Rheumatology throughout the Ages
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Objectives

• By the end of this Symposium participants will be able to:
  • To augment the knowledge and understanding of the history of rheumatology.
  • To augment the understanding of the influence of past medical information, ethics, professionalism and practices on present day rheumatology and other specialties.
  • To apply formal decision making from past masters not taught in medical school today into present evidence-based medicine.
  • List the various components of cultural diversities where applicable in rheumatology.

Rheumatology, the final frontier. These are the voyages of the Starship Enteropathy. Its five year mission to explore strange new diseases, to seek out new methods of evaluation and new treatments, to boldly go where no man has gone before!
Rheumatrek

Staring Your Host

• Captain William Rheumos Kirk and a Host of Famous Characters known as the Arthridites

What is Rheumatology?

• “The rheumtism is a common name for many aches and pains, which have yet no particular appellation, though owing to very different causes.”
  William Heberden (1710-1801)
  Commentaries on the History and Cure of Diseases, chapter 79

From arguably, one of the greatest physicians in modern times,

“When I noticed a patient suffering from arthritis coming in the front door, I felt like escaping through the back one.”
  Sir William Osler
So Let Us Begin Our Journey!

Starship Date 1111.1

• The Starship Enteropathy is near the planet Rheuma in the Heberden Galaxy. We have run into a meteor shower and are blasting our way out.
• The Enteropathy is significantly damaged and we will need to land on the Planet Rheuma to search the chemical TNF-alpha which provides the energy to go into warp speed.

We Find the Palace of Joints.

Here we meet Mr. Skeletos and his sidekick Bony Marone

Skeletos

• Skeletos invites us to view his palace and shows us his passion: Rheumatology.
• We viewed endless halls with paintings, sculptures, artifacts on Rheumatology from the planet Earth.

Then, Skeletos began to tell us the History of Rheumatology.

"Who controls the past controls the future. "Who controls the present controls the past."

George Orwell, 1949

Investigative Tools
The Historical Perspective

Historical Clues to Rheumatology
- Paleopathology
- Visual Arts
- Early Medical Literature
- Historical Figures
- Medical Museums

Paleopathology
- Paleopathology, a term popularized by Sir Marc Armand Ruffer (1859-1917), Professor of Bacteriology at the Cairo Medical School at the turn of the century, consists of the study of disease in human populations as revealed by their mummified and skeletal remains.

Dieppe and Rogers have commented that paleopathology provides the addition of a time dimension to the study of disease, which they aptly described as “two-dimensional epidemiology.”

Pitfalls with Paleopathology
- Circumstances of burial, often unknown
- Nature of the soil since burial in chalk will result in chemical changes so that the bones become light and pliable.
- Fossilized specimens undergo chemical changes, known as purites disintegration, which can lead to changes simulating periostitis.

Pitfalls with Paleopathology
- Roots encircling bones can also produce lesions on the surface of bones which may be interpreted as periosteal reactions
- Erosions of joints may occur as a result of soil erosion as well as a number of conditions, including frostbite, syringomyelia, leprosy and peripheral gangrene.
- Artefacts are innumerable and precipitate judgments and hasty conclusions which are best avoided.
Visual Arts and Literature

Early Medical Literature

- The study of early medical literature is seldom of particular value in view of the vagueness of the description.
- For example, Soranus of Ephesus (98-138AD) in his treatise *On Chronic Disease* describes polyarthritis affecting middle-aged men, causing the joints to "become twisted, with the toes and fingers either turned sideways, or bent over backwards, or rest immovable upon their neighbours."

Early Medical Literature

- This might not unreasonably be interpreted as RA, unless it is appreciated that the description includes an acute attack of gout with discharging tophi.
- Translators of early medical writings were often nonmedical.
- Usually, it is not possible to verify the accuracy of the translation so that the diagnosis can only be tentative.

