

Inflammatory Diseases, Processes and Outcomes

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The underlying causes for many diseases are the result of chronic systemic inflammation, such as obesity, diabetes, inflammatory bowel disease, rheumatoid arthritis, and osteoarthritis, vascular diseases and even cancer and Alzheimer's disease.

Lifestyle-related diseases are becoming more synonymous with chronic systemic inflammation because of an imbalance of the internal environment in the body.

Atherosclerosis is now recognized as a diffuse, multisystemic, and chronic inflammatory disorder involving the vascular, metabolic, and immune systems, with various local and systemic manifestations.¹

Considerable evidence gained over the past decade has supported the conclusion that neuro-inflammation is associated with Alzheimer's disease pathology.²

Low-grade infection plays a significant role in cardiovascular disease. Chlamydia pneumoniae, helicobacter pylori, herpes simplex virus, streptococcus, or cytomegalovirus, can lead to chronic inflammation. This results in high levels of C-reactive protein (CRP), which is produced in the liver, and which indicates chronic inflammation. Initially it is produced to fight infection, help clear away dead bacteria, and promote healing. As long as inflammation persists, blood levels of CRP remain high. If this condition is prolonged, it will likely play a role in atherosclerosis. CRP levels are one of the best tools for identifying future risk of cardiovascular disease.³

Inflammation may occur in the absence of infection when tissues are damaged, and this inappropriate response contributes to diseases such as heart attacks and strokes.

Researchers at the University of Calgary are using an innovative new imaging technique to study how white blood cells (neutrophils) respond to inflammation, and have revealed new targets to inhibit the response. This is done by examining real-time videos of the white

blood cells activity at the sites of inflammation. Damaged tissue can release signals that attract white blood cells, and blocking this signal can prevent inappropriate inflammation.⁴

Researchers examined levels of several inflammatory markers. People who were metabolically healthy had reduced counts of white blood cells and acute-phase response proteins, which proliferate when inflammation occurs. Metabolically healthy people also had higher levels of adiponectin, a hormone that has an anti-inflammatory effect, compared to their metabolically unhealthy counterparts. Researchers found this inflammatory profile in both obese and lean people who were metabolically healthy. "Regardless of their body mass index, people with favorable inflammatory profiles also tended to have healthy metabolic profiles."⁵

The British Journal of Diabetes and Vascular disease has shown an important relationship between systemic inflammation and markers of liver function in overweight women. There is an incremental increase in the number of features of the metabolic syndrome and liver enzyme abnormalities, with increasing inflammation.⁶

Three Main Processes in Inflammation

1. The *arterioles* supply blood to the injury, resulting in an increase in its blood flow. There are changes in the vascular flow.
2. The *capillaries* become more permeable enabling blood proteins and fluid to penetrate into the interstitial spaces, i.e. between the tissues. This leakage of fluid is exudate, not transudate.
3. The *neutrophils* as well as *macrophages* move out of the capillaries and venules into the interstitial spaces. Both neutrophils and macrophages are white blood cells which have the ability to digest the invading microorganism.

Acute inflammation - pathway 1

The acute inflammatory response is the initial and rapid response of the body to the offending agent. It is of short duration, usually lasting from a few minutes to several days.

Sudden changes in excess of qualities will result in symptoms, which manifest at the qualitative level – acute conditions - and may impair functions of the body. Examples include rhinitis and seasonal affective rhinitis:

There is a formation of inflammatory exudates, which is a slow release of liquid, which contains proteins and leucocytes (white blood cells). They pass through the walls of intact vessels into the tissues which then become inflamed.

Its aim is to defend the body from further damage and/or invasion of pathogens. It does this by:

- Altering the vascular permeability of the capillaries;
- Increasing the flow of blood;
- Changing the structure of the cells to enable leucocytes and plasma proteins to leave the circulation and to accumulate at the site of the injury, in order to eliminate the offending agent.

This phase may be accompanied by the five cardinal signs of inflammation, which typically lasts for about 1-3 days. Not all of these signs may be present.

Examples of Acute Inflammation of Pathway 1:

- Acute rhinitis, also known as 'hay fever' – has qualities of Dryness with Heat.
- Acute bronchitis – has qualities of Heat with Dryness.
- Conjunctivitis – has qualities of Heat with Dryness.

