Focal infection: with special consideration of experimental work on the theory and disease entities resulting from it

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Focal Infection: With Special Consideration of Experimental Work on the Theory and on Disease Entities Resulting from it.

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Introduction

Focal infection is a clinical term implying the inter-relationship between a circumscribed area of infection and an infection elsewhere in the body. (Nickel 1935). It is the most universal of known ailments (Cecil 1934).

It is a common primary cause of chronic ill-health, but is more usually a contributing factor to the diseased condition. (Graham 1931).

Holman (1928) thinks that the subject is often misunderstood and misinterpreted. Focal infection has progressed from a theory to a principal of infection and of necessity involves the primary elements of medicine. There are few branches of medicine that it does not touch on. It is self-evident that all bacterial, protozoal and virus infections must have a portal of entry, which becomes a primary focus from which the distribution of the micro-organisms, or its toxins, occur if not immediately neutralized by body defense. This is much too broad an application for such terminology, as this would necessarily incorporate the entire bacterial origin of disease. The object, then, is to obtain a general conception of the problem as a whole.
Definition

A focus of infection may be defined as a circumscribed area of tissue infected with pathogenic bacteria. They may be primary and are then usually located in tissues communicating with a cutaneous or mucous surface. They may also be secondary foci, and are then the direct results of infection from other foci, either by contiguous tissue or by the blood stream or lymph channels. (Billings 1913).

Ogilvie in 1935 termed the condition "latent sepsis". The former word implied dormancy or concealment, while the latter word indicated that there was an infection by an organism capable of producing an inflammatory reaction. He says that the manifestations of this condition are brought about by one of two mechanisms:

1) A liberation of showers of bacteria into the blood stream or

2) The action of their toxins distributed by the circulation.

Taquino (1935) agrees, but insists that bacteria are also conveyed via the lymphatics in many cases especially those involving lymphoid tissue of the throat.

Holman (1928) does not include the dissemination of toxins as coming under the term "focal infection", but says that the term implies the following points:

1) That there exists or has existed a circum-
scribed lesion or focus.

2) That the lesion is of a bacterial nature and as such is capable of dissemination.

3) That from this focus there has resulted systemic infection or infection of other contiguous or non-contiguous parts. Blum (1918) is of the same thought.

In 1934 Wiltsie stated that it was merely a chronic infection in which neither the invader nor the defense mechanism of the host is fully able to predominate. Immunity has been inadequate, but has held the invader in check. On the other hand the invader intrenches himself, but gradually loses his virulence.

**History**

The theory of focal infection is not a recent or modern one, in any meaning of the word. It was not even original to the Middle Ages, but was a product, as was a good share of original medical knowledge, of the fertile mind and writings of Hippocrates (Mayo 1922)(Kerr 1936 and others). This great doctor recorded two cases in which eradication of infections of the mouth had relieved patients of rheumatic troubles of the joints. There was no further record in the literature, as is the case with most medicine, until a few years previous to 1700 A.D. At this time the poet Dryden wrote the following:

"The throttling quinsy 'tis my star appoints
And Rheumatism descends to wrack my joints." (Kerr 1936)
In 1796, John Hunter published his "Treatise on Blood Infection, etc." in which the idea of a focus of infection causing manifestations in other parts of the body was brought out.

Benjamin Rush, signer of the Declaration of Independence and one of America's noted physicians, began an article in 1801 which was published in 1818. It consisted essentially of several cases demonstrating the theory of focal infection. There was one case of rheumatism, one case of dyspepsia, and toothache, one case of epilepsy, and one case having inflammation, pain, and ulcers of the upper and lower right jaw with scanty menses. All of these cases were cured by the removal of bad teeth.

In America there was much in the literature until the latter part of the Nineteenth century, but in Germany several references to the subject. In 1869 Winge recorded cases of malignant endocarditis in a man who died of septicemia from an abscess of the foot. In 1872 Heiberg (Hjelmar) recorded cases of ulcerative endocarditis occurring in women who had died of puerperal septicemia, and these were proven on autopsy (Blum 1918).