Historical Figures

- In 1989, Appleboom reviewed a host of famous people who suffered from arthritis in his "The Past: A Gallery of Arthritis."
- Illnesses in notable historic figures can be useful in teaching medical students, both in terms of diagnosis and in highlighting the misery of the affliction suffered by patients such as the torment of Erasmus’s pustulotic arthro-osteitis and of Renoir’s RA.

Historical Figures

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<td>Renoir (1841-1919)</td>
<td>RA?</td>
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Museums

- Sadly, there has been a decline in interest in medical museums, despite the fact that many of the older museums contain much of current interest.
- For example, there is a remarkable collection of pathologic specimens in William Hunter’s collection in the University of Glasgow. This collection is of particular value because clinical histories, including details of surgical operations and postmortem findings, are available.
Sir William Osler (1849-1919), in his introductory lecture at the 45th Session of the Medical Faculty, McGill University in Montreal said the following of medical history:

"Remember you enter upon a glorious heritage; you will reap where you have not sown and gotten where you have not strained and the knowledge which is your privilege today to acquire so early has cost others. We are, all of us, debtors to our profession."

Hippocrates’ View

- In the fourth century B.C., the Greek physician Hippocrates developed a medical theory called humorism, which held that four humors (liquids) coursing through the human body determined one’s temperament and state of health.
- He used the term rheuma, which literally means "flowing," to describe an excess of the watery humor thought to flow down from the brain.
- The words rheuma and catarrhos ("flowing down") were used interchangeably by ancient Greeks to describe a variety of illnesses including joint problems.

Roots of Rheumatology

- 1st century AD—the term rheuma first appears in the literature.
- Rheuma refers to a substance that flows and probably was derived from phlegm, an ancient primary humor, which was believed to originate from the brain and flow to various parts of the body causing ailments.

Dr. Guillaume de Baillou, 
_L. Ballonius_ (1538-1616)

- 1642—the word rheumatism is introduced into the literature influenced by the French physician Dr. Guillaume de Baillou (Latin: Ballonius) who emphasized that arthritis could be a systemic disorder.
- The term rheumatism was used by the French physician Dr. Guillaume de Baillou who sought to distinguish noxious humors that affected joints from those that caused catarrh (hay fever, head colds, sinusitis, and the like).


Roots in Rheumatology

- 1928—The American Committee for the Control of Rheumatism is established.
- 1934—Renamed American Association for the Study and Control of Rheumatic Disease
- 1937—Renamed the American Rheumatism Association
- 1940—The terms rheumatology and rheumatologist were first coined by Drs. Hollander and Comroe.
- 1988—The American College of Rheumatology

Joel Ernest Goldthwait (1866-1961)

- A surgeon, organizer, innovator and fund-raiser, Joel Ernest Goldthwait, MD, was influential in the evolution of orthopedics and rheumatology.
- The 1912 report described the cases seen in the fledgling orthopedic department: diseases of the joints; chronic joint affections; congenital and acquired deformities of paralysis; static conditions of the feet; and affections of the spine, including scoliosis and postural deformities. It noted that a high proportion of research being performed arthroplasty and investigative treatments for scoliosis and secondary infected tubercular sinuses.
- An accomplished professional, Goldthwait continued to see patients until he reached 90.
The Classification of Rheumatic/Musculoskeletal Disorders

- 1904—Dr. Goldthwait, an orthopedic surgeon makes the first attempt to classify the arthridites
- 1964—The American Rheumatism Association (ARA) classification
- 1983—The ARA classification is revised
- Today, there are over 120 rheumatic/musculoskeletal disorders

Kirk:Skeletos and Bony Marone, What Do You Want for @TNF?

- Skeletos: My Dear Captain Kirk, all you have to do is to guess what rheumatic disease that I have and I will give you all the @TNF you want. Listen and you will learn!