Chronic inflammation - Pathway 2

Chronic inflammation may be due to continued physical or chemical stress, such as smoking, or infection. More often it is the result of biochemical influences, such as the imbalance of dietary fats, absence of specific substances that adversely affect the production of anti-inflammatory cells, as well as specific nutrient problems.⁷

Examples of Chronic Inflammation of Pathway 2:

- Tuberculosis - has qualities of Heat with Dryness.
- Bronchial asthma – of a Phlegmatic nature, has qualities of Cold with Moistness.
- Bronchial asthma – of a Melancholic nature, has qualities of Dryness with Cold.
- Rheumatoid arthritis – has qualities of Moistness with Heat.

Homeostasis and health are restored when inflammation is limited by anti-inflammatory responses that are redundant, rapid, reversible, localized, and adaptive to changes in input and integrated by the nervous system.⁸

Steps in the process of inflammation

1. Damaged tissues release histamine which causes increased blood flow to the site.
2. Histamines dilate the capillaries and cause a leakage of fluid which releases phagocytes and clotting factors.
3. Phagocytes engulf debris, bacteria and dead cells.
4. Platelets move out of the capillaries to seal wound.

The Stages of Inflammation

1. The first stage - The irritation

The irritation results in an inflammation in an effort for the body to aid in the healing process.

2. The second stage – Suppuration (the formation of pus)

The body produces pus in an effort to expel the toxins out of the body. The chemicals produced as a response to the damaged cells include histamine, bradykinin, and prostaglandins, which attract white blood cells called phagocytes that "eat" germs and dead or damaged cells. This process is called phagocytosis. Phagocytes eventually die. Pus is formed from a collection of dead tissue, dead bacteria, and live and dead phagocytes.⁹

3. The third stage – Granulation

Granulation is the formation of rounded, fleshy masses of tissue which is formed in the wound, which aids in the healing response.¹⁰

The Histology of Inflammation

There is a complex series of events:

- *Dilatation* of the arterioles, capillaries and venules;
- There is an *increase in permeability* and blood flow;
- There is an *exudation of fluids*, including plasma proteins, and
- There is *leucocyte migration* to the site of the focal point.¹¹

Outcomes of Inflammation

1. Complete resolution or remission

Physis has restored the harmony of the body. There are no permanent damages incurred in the body.

2. Healing by fibrosis occurs when:

- There is substantial loss of tissue
- Inflammation occurs in tissue which is unable to regenerate
- There is an excess of fibrin exudates which cannot be cleared. Fibrosis is the thickening and scarring of connective tissue, usually as a result of a physical injury and inflammation. In complete resolution and healing by fibrosis, connective tissue grows into the damaged tissue.

3. Formation of an abscess

Pus accumulates around the inflamed tissue, such as a boil, which has qualities of Dryness and Heat. Pus contains dead white blood cells, bacteria (alive and dead), and fragments of dead tissue. The reason for the formation of an abscess is the inability of Physis to overcome the offending agent, which is often from a bacterial infection.

4. Chronic inflammation occurs when:

- There is persistence of the agent causing the inflammation

- There is interference with the normal process of healing, which prevents Physis from overcoming and destroying the offending agent. The inflammation remains unresolved.

Chronic inflammation is a long-term inflammation, which can last for several months and even years. It can result from:

- Failure to eliminate whatever was causing an acute inflammation
- A chronic irritant of low intensity that persists.

Examples of diseases and conditions with chronic inflammation include: asthma, chronic peptic ulcer, tuberculosis, rheumatoid arthritis, chronic periodontitis, ulcerative colitis and Crohn's disease, chronic sinusitis, and chronic active hepatitis (there are many more).¹⁰

Factors affecting the outcome of acute inflammation

1. The severity of tissue damage.
2. The capacity of cells to divide.
3. The type of agent causing the damage.
4. The responsiveness of the host.
5. The site involved.

Examples of Inflammation of Tissues

1. Inflammation of the membranes of the nervous system - covering the brain and spinal cord producing, meningitis or of the brain itself, producing encephalitis.
2. Inflammation of the heart - producing myocarditis or endocarditis.
3. Inflammation of joints - producing rheumatoid arthritis.
4. Inflammation of the gut - causing inflammatory bowel disease.
5. Inflammation of the lung - causing pneumonia.¹²

The following examples will be discussed from a Tibb perspective, from pathway 1 and pathway 2:

A. Pathway 1 from a Tibb perspective

The following examples of rhinitis and seasonal rhinitis will illustrate the inflammatory process of pathway 1:

The Inflammatory Nature of Rhinitis

Rhinitis is inflammation of the mucous membrane of the nose. In acute catarrhal rhinitis, or coryza, there is an acute congestion of the mucous membrane of the nose, marked by dryness, followed by increases mucous secretion from the membrane, impeded respiration

through the nose, and pain.¹¹ This may also be accompanied by sneezing, itching of the nose and postnasal discharge.