In England, John Abernathi in 1809, recorded several cases which were manifestations of distant diseases. He had a case of "stomach and bowel disorders" which produced "weakness in the lower extremities, pain in loins, rheumatism and dysuria". Another case of "diseased lungs"
which was associated with marked sacro-iliac pain. In still another case, a diseased gall bladder was found to cause "weakness and back pain". In a case, which on autopsy was found to have iliac ulcers, presented paralysis of the lower limbs, epileptic paroxysms, and slight temporary diarrhea. He states that disorders of the digestive organs can be caused by "lumbar abscesses, diseased joints, compound fractures, and all kind of local diseases".

Graves (1835) recorded that the first case of hyperthyroidism was in a woman convalescing from acute rheumatism. This was probably a coincidence, but he did not think so at that time.

During the last decade of the nineteenth century, and the first two decades of the twentieth century, the literature became voluminous and will be referred to under the various branches of the subject as taken up.

**Etiology**

As in all types of disease there must be a cause for the formation of foci of infection. Cecil (1934) is of the thought that many factors can predispose to this type of infection as in general disease. He lists long-protracted illness, old age, exposure, addiction to alcohol or drugs, and poor personal hygiene. The modern city life of the average person appears to add to the prevalence of infected tonsils. As to vitamin deficiencies, Daniels, Armstrong and Hutby (1923) show that nasal sinusitis can
be produced by deficient Vitamin A in the diet. According to Cecil (1934), David Smith showed that the guinea pig deprived of all Vitamin C developed pyorrhea and ulcers of the stomach.

In addition to the above predisposing factors must be added the common cold; the effects of heat and cold if too extreme and suddenly changed especially; fatigue, either physical or mental; and elective localization of which more will be said later (Holman 1928).

As to the exciting causes the usual offender appears to be the streptococcus. Haden (1923) showed that 92½% of his group of apical abscesses of the teeth were caused by streptococcus. Cecil (1934) says that acute and chronic tonsilitis are almost 100% produced by forms of the streptococcus. Steffen and Cecil (1921) actually produced experimental tonsilitis in a human volunteer by swabbing his tonsils with a pure culture of streptococcus hemolyticus. Any bacteria can cause this condition however; of more frequency are staphlococcus, gonococcus, pneumococcus, bacillus proteus, etc.

Here we must discuss the two theories championed by Rosenow and Billings as explanatory of focal inception. The first consists essentially of the transmutation within the members of the streptococcus-pneumococcus group, of bacteria, in variations of morphology, cultural characteristics, biological reactions, and of general and special pathogenicity. Schottmüller (Billings 1918) isolated streptococcus from patients with chronic infectious
endocarditis which was of the non-hemolyzing type and produced a greenish halo around the colonies on blood agar. It was a streptococcus viridens and was of low pathogenicity for animals. In 11 patients streptococcus viridens was cultured on various media and animals were inoculated with successive strains. The end result was a pneumococcus with a specific pathogenicity for animals producing pneumococcemia and pneumonia (Billings 1909)(Rosenow 1909–1910). In 1914, Rosenow took hemolytic streptococcus strains from patients with erysipelas, puerperal fever, scarletina, acute tonsilitis, acute polyarthritis and cows' milk. He took strains of streptococcus viridens from tonsils, alveolar abscesses, blood, and cows' milk. He took the streptococcus mucosa from sputum, tonsils, and elsewhere; and he took strains of pneumococcos from sputum, blood, exudate of empyema, hepatized lung, and Cole's strain I and II. He successfully made these strains assume the varying types as to form, cultural characteristics, biological reactions, and special and general pathogenic virulence of the entire group. The possibility of transmutation into form, etc., is used by many authors to explain the conflicting results of animal inoculation with undifferentiated strains of streptococci.