Gout

- Has been recognized since antiquity.
- Descriptions of the disease date back to the times of Babylon.
- It was certainly well described by Hippocrates and evidence of the disease has been found in early skeletal remains.
- Lead detected in some of those remains suggests the possibility that some of this gout may have been saturnine.

Gout

- Called the ‘king of diseases’ and the ‘disease of kings’, gout is perhaps more the ‘disease of plenty’.
- The term ‘gout’ was not used until the 13th century, being derived from the Latin “gutta” (a drop) which reflects the notion that gout resulted from a local instillation of malevolent humor.
- These concepts are well illustrated in paintings of persons afflicted with gout.

Important Landmarks in the Hx of Gout

- 5th Century BC—Hippocrates described gout
- 1st Century AD—Seneca described the familial nature of gout
- 3rd Century AD—Galen described tophi
- 13th Century AD—Vieledherdouin drives the term ‘gout’
- 1679 Van Leeuwenhoek identified crystals in a tophi

Important Landmarks in the Hx of Gout

- 1683—Sydenham’s classic description of gout
- 1776—Scheele demonstrated uric acid in renal calculi
- 1798—Wollaston demonstrated uric acid in tophi
- 1814—Colchicine showed to be the effective component of Colchicum autumnale used in acute gout
Important Landmarks in the Hx of Gout

1848-Garrod demonstrated hyperuricemia in gouty patients
1896-Huber reported the first radiologic description of gout
1898-Fischer demonstrated uric acid to be a purine compound
1899-Freudweiler reproduced about gout by the injection of urate crystals
1913-Folin and Denis measured serum urate concentration biochemically
1936-Colchicine prophylaxis demonstrated to be efficacious
1950- Talbott et al and Gutman and Yu demonstrated probenecid to be a clinically useful uricosuric agent
1961-McCarty rediscovered urate crystals in gouty effusions
1963-Allopurinol developed as a clinically useful xanthine oxidase inhibitor
1967-Kelly et al. described HGPRT deficiency in patients with gout
1972-Sperling et al. demonstrated PRPP synthetase overactivity to be a cause of urate overproduction
1979-Schumacher demonstrated urate crystals in some uninvolved joints of patients with gout

13th-Century Europe and Gout

- In 13th-century Europe any joint ailment was called gutta (Latin, meaning "a drop") for a noxious humor falling drop by drop into the joint. Gout and gouty diathesis were used as broadly as the term arthritis is used today. Thomas Sydenham (1624-1689), a London physician who himself suffered from gout, distinguished this episodic disorder from acute arthritis that attacked young people (probably rheumatic fever) and from chronic crippling arthritis (probably rheumatoid arthritis) that came to be called rheumatic gout.

Punch Cures the Gout, the Colic and the ‘Tisick

- By James Gillray on 7/13/1799 and published by H.Humphrey
- Gillray juxtaposes a popular 18th century drinking song with a social commentary on alcohol abuse of the upper class.
- The song is known as “Landlord Fill the Flowing Bowl” or the “Three Jolly Coachmen.” A verse applicable to this picture is the following:

Punch cures the gout, the colic and the physic,
Punch cures the gout, the colic and the phylitic,
And is to all men, And is to all men, the very best of physic
Punch Cures the Gout, the Colic and the ‘Tisick

- In this etching, 3 individuals find medicinal cure for their ailments in the punchbowl.
- The bowl is filled with punch, a mixture of at least 5 or more ingredients of liquor and fruit juices made popular in the 18th century.
- Only the wealthy could have afforded the Chinese porcelain vessel on the table.

Pseudogout

- With the advent of skeletal radiography, it became apparent that articular cartilage calcification (chondrocalcinosis), first noted in pathologic specimens in the 19th century by Adams (1857), is a common phenomenon occurring alone or in association with arthritis.