The allergic inflammatory cascade is often characterized as having 3 components, including sensitization followed by an early- and late-phase response. These pathways work together within a complex interaction of a variety of cells, mediators and cytokines. It is within these pathways that targets for immunomodulation offer the greatest opportunities for pharmacologic interventions to prevent or ameliorate the signs and symptoms of allergic rhinitis.¹³

From a morphologic standpoint, the inflammatory nature of allergic rhinitis is readily apparent by the characteristic presence of basophilic and eosinophilic cells in nasal secretions, accompanied by mast cell and eosinophil infiltration of the epithelium and an increase in mucosal antigen-presenting cells, activated T lymphocytes, and up regulated endothelial expression of adhesion molecules.

Seasonal Allergic Rhinitis (SAR)



In seasonal allergic rhinitis antibodies coating the mucosa of the nose and conjunctiva and specific to a given pollen (antigen), combines with the pollen. This results in cell injury, causing a large amount of secretions, oedema of the mucosa, sneezing and local itching. When the offending pollen is blown away, or flushed out of the nasal passages with a nasal spray, the allergic condition ceases.

The cause of this cell stimulation is due to the release of histamine, which is a chemical compound of mammalian tissues Histamine causes:

- Dilation of capillaries,
- Contraction of smooth muscles, and
- Stimulation of gastric acid secretion that is released during allergic reactions causing the decarboxylation of histidine.¹⁴

Relief may be obtained by:

- Hypo-sensitization by repeated infections of the offending pollens in low concentrations.
- Administering anti-histamines, such as allergy pills or nasal sprays.
- Removal of the offending pollen, such as the use of an air conditioner in the home.
- Suppression of the immune response by means of corticosteroids.¹⁴

Tibb views seasonal allergic rhinitis as an excess of dryness with heat in the body resulting in inflammation. The body's own innate ability to heal itself, known as Physis, reacts by expelling the toxins from the body by stimulating the Phlegmatic Humour to reduce the dryness with heat by increasing moistness. This results in a watery nasal discharge, sneezing, itchy and watery eyes.

Individuals with a dominant/sub dominant bilious temperament (hot and dry) are mostly predisposed to SAR. Other Temperaments may also be affected by the sudden changes from a hot/dry environment.¹⁵

Treatment is aimed at:

- Avoiding the cause of the allergen.
- Supporting the body to assist in the elimination of toxins, such as:
- Nasal irrigations and steam inhalations.
- Cupping.
- Tibb medication, such as Joshina

It must be noted that the use of air conditioners increase the qualities of dryness with cold of the immediate environment.

B. Pathway 2 from a Tibb perspective

The following examples of rheumatoid arthritis and gout will illustrate the inflammatory process of pathway 2:



Rheumatoid arthritis

This is also known as low grade or systemic inflammation. If the inflammation is prolonged and has not resolved within a month, then the inflammation becomes chronic. The body does not have enough energy to cope with the immune defences, as the body is in contact with a persistent, injurious stimulant. This may last for a few months, which results in further destruction of tissue, resulting in fibrosis.

Prevention and effective treatment is important in managing chronic inflammation and reducing the risk of chronic disease.

Tibb's view on the types of arthritis and their management is dependent on the temperament of each person. For example, osteoarthritis is linked to an excess of coldness and dryness, whilst rheumatoid arthritis is generally associated with heat and moisture. Treatment would therefore be tailor-made to the specific condition, taking into account all aspects of the patient. In all cases, lifestyle adjustments would be advised. A diet high in

fruit and vegetables, whole grains and increased water intake would be beneficial, and avoiding caffeine products and smoking is strongly encouraged. Yoga exercises and walking would also assist patients in delaying degeneration. Tibb practitioners further recommend cupping and massage to relieve pain.¹⁶

Chronic inflammation may be due to continued physical or chemical stress, such as smoking, or infection. More often it is the result of biochemical influences, such as the imbalance of dietary fats, absence of specific substances that adversely affect the production of anti-inflammatory cells, as well as specific nutrient problems.⁷

Examples of Chronic Inflammation of Pathway 2:

Tuberculosis - has qualities of Heat with Dryness.