Wherry (1905) says that the cholera-red reaction, which is typical of the spirillum of this disease, depends on the kind of medium in which the organism grows. If it cannot produce a nitrite out of the medium in which
it lives, the reaction does not develop. He thinks that this is significant of a change in the organism.

Wherry (1913) found that he could produce the "spore-bearing type of tuberclebacilli" and also the ordinary type at will by varying the composition of the culture medium. He could also vary the "acid-fastness" of the bacilli by varying the type of medium. Also by alterations of surrounding media, he has made certain amebae change into free-swimming flagellates and back again. If these facts are true why cannot any bacteria change its characterizations with changes in associated media? According to Smith (1894) bacteria in mixed cultures can be modified in many ways. There appears to be an antagonistic action of various bacteria on each other. There is also an inhibiting action of the products of metabolism of certain bacteria on the growth and virulence of other bacteria. The same author lists a condition called by Neneki "enantibiosis". This is, that in the associated growth of two species of bacteria the products of fermentation may be different than those in pure culture of either specie. V. Schreider found toxalbumoses from mixed cultures of diphtheria bacilli and streptococcus more speedily fatal to the guinea pig than the albumoses of either specie alone. In his experiments on hog-cholera bacillus and bacillus proteous he found that the virulence was attenuated, but later regained and advanced when the proteous was removed.

The second theory is essentially acquisition of
pathogenic elective tissue affinity by bacteria from foci of infection, cultural media, and in serial animal passage. 

Fors<er (Billings 1916) cultured ordinary streptococcus pyogenes (hemolysans), which had no pathogenic elective affinity for the kidney, in kidney and kidney extract. The bacteria were converted into a strain, which when injected intravenously into animals, constantly produced outspoken anatomical lesions of the kidney. This he believed, proved that bacteria of a local infection may attain specific pathogenicity and elective tissue affinity.

Poynton and Paine (1902)(1900) isolated a diplococcus in cases of patients with acute rheumatic fever. When injected into rabbits, they caused acute non-suppurative arthritis and simple rheumatic endocarditis. After a few months in culture the same strain caused malignant endocarditis in rabbits. They recovered a smaller diplococcus in pure culture from the large vegetations and contains thrombi of the malignant endocarditis, but did not recover diplococci from the simple rheumatic endocarditis. Rosenow (1914) recorded clinical examples of acute appendicitis, cholecystitis, acute gastric and duodenal ulcers, acute and sub-acute glomerulonephritis, rheumatic fever, erythema nodosum, herpes, zoster, malignant endocarditis, simple endocarditis, myo-carditis, and others. There are associated with focal infections of tonsils, accessory sinuses, dental alveoli, skin and its appendages, fallopian tubes,
prostate and seminal vesicles, and other foci. The dominant pathological bacteria were cultured from tissue removed at operation, and from the primary foci at the same time. Both cultures were injected intravenously in different animals at the same time. The evidence of the specific elective affinity of pathogenic streptococcus from the various tissues and likewise from the foci was very marked. Hendrich (1916) and Moody (1916) through work with the injection of rabbits with streptococcus from infected teeth also proved the theory of elective localization. Pern (1934) likewise upholds the theory.

Nickel (1935) interprets Rosenow's work on elective localization as meaning that certain bacteria usually streptococci although not necessarily so, when injected into certain experimental animals locate in and produce lesions in the same organs or tissues as were infected in the patient. This is not to the exclusion of all other places however. Manwaring (Nickel 1935) made the following statement: "Under the magic touch of the hybridization metaphor, this ostracized heresy (meaning Rosenow's theory of elective localization) becomes the consistent logic of clinic expectancy".