Rheumatic Fever

- “The sad list of symptoms begins with chills and shivers; these are followed immediately by heat, disquietude, thirst, and the other concomitants of fever. One or two days after this (sometimes sooner) the patient is attacked by severe pains in the joints... This pain changes its place from time to time, takes the joint in turns, and affects the one that it attacks lasts with redness and swelling. Sometimes during the first days the fever and the above-named symptoms go hand in hand; the fever, however, it grows worse. The febrile has, in that case, been transferred to the joints.”
  

Punch Cures the Gout, the Colic and the ‘Tisick

- The 3 jolly characters suffer from maladies in the song.
- The obese gentleman has gout in his extremities. Gout was believed to attack men who indulged in heavy wines and rich food. The man has wrapped his legs, feet and hand in soft flannel as a means to induce perspiration, thought to be a safe and efficacious method to discharge gouty material.

Pseudogout

- Clinical and pathologic diversity was first emphasized by Mandl (1927) who distinguished in the knee primary CC (asymptomatic, bilateral, no cartilage damage) from secondary CC (symptomatic, localized, often post-traumatic, with cartilage fibrillation.

Rheumatic Fever

- Heart failure in young people with "acute rheumatism" was first designated rheumatic fever in 1808, and this is one of the few rheumatology terms whose meaning hasn't changed.
Rheumatoid Arthritis

- Evidence of RA in Europe first appeared in early 17th century art, especially by the Dutch Masters.
- It is possible that RA was recognized in 1676 by Sydenham who mentioned a joint disease characterized by chronicity and deformities, possibly including swan neck deformities, suggestive of RA.

“La Goutte Asthénique Primitive”

- The first entirely convincing description of RA was published in the year 1800 by Landré-Beauvais.
- He named the disease “la goutte asthénique primitive,” and he felt that it had not been described previously.

Rheumatoid Arthritis

- In 1703, Musgrave described a chronic polyarthritis which, he felt, was different from gout and rheumatic fever.
- Heberden may have known the disease near the end of the 18th century.

“La Goutte Asthénique Primitive”

- The patients described by Landré-Beauvais were 9 women, who were asthenic, unlike the robust and wealthy persons who were mostly male, robust and wealthy with gout.
- Furthermore, this new disease started as a polyarthritis, not as an episodic monoarthritis, the way that gout usually does.
**“La Goutte Asthénique Primitive”**

- According to Landré-Beauvais, the new disease caused permanent swelling of the joints and deformities, and after several years, some patients became severely disabled.
- Autopsy showed ulcers of the cartilage, bone destruction and osteopenia, but no tophi.

**Rheumatoid Arthritis**

- Although intermittent case series were subsequently reported, the disease was not fully recognized until it was defined by Garrod in 1859.
- He named it ‘rheumatoid’ arthritis to distinguish it from the two well-known forms arthritis, rheumatic fever and gout.

**Alfred Garrod and RA**

- British physician A. B. Garrod, whose practice was devoted to studying “articular affections,” introduced the term rheumatoid arthritis (from the Greek arthron, “joint”) in 1858 because, he insisted, the majority of patients said to have “rheumatic gout” had an affliction that was related “neither to true gout or to true rheumatism.” Although the British Ministry of Health officially adopted the name in 1922, rheumatoid arthritis remained a controversial term until the early 1940s when the American Rheumatism Association followed suit.

**Rheumatoid Arthritis**

- By the early 20th century, RA was viewed as separate from osteoarthritis (‘arthritis deformans’).
- In 1957, Charles Short described RA definitively and clearly set it apart as a defined clinical entity distinct from the seronegative spondyloarthropathies, crystal-induced disease, osteoarthritis, systemic lupus erythematosus, and many other conditions.

**Rheumatoid Arthritis**

- Examination of skeletal remains from antiquity in Europe and North Africa shows various forms of arthritis, including osteoarthritis, ankylosing spondylitis and gout.
- But characteristic rheumatoid lesions with marginal erosions at the bone–cartilage interface of the small joints are strikingly absent.
- In contrast, palaeopathological studies of specimens dating back several thousand years show clear evidence of rheumatoid arthritis (RA) in Native American tribes in North America.
- The prevalence of RA in the same regions today remains extraordinarily high, with over 5% of individuals affected in some groups.