- Bronchial asthma – of a Phlegmatic nature, has qualities of Moistness with Cold.
- Bronchial asthma – of a Melancholic nature, has qualities of Moistness with Heat beginning stage and can lead to dryness with cold (nodular stage).
- Rheumatoid arthritis – has qualities of Moistness and Heat.

Homeostasis and health are restored when inflammation is limited by anti-inflammatory responses that are redundant, rapid, reversible, localized, and adaptive to changes in input and integrated by the nervous system.⁸

The immune system involuntarily mobilises an inflammatory response to get rid of pathogenic threats. If the inflammatory response is either deficient or excessive, it will have dire consequences, as follows:

- If there is a **deficient response** to the invading organism or substance this will result in an immunodeficiency, leading to infection and cancer.
- If there is an **excessive response** this will result in mortality and morbidity, such as in rheumatoid arthritis, diabetes and Alzheimer's disease (Tracey, 2002). The body tries to prevent collateral damage to tissues due to excessive immune activation.^{17,8}

Gout



Too much lactic acid results in an excess production of free radicals and inflammation by changing the pH (potential of Hydrogen) levels in the fluid surrounding the cells. This results in the poor functioning of muscles, with resultant injuries while doing exercises or in sports.¹⁸

The pH level in the body is the measurement of acidity and alkalinity. Lack of rest and exercise, chronic stress, and not eating enough fresh fruits and vegetables all contribute to creating more acidic environment in the body.

The pH level drops when the body becomes acidic, resulting in the loss of calcium and a depletion of oxygen in the blood. This leads to tiredness and exhaustion and the immune system is compromised, resulting in the growth of fungi, moulds, parasites, bad bacteria, and viral infections. Cancer thrives in an acid tissue pH/oxygen deficient environment.

An excess of acid in the blood causes acidic metabolic acidosis, which has destructive consequences, leading to chronic diseases, inflammation, auto-immune disorders, accelerated aging, as well as reduced physical performance and low energy.

The alkaline diet is the healthiest one, which is mostly vegetarian, and it includes, for example, fresh vegetables, some fresh fruits, soy products and some nuts, grains, and legumes. Foods which promote acidity include, for example, processed foods, white sugar, caffeine and alcohol.

Gout is inflammation of the joints which is associated with an excess of uric acid in the blood. Uric acid is produced in the liver and enters the bloodstream. If too much lactic acid is produced, or if the body excretes too little of the lactic acid, monosodium urate crystals accumulate, which cause inflammation and pain. People who have gout are more at risk of developing kidney stones.

Chronic gout occurs can lead to a condition called Tophaceous gout, which is the accumulation of a large amount of uric acid in the joints, cartilage and bones. The urate causes a nodule (tophus) which causes an erosion of bone which it is near to. It can cause inflammation which is similar to an acute gouty attack.¹⁹

Summary

In Tibb, every illness has one or more identifiable causes/s with a definite pathway from health to disease, as well as the reversal of a diseased state to health. Tibb believes that a disease results from an alteration in the temperament, humour, structure and function of a cell, tissue or organ of an individual from any internal or external cause. Pathology is viewed by Tibb as a state of imbalance in the body which alters the stability of the internal environment of the body.

Acute inflammation is the initial and rapid response of the body to try to get rid of the offending agent, which may temporarily impair the functioning of the body, as in rhinitis.

Chronic inflammation is a long-term inflammatory response as a result of the failure of the body to rid itself of the offending agent, as in rheumatoid arthritis.

Inflammation actually assists the body to heal wounds and damaged tissue, which would otherwise cause more and more destruction of the affected tissue and organ. The stages

and processes of inflammation play an integral role in the healing response by releasing immune cells into the bloodstream. Inflammation prevents the spread of damaged cells to other areas of the body by getting rid of the dead cells.

However the inflammatory responses may be harmful, such as in an anaphylactic shock or it may form fibrous bands and plaques, leading to intestinal obstruction and impair the functioning of the heart.

As inflammation is an important manifestation of the natural body's response to injury, this process should not be impeded, but rather to assist Physis to go through the various stages of the inflammatory process in order to facilitate healing.