As further verification of the fact of elective localization, (Nickel 1935) mentions Jensen and Rosenow's work where they used the cataphoretic potential as a distinguishing and identifying means between the streptococci which produced encephalitis, ulcer, and arthritis. One of the main criticisms of the above theories was the fact
that they had not considered the sex litters or diet of the animal. These facts do not materially change the results. The difference in per cent is so slight and besides they do not change the site. Another criticism is that a low per cent of positive results are obtained in experimental animals. This is absurd because one hundred radishes do not grow from one hundred radish seed, and all people consuming typhoid bacilli do not contract typhoid. Another criticism is that the bacteria are not the cause of the disease, but secondary invaders. Like Sir John Burden in 1880 (Nickel 1935) who injected guinea pigs with dust from St. Paul's Cathedral, Westminster Abby, and from his own drawing room, and produced scrofula in all the cases. He therefore deduced that the disease could not be caused by specific cause because it was produced with dust from three widely separated sources. Next year Koch nullified his work with the discovery of tubercle bacilli. We know fatigue, lack of resistance, hereditary pre-disposition all must be reckoned with and yet no one will posit a statement that the tubercle bacillus is a secondary invader and of no etiological significance. Likewise the green streptococcus is not the only factor, and no advocate of elective localization says that it is the only factor. Rosenow's work is based on quantitative evidence and nothing but quantitative evidence of the same sort and of like volume which sufficed to disprove this thesis. Any worker following Rosenow's technique verbatim
in a respectable series of experiments will reproduce a phenomenon of elective localization - at least none have yet failed.

Nickel (1926) in a series of animal experiments, discarded all animals over two in number injected with the same strain, and took only the first and second animals injected irrespective of findings. In other tabulations, he rejected the rabbits injected with culture obtained a second time from a focus or the rabbits injected with strains obtained after an animal passage and still his figures demonstrated very decisively the fact of elective localization.

Jones and Newsome (1932) corroborated the above works from chronic foci produced in the tooth usually of the dog. The animals developed lesions comparable to lesions of the patient in the majority of the cases.

Hendrici (1916) took 53 strains of streptococci from various sources and inoculated them into 225 rabbits and a virulent elective organ affinity compared with the powers of hemolysis and carbohydrate - fermentation. He found that the carbohydrate - fermentation tests were of no value from the standpoint of virulence and of little value from the standpoint of tissue localization. Hemolytic and non-hemolytic streptococci although different in virulence, localize in the same tissues frequently. Flexner (1896) thinks that there is a relation between the predilection shown by various micro-organisms for
certain viscera, and certain chemical substances in these and peculiar to these organs. It is not possible to explain the distribution of bacteria by peculiarities of the blood supply.

As a pragmatic test, Nickels (1935) cites the following facts: Following the removal of foci of infection or the use of vaccine made from strains that localized electively, the patient often is improved or gets well. For example, the clearing up of an iritis in a patient after the removal of his tonsils. Sometimes they do not improve, which means that the foci was not the cause. There are patients who are better following vaccination, but when discontinued relapse and then get better again when the vaccine is resumed. These usually get no benefit from nonspecific therapy. This has occurred often enough to convince many that the organism involved is causal and not coincidental.

Although the exact role of allergy is unknown, it is quite possible that the focus may discharge allergens which would react on the sensitive tissue. It is well known that asthma may be caused by chronic infection of the accessory sinuses. (Cecil 1934).

Swift, Derick and Hitchcock (1928) cites rheumatic fever as a disease which presents evidence of a focus somewhere in the body and usually this focus is a tonsillitis, sinusitis, or upper respiratory infection. These foci present areas where the sensitizing substances are
produced and from where it is distributed to the entire body as well as localities whose bacteria may be fed into the blood stream.

Wiltsie (1934) thinks that such conditions as arthritis, asthma, colitis, eczema, hyper-tension, and spastic states although commonly the result of foci are essentially allergic in nature.