**Rheumatoid Arthritis as seen by Van Gogh 100 years ago**
Osteoarthritis

- Osteoarthritis (from the Greek osteon, "bone") was commonly used as a synonym for rheumatoid arthritis beginning in the 1860s. A clear distinction between the two ailments began emerging at the turn of the century. In 1904, Boston physician Joel E. Goldthwait described differences he saw using X-rays. In 1909, physicians Edward H. Nichols and Frank L. Richardson of New York reported on the pathological differences between osteoarthritis and rheumatoid arthritis. Since that time, the labels have stuck.

Ankylosing Arthritis

- The first description of ankylosing spondylitis (from the Greek ankylos, bent or crooked, and spondylos, spine or vertebra) appeared in 1695 when a skeleton unearthed from a French cemetery was found to have a spine with vertebral bones "so straightly and intimately joyned...they really made but one uniform continuous Bone." Several clinical reports published during the 1850s described patients with bent, inflexible spines including a 31-year-old man whose spine had scarcely any perceptible flexure in it, the stooping being apparently confined to the motion of the pelvis on the thigh. Thought by some doctors to be caused by trauma to the spinal cord, the condition was generally accepted to be a rheumatic disease by the early 1900s and was called "rheumatoid spondylitis." The term ankylosing spondylitis was officially adopted by the American Rheumatism Association in 1963.

Systemic Sclerosis

- Although there is evidence in the writings of Galen and Hippocrates of scleroderma, the first convincing description was of a 17-year-old woman in Naples in 1753. Her attending physician, Cario Curzio, successfully managed her case with bloodletting, warm milk and 'small doses of quicksilver.'

- However, it was only in the mid-19th century that scleroderma was established as a clinical entity and given its current name.

- Maurice Raynaud described Raynaud’s phenomenon in 1865 and Jonathan Hutchinson reported a case of Raynaud’s phenomenon who had definite features of scleroderma in 1883.

- Although William Osler referred to the systemic nature of the disease in his 1894 textbook of medicine, it was not until 1945 that Goetz proposed the term, progressive systemic sclerosis to emphasize the visceral disease.

- In 1964, Winterbauer described the CRST syndrome (now the CREST syndrome of calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia).

- In 1969, a major pathologic review delineated the widespread fibrotic and vascular disease of scleroderma.
**Inflammatory Muscle Disease**

• Between 1886 and 1891, several German clinicians published accounts of patients with polymyositis and/or dermatomyositis.
• Two thirds of the 19th century descriptions best fit polymyositis, a term introduced by Wagner in 1886, while one third described dermatomyositis, a term coined by Unverricht in 1891.

**Sjögren’s Syndrome**

**Synonyms of Sjogren’s Syndrome**

• Mikulicz’s disease
• Gougerot’s syndrome
• Sicca syndrome
• Autoimmune exocrinopathy
• Autoimmune epithelitis

• The first reported case of unequivocal dermatomyositis associated with carcinoma was in 1916, although a causal association between these two disease processes was not suggested until 1935.

• The various clinical features of keratitis, dry mouth and salivary gland enlargement were first described in the late 1800s by Hadden, Leber, and Mikulicz.
• However, it was not until the work of Gougerot in France in 1925 and of Sjögren in 1933 that association of these findings with polyarthritis and systemic disease was fully appreciated.