References

1. Spagnoli L.G.; Bonanno, E.; Sangiorgi, G.; Mauriello, A. *Role of Inflammation in Atherosclerosis*. J Nucl Med 2007; 48:1800–1815. [Online]. Available <http://interactive.snm.org/docs/jnm038661.pdf>
2. Tuppo EE, Arias HR. (2005). *The role of inflammation in Alzheimer's disease*. Int J Biochem Cell Biol. 2005 Feb;37(2):289-305. [Online]. Available <http://www.ncbi.nlm.nih.gov/pubmed/15474976>
3. Giampapa, V.; Pero, R.; Zimmerman, M. (2004). *The Anti-Aging Solution 5 Simple Steps to Looking and Feeling Young*. [Online]. Available http://healthpsychology.ir/files/site1/pages/Free_Books/6the_anti_aging_solution.pdf
4. Kubes, P. (2010). *Images shed new light on inflammation*. [Online]. Available <http://medicine.ucalgary.ca/about/inflammationpaulkubes>
5. Gingery, J.G. (2013). *Low inflammation may explain healthy metabolic status in some obese people. Chronic inflammation could signal higher risk of diabetes, heart disease*. [Online]. Available http://www.eurekalert.org/pub_releases/2013-08/tes-lim082313.php
6. Browning, L.M.; Krebs, J.D.; Siervo, ; Hall, R.H.; Finer, N. Allison, M.E.; Jebb, S.A. (2008). *Inflammation Is Associated With Liver Function Markers, Independent of Other Metabolic Risk Factors in Overweight Women*. British Journal of Diabetes and Vascular Disease. 2008;8(2):73-76. [Online]. Available http://www.medscape.com/viewarticle/574651_2
7. Maffetone, P. (2002). *The ABCs of Chronic Inflammation*. [Online]. Available [http://content.bandzoogle.com/users/cippianhotmail/files/ABCs_of_Inflammation_-_update_4-08\(1\).pdf](http://content.bandzoogle.com/users/cippianhotmail/files/ABCs_of_Inflammation_-_update_4-08(1).pdf)
8. Tracey, K.J. (2002). *The Inflammatory Reflex*. Laboratory of Biomedical Science, North Shore-LIJ Research Institute: New York. [Online]. Available http://www.tedpriebe.com/documents/the_inflammatory_reflex.pdf
9. Dugdale, D.C., Henochowitz, S.I.; Zieve, D. (2013). *Immune Response*. [Online]. Available <http://umm.edu/health/medical/ency/articles/immune-response>

10. Nordqvist, C. (2012). *What Is Inflammation? What Causes Inflammation*. [Online]. Available <http://www.medicalnewstoday.com/articles/248423.php>
11. Saunders. (2007). *Dorland's Illustrated Medical Dictionary*. USA: Elsevier.
12. Dean, J. (2011). *Hyperbaric oxygen and inflammation*. [Online]. Available http://www.foodsmatter.com/natural_medicine_comp_therapies/oxygen_therapy/articles/oxygen_inflammation.html
13. No author. (2006). *Inflammatory Nature of Allergic Rhinitis: Implication for Future Therapies*. *Medscape Allergy & Immunology*. 2006;6(1). [Online]. Available http://www.medscape.org/viewarticle/532192_2
14. William, D. (2011). *Pathophysiology of Pollinosis - Seasonal Allergic Rhinitis Caused by Pollens and other irritants*. [Online]. Available <http://dwilliam.hubpages.com/hub/PATHOPHYSIOLOGY-OF-POLLINOSIS-Seasonal-Allergic-Rhinitis-Due-to-Pollens>
15. Tibb Institute. (2013). *Tibb Training Manual. Lifestyle Advisor Training Course (revised)*. Johannesburg: IbnSina Institute of Tibb.
16. Bhikha-Vallee, N. (2009). *About Arthritis*. [Online]. Available <http://www.tibb.co.za/articles/about%20arthritis.pdf>
17. Van Westerloo, D.J. Giebelen, I.A.J.; Florquin, S.; Daalhuisen, J.; Bruno, M.J.; van de Vos, A.F.; Tracey, K.J.; van der Poll, T. (2005). *The Cholinergic Anti-Inflammatory Pathway Regulates the Host Response during Septic Peritonitis*. *J Infect Dis*. (2005) 191 (12):2138-2148. [Online]. Available <http://jid.oxfordjournals.org/content/191/12/2138.full>
18. Richards, B. (2013). *Reduce Excess Lactic Acid and Cellular Waste: Wellness resources*. [Online]. Available http://www.wellnessresources.com/health_topics/detoxification/lactic_acid.php
19. Kroner, Z. (2013). *Dr. Ronald Hoffman. Gout: A Detailed Discussion*. [Online]. Available <http://www.drhoffman.com/page.cfm/547>