As to the bacteriicidal powers of the blood playing a part in the cause of focal infection, Lubarsch (Pern 1934) showed that small numbers of anthrax bacilli are sufficient to kill a rabbit when injected into the blood stream. However 1 cc. of blood in vitro was able to destroy a much larger number. This was accounted for by the liberation of cytases from the disintegrating leukocytes. There are times when blood loses all bacteriicidal power for a certain organism and even fails to kill it in vitro. This is shown by trying to culture organisms in the patient's own blood, the type multiplying and surviving indicates the type for which the blood's resistance is lost. This gives us a clue as to why some people with gross infection fail to suffer any serious damage to their tissues, while others with small infection may suffer severely. Also the fact that disease is as much due to the organism as to the lack of resistance of the patient; and that in trying to produce the same identical changes in other animals one has little hope of even expecting to find the same condi-
tions of lower resistance as that found in the patient. In one, the defense is much reduced while in the others it is much alive.

Some think that bacteria lie dormant in a given region and flare up when the tissue has a lowered vitality. Fern (1934) cites the following case to disprove that idea. A friend of his who received a shrapnel wound to his tibia during the World War, found that if he jarred his leg by playing tennis on an asphalt court, the old wound would flare up and incapacitate him for several days. With removal of some badly infected tonsils, the friend had no further relapses regardless of how much tennis he played.

Interference with cell respiration is said by Roenow (1915) to play a prominent part in this subject. He bases his conclusions on pathological findings (see pathology) and the fact that bacteria and their product are powerful reducing agents. He thinks that the predisposing action of trauma, exposure to cold, drunken bouts, etc., can be explained on the basis of lack of oxygen.

**Teeth**

As a primary focus, these organs are well known, and the literature is voluminous from this angle. I will refer to some of the experimental work in this connection under other headings, but will not attempt to cover the subject fully.
Duke (1918) thinks that oral sepsis acting as a focus of chronic active infection, may be a source of ill health in many different ways. It may either distribute organisms themselves or their toxins. It may favor in advance diseases, which are not related to the focus, or it may cause functional disturbances in relatively normal organs by furnishing foreign protein to which the individual may become sensitized. It may also increase functional disturbances due primarily to organic disease.

Ogilvie (1935) records four cases of "tennis elbow" which cleared up "like magic" after the removal of infected teeth plus the curettage of the alveolar margin.

M. H. Fletcher (Fischer 1921) reports thirteen cases of trifacial neuralgia. Twelve of these cases were cured by treatment of infections around the teeth.

**Accessory Nasal Sinuses**

Here again as this is a common source of focal infection, and as the literature is so voluminous as to make it impossible to incorporate it all into this thesis, I will only mention some outstanding work which appears to represent majority of opinion.

Solis-Cohen (1924) made 230 pathogen-selective cultures of the nares and 35 such cultures of the sinuses of patients being treated for sinus disease, and found infecting organisms in 180 (78%) of the nasal cultures
and in 20 (57%) of sinus cultures. Sinus operations failed to cure the disease in the opinion of Solis-Cohen, Shollern, Pratz, Carter, Pond. (Solis-Cohen 1934).

Taquino (1935) thinks that the position of the sinuses and the middle ear at the top of the respiratory and digestive tracts, favors the entrance of bacteria by gravity into the pharynx, larynx, bronchial tree, stomach and intestinal tracts.

Parkinson (1935) cultured the nasal and rectal bacterial flora in patients having a focal infection with gastrointestinal upsets. He found that there was apparently more than a causal relationship between the pathogens grown from the two areas.

Byfield (1918) cites cases of chronic digestive disturbances, persistent cough, occult temperature, poor general health, asthma, infectious deforming arthritis, and cyclic vomiting. He established a definite relationship with a sinusitis by X-ray examination.

_Tonsils and adenoids_

As these organs are one of the more usual primary foci they will be discussed more in length in relation to other foci under the corresponding titles. A complete discussion would form a complete thesis in itself.