• Sjögren, a Swedish ophthalmologist, wrote the classic monograph on the disease in which he emphasized that the eye manifestations are local findings of a systemic disorder.
• In 1953, Morgan and Castleman showed that the intense focal lymphocytic infiltrate of the parotid gland, described in Mikulicz’s patient about 60 years earlier, was identical to the characteristic findings in Sjögren’s Syndrome.
• This resolution of nomenclature was followed by an increasing recognition of the diverse clinical spectrum of Sjögren’s syndrome and, in the 1960s, by the discovery of autoantibodies in Sjögren’s syndrome patients.
"Three Stages of Women" by Klimt, 1905

- The painting presents its elemental message—"in life we are in death"—not only through the three principal characters, but also via a complex network of adjunct symbols.

- The women are encapsulated in a sea of bobbles representative of the life force.

- However, now the "column of life" is isolated within a surrounding void, which, despite the touch of Klimt's decorating hand, offers a far gloomier, more barren environment than the teeming cocoon within which the protagonists rest.

- Death—here, is represented by the color blue—awaits ominously on the horizon, winding its gossamer threads even about the legs of the innocent young mother.

Evidence of Temporal Arteritis: painting by Jan Van Eyck (c. 1385-1440) entitled "The Virgin with Canon Van der Paele," 1436. Notice the prominent arteries on the temples of the bishop.

Names Suggested for Giant Cell Arteritis by Various Authors

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<td>Hutchinson 1890</td>
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<td>Temporal arteritis</td>
<td>Horton et al 1932</td>
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<td>Horton's disease</td>
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<td>Giant cell arteritis</td>
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<td>Cranial arteritis</td>
<td>Kilbourne &amp; Wolff, 1946</td>
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<td>Granulomatous arteritis</td>
<td>McMillan, 1950</td>
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<td>Senile arteritis</td>
<td>Olhagen, 1963</td>
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<td>Polymyalgia arteritica</td>
<td>Hamrin, 1964</td>
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Title page of the article in the Archives of Surgery in which Hutchinson described a case of giant cell arteritis under the name thrombotic arteritis of the aged.

Title page of the article by Horton et al describing giant cell arteritis under the name temporal arteritis. This article contained the details of the first 2 cases described briefly in the Proceedings of the Staff Meetings of the Mayo Clinic (currently, Mayo Clinic Proceedings) in 1932.

From the article by Horton et al in which the details of the first 2 cases were described.

Names Suggested for Polymyalgia Rheumatica by Various Authors

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<td>Senile rheumatic gout</td>
<td>Bruce, 1888</td>
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<td>Secondary fibrositis</td>
<td>Slocumb, 1936 &amp; 1943</td>
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<td>Periarthrosis humeroscapularis</td>
<td>Meulengracht, 1945</td>
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<tr>
<td>Peri-extraarticular rheumatism</td>
<td>Holst &amp; Johansen, 1945</td>
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<td>Special arthritis of old age</td>
<td>Porsman, 1951</td>
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<td>Myalgic syndrome of the aged with systemic reaction</td>
<td>Kersley, 1951</td>
</tr>
<tr>
<td>Pseudo-polyarthritis rhizomélique</td>
<td>Forestier &amp; Certonoiny, 1953</td>
</tr>
<tr>
<td>Anarthritic rheumatoid disease</td>
<td>Bagratuni, 1953</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>Barber, 1957</td>
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</tbody>
</table>

Title page of the article by Bruce in the British Medical Journal in 1888 in which he described 5 cases of polymyalgia rheumatica under the name senile rheumatic gout.

History of Necrotizing Arteritis

Karl Rokitansky 1862
Adolf Kussmaul 1866
Rudolf Maier 1866
1903 Ferrari
1930 Arkin
1948 Davson, et al.
1948 Zeek
1954 Godman & Churg

Adolf Kussmaul
Historical Background of Vasculitis

- Some of the earliest investigations of patients with vasculitis were prompted by the recognition of arteritis, which in fact could be seen grossly as nodular enlargements in the arteries within the parenchyma and even in main visceral arteries such as the renal arteries, hepatic artery.
- There were many early reports. Certainly Karl Rokitansky described patients with what was in fact arteritis in his discussions of patients with aneurysms.
- But Kussmaul and Maier in 1866 really published one of the first detailed descriptions of vasculitis in patients. In the one patient that they described most carefully, the involvement was predominantly, at least, within arteries and could be seen grossly; but microscopically, it involved very small vascular radicals as well.

