Journal*, 2012, 5, 1-9. [Online]. Available <http://benthamscience.com/open/toinfj/articles/V005/1TOINFJ.pdf>

Gabalawy, H.; Guenther, L.C.; Bernstein, C.N. (2010). *Epidemiology of immune-mediated inflammatory diseases: incidence, prevalence, natural history, and comorbidities*. *J Rheumatol Suppl*. 2010 May; 85:2-10. doi: 10.3899/jrheum.091461. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/20436161>

Glynn, J. (2013). Personal notes from an email to Linda Mayer.

Wood, R. (2004). *Current prevalence of chronic diseases in the United States*. [Online]. Available <http://mpkb.org/home/pathogenesis/epidemiology>

Van Cleave, J.; Gortmaker, S.L.; Perrin, J.M. (2010). *Dynamics of obesity and chronic health conditions among children and youth*. *JAMA*. 2010; 303:623-30. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/20159870>

Hernandez, H.R.; Simental-Mendia, L.; Rodriguez-Ramirez, G.; Reyes-Romero, M. (2013). *Obesity and Inflammation: Epidemiology, Risk Factors, and Markers of Inflammation*. [Online]. Available <http://www.hindawi.com/journals/ije/2013/678159/>

Molodecky, N.A.; Soon, I.S.; Rabi, D.M.; Ghali, W.A.; Ferris M.; Chernoff, G.; Benchimol, E.I.; Panaccione, R.; Ghosh, S.; Barkema, H.W.; Kaplan, G.G. *Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review*. *Gastroenterology*. 2012 Jan; 142(1):46-54.e42; quiz e30. doi: 10.1053/j.gastro.2011.10.001. Epub 2011 Oct 14. Available <http://www.ncbi.nlm.nih.gov/pubmed/22001864>

Sanga, O. (2000). *Epidemiology of Rheumatic Diseases*. *Rheumatology* 2000;39 (suppl.2):3-12. [Online]. Available [http://rheumatology.oxfordjournals.org/content/39/suppl\\_2/3.full.pdf](http://rheumatology.oxfordjournals.org/content/39/suppl_2/3.full.pdf)

Wiley-Blackwell. (2011). *Gout Prevalence Swells in U.S. Over Last Two Decades; Increase in Obesity and Hypertension Are Likely Contributors*. [Online]. Available <http://www.sciencedaily.com/releases/2011/07/110728082551.htm>

Leday, T. (2006). *Use of an Animal Model of Group A Streptococcal Infection to Identify Factors Important for Virulence*. PDF version: [Kevin S. McIver Melanie H. Cobb Eric J. Hansen - Repositories](#). [Online]. No web page reference.

Rather, L.J. (1971). *Disturbance of function: The legendary fifth cardinal sign of inflammation, added by Galen to the four cardinal signs of Celsus*. Department of Pathology Stanford University School of Medicine. [Online]. Available <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1749862/pdf/bullnyacadmed00204-0099.pdf>

No author. *Sepsis History*. German Sepsis Society. [Online]. Available <http://sepsis-gesellschaft.de/DSG/Englisch/Disease+pattern+of+Sepsis/Sepsis+History?iid=2>

Edwards, S.A. (2013). *Rudolph Virchow, the father of cellular pathology*. [Online]. Available <http://membercentral.aaas.org/blogs/scientia/rudolph-virchow-father-cellular-pathology>

Silva, M. R. E. (1978). *A Brief Survey of the History of Inflammation*. Agents and actions vol. 8/1-2, Basel. [Online]. Available <http://link.springer.com/article/10.1007%2FBF01972401#page-2>

Heidland, A., Klassen, A., Rutkowski, P, and Bahner U. (2006). *The contribution of Rudolf Virchow to the concept of inflammation: what is still of importance?* *J. Nephrol.* May-Jun; 19 Suppl 10:S102-9. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/16874721>

Gordon, S. (2008). *Elie Metchnikoff: father of natural immunity*. *Eur J Immunol.* 2008 Dec; 38(12):3257-64. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/19039772>

Savill, J. (1997). *Apoptosis in resolution of inflammation*. [Online]. Available <http://www.jleukbio.org/content/61/4/375.full.pdf>

Lamont, A. (1992). *Joseph Lister: Father of Modern surgery*. [Online]. Available [http://www.answersingenesis.org/articles/cm/v14/n2/joseph-lister#fnList\\_1\\_5](http://www.answersingenesis.org/articles/cm/v14/n2/joseph-lister#fnList_1_5)

Heidland, A., Klassen, A., Sebekova K, Bahner U. (2009). *Beginning of modern concept of inflammation: the work of Friedrich Daniel von Recklinghausen and Julius Friedrich Cohnheim*. *J Nephrol*. 2009 Nov-Dec; 22 Suppl 14:71-9. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/20013736>

Prichard, R. (1961). *Selected Items from the History of Pathology*. *Am J Pathol*. 1979 November; 97(2): 314. [Online]. Available <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2042458/pdf/amjpathol00237-0113.pdf>

Rittirsch, D.; Flierl, M.; Ward, P. (2008). *Harmful mechanisms in sepsis*. *Nat Rev Immunol*. 2008 October; 8(10): 776–787. [Online]. Available <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2786961/>

Balk, R. (2011). *Roger C. Bone, MD and the evolving paradigms of sepsis*. *Contrib Microbiol*. 2011; 17:1-11. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/21659744>

Amagai, M.; Matsushima, K. (2010) *Overview on autoimmunity and auto inflammation*. [Online]. Available [http://www.jsir.gr.jp/journal/Vol31No1/pdf/06\\_S1\\_50.pdf](http://www.jsir.gr.jp/journal/Vol31No1/pdf/06_S1_50.pdf)