1866: Periarteritis Nodosa
Adolf Kussmaul and Rudolf Maier

- In their patient, the presentation was similar to what I’m sure you’ve seen in your own patients. There were the non-specific manifestations of a systemic inflammatory process—fever, anorexia, weakness. There were also indications of vascular involvement in the tissues—myalgia, paresthesia, abdominal pain, cutaneous nodules, and there was oliguria. The gross pathology, as I mentioned and, as was illustrated here in the article by Kussmaul and Maier, was predominantly nodular thickenings along arterial radicals. Histologically this was shown to be inflammation and necrosis.

The Beginnings of Classification Emerge

- So you can see that from the initial single category of necrotizing arteritis, some entities with specific features were being separated.
- At this point we really had still polyarteritis nodosa, Wegener's granulomatosis, and Churg-Strauss Syndrome.
- Zeek and Godman and Churg in the early 50s, and in fact beginning in the late 40s, added some substantial insight into the categories of necrotizing vasculitis.

Zeek and Classification of Vasculitis

- Although Zeek’s 1952 article is better known, her 1948 article really describes more carefully her perception of necrotizing vasculitis.
- And what she concluded was that there were two major forms of necrotizing vasculitis.
- There was what had been described, she felt, by Kussmaul and Maier that she was at that time calling periarteritis nodosa that had involvement of arteries but had no involvement of the lungs, and it had no involvement of vessels smaller than arteries.
Zeek's 1952 classification system for vasculitis

- Her 1952 article proposed an actual classification system for vasculitis:
  - What she called periarteritis nodosa; hypersensitivity angiitis, which is a small-vessel necrotizing vasculitis;
  - She was aware of the allergic granulomatosis and angiitis that we now call Churg-Strauss Syndrome;
  - She apparently was not aware of Wegener's granulomatosis being a type;
  - She also was aware that patients with rheumatic diseases developed forms of vasculitis;
  - And was aware of the large vessel form of vasculitis called temporal arteritis, which is now designated giant cell arteritis because it doesn't always affect just the temporal arteries.

Godman and Churg (1954)

1. Periarteritis nodosa (PAN) should be reserved for arteritis with macroscopic involvement of arteries.
2. A "microscopic" form of periarteritis nodosa (MPA) is more common and was called "hypersensitivity angiitis" by Zeek.
3. Wegener's granulomatosis and "allergic angiitis and granulomatosis" (Churg-Strauss) are related to each other and to MPA.

Vasculitis

- Godman and Churg also looked at systemic vasculitides. Of course, Churg had been involved with Strauss earlier in describing Churg-Strauss Syndrome.
- They came to some conclusions in 1954 which are basically, in my opinion, where we are today. They recognized again that periarteritis nodosa, as it was designated, affected mainly arteries and grossly visible arteries. But they concluded that there was a more common form of vasculitis that they referred to as the "microscopic form of periarteritis nodosa." They concluded that, in fact, this was the same category of vasculitis that Zeek was calling hypersensitivity angiitis. But they pointed out that there really was not good evidence for allergy in these patients and that isn't a good terminology. So they preferred the term "microscopic form of periarteritis." They also, of course, were aware of Wegener's granulomatosis.

Vasculitis

- In this 1954 article, they clearly described the major triad of Wegener's granulomatosis with systemic necrotizing angiitis, as they called it, necrotizing glomerulonephritis; and, of course, the granulomatous inflammation. And they also were, of course, aware of Churg-Strauss Syndrome since Churg had just been involved with describing this earlier. They concluded that because of the pathologic similarity, especially of the underlying small-vessel vasculitis, that Wegener's granulomatosis, Churg-Strauss Syndrome, and microscopic form of periarteritis were related and were distinct from and probably pathogenetically distinct from periarteritis nodosa or what we call polyarteritis nodosa. I would suggest that more recent data that I will review later supports this position that they put forward in 1954. These do appear to be related because they all are associated with ANCA. This process [polyarteritis nodosa], I believe, is distinct and now uncommon as we've pulled away from it many more specific forms of vasculitis.

Kawasaki's Disease

- In the 1960s, the final major category of necrotizing vasculitis was separated from the polyarteritis nodosa group, and this is Kawasaki's disease.
- Up until this point, there were other descriptions of this process sometimes referred to as infantile form of polyarteritis nodosa because Kawasaki's disease occurs most frequently in young children.
- However, Kawasaki's disease has another very distinctive component, and this is the mucocutaneous lymph node syndrome.
- So basically the diagnostic characteristic that separates Kawasaki's disease from polyarteritis nodosa is this mucocutaneous lymph node syndrome with erythematous and scaly mucosa and skin, especially on the digits, with a lymphadenopathy and with this necrotizing vasculitis that has a predilection for the coronary arteries and can produce aneurysms with thrombosis and myocardial infarction.
- The necrotizing lesion is similar to that of polyarteritis nodosa, although there are some subtle differences in general— a little less fibrinoid necrosis, a little more cellular character to the initial injury.
Lyme Disease

- Was first described as a separate entity in 1976 because of geographic clustering of children in Lyme, Connecticut who were believed to have juvenile rheumatoid arthritis.
- The rural setting of the case clusters and the identification of erythema migrans as a feature of the illness suggested that the disorder was transmitted by an arthropod.
Lyme Disease

• It soon became apparent that Lyme disease was a multisystem illness that affected primarily the skin, nervous system, heart or joints.
• Epidemiologic studies of patients with erythema migrans implicated certain *Ixodes* ticks as vectors of the disease.

Lyme Disease

• Lyme disease or Lyme borreliosis is now recognized as an important infectious disease in North America, Europe and Asia.
• In the USA, the infection is caused by *Borrelia burgdorferi*, whereas in Europe it is caused primarily by *Borrelia afzelii* and *Borrelia garinii*, and only these two species are responsible for the illness in Asia.

"He who can no longer pause to wonder and stand rapt in awe, is as good as dead; his eyes are closed."
by Albert Einstein

And Now The Quiz!

Question #1

Historical Clues to Rheumatology include all except for which of the following?

a. Paleopathology  
b. Astrological Information  
c. Visual Arts  
d. Early Medical Literature  
e. Historical Figures  
f. Medical Museums
**Question #2**
Who was the first physician to attempt to classify the arthritides?

a. Hippocrates  
b. Galen  
c. Sydenham  
d. Goldthwait  
e. Osler

**Question #3**
Gout comes from the Latin term *gutta* which means which of the following?

a. A Drop  
b. Pus  
c. Inflammation  
d. Swelling  
e. Redness

**Question #4**
Rheumatoid Arthritis was defined by Garrod in 1859 to distinguish this disease from which two well-known forms of arthritis?

a. Gout and Pseudogout  
b. Rheumatic Fever and Osteoarthritis  
c. Gout and Rheumatic Fever  
d. SLE and Vasculitis

**Question #5**
Lyme's Disease was named after which of the following?

a. Dr. Lucious Lyme who first described the disease  
b. The First Patient who had the disease, Lois Lyme  
c. The Lyme Phenomenon  
d. Lyme, Connecticut where it was first described.

**Answers to the Questions**
1. b—Astrological Information  
2. d—Goldthwait  
3. a—A Drop  
4. c—Gout and Rheumatic Fever  
5. d—Lyme, Connecticut where it was first described.
You All Deserve a Green Star, Well Maybe a Green Comet!

See You Next Year!

The End