Solis-Cohen (1934) is of the opinion that the bacteria are not only present in the diseased tissue, but also in the surrounding mucous membrane of the oral and
pharyngeal cavities. When the tonsil is removed, the stumps may become infected, recurring tonsils (i.e. infratonsillar tissues which has worked up into the empty fossae) may become infected, or normal appearing tonsillar fossae may also harbor infected organisms. Solis-Cohen (1921) made 74 pathogen-selective cultures of apparently clear tonsillar fossae and found infecting bacteria in 73 (97%). The apparently normal naso-pharynx frequently becomes the habitat of infecting germs and thus serves as a focus of infection. In 1924 Solis-Cohen made 147 pathogen-selective cultures of the naso-pharynx in suspected infections of the upper respiratory tract, and found infecting organisms in 140 (95%).

The tonsils are always primarily infected according to most authors, but rarely may become secondary foci. Seawell (1911) recorded cases of the tonsils becoming infected in tuberculosis, the primary lesion or focus being in the lungs.

**Middle Ear**

Here again the literature dealing with this organ alone as a focus of infection is so great as to form the body of a thesis itself. I will not attempt to cover it thoroughly therefor.

V.V. Wood (Taucino 1935) thinks that bacteria gain entrance to blood and lymph more readily from lymphoid
tissue of the throat and middle ear, which have abundant lymph and blood supply; and from the sinuses which have a poor supply. Taquino (1935) states that the sinus stands first with the exception of the middle ear as a primary focus.

Gynecological and Urological Foci

Here is a source of infection that is referred to by many authors of not only gynecological and urological works, but general medicine as well. The literature is again so vast that an attempt to discuss it fully will not be attempted. There appears to be no doubt in anyone's mind as to the existence of these foci, Chronic prostatitis and seminal vesiculitis, salpingitis, chronic endocervicitis, endometritis, cystitis, etc., are all included as foci by Rosenow, Billings, and others.

Nickel (1930) claims that the streptococci from chronic prostatitis and seminal vesiculitis show, as do most streptococci, elective localization.

Curtis (1935) even mentions two cases of arthritis and iritis which cleared up after the treatment of infected Skene's glands.

Delee (1934) mentions a type of endogenous puerperal infection arising from a focal mastitis. He refers to many cases as coming from infected cervixes.

Curtis (1925) records cases of spontaneous recurring
abortions being stopped by the removal of foci of infection.

Chronic Intestinal Toxemia

This is a condition said by Wiltsie (1933) to be consistently present in all cases of focal infection. Usually the liver and biliary systems are secondary foci by the time symptoms are evident. These in turn add new strain to the already involved cecum and colon and thus these organs become foci of major importance. These organs then cause contamination of the portal circulation with bacteria and toxins, and a second vicious circle is started.

The lymphatic draining from the cecum and colon through the mesentery system of glands and channels to the recepta-culum chyli and then to the blood stream, becomes a third vicious circle because every infected node is a focus in itself (Mayo 1923). When drainage becomes blocked, new groups of glands are involved even to the gastro-epiploic and subpyloric ones. Thus much pathology around the duodenum, gall bladder, and head of the pancreas is really secondary to the colon.

In time the liver becomes chronically congested resulting in portal stasis with the formation of hemorrhoids and proctitis. This leads to the shunting of large volumes of the infected blood through the interior hemorrhoidal
veins to the iliac veins and so to the general circulation. This forms the fourth great vicious circle. Thus the colon and cecum are in possession of the key position to cure and must of necessity be cleared up to bring about relief.

In this connection, it must be remembered that Posner and Lewin (Adami 1899), tied the rectum in rabbits without causing any gross lesions of the mucous membrane. They found that within 18 to 24 hours the whole organism, including the heart blood became infected with intestinal bacteria.

**Acute Rheumatic Fever**

The true infectious cause of acute rheumatic fever is a diplococcus (Micrococcus Rheumaticus) (Streptococcus Rheumaticus) as proven by Poynton and Paine (1900). These experiments were confirmed by Beattie, Walker and Ryffel, and finally and conclusively by Rosenow (1914). This latter worker isolated three different types of cocci from the joint exudate of patients with acute rheumatism. Although they all varied in cultural characteristics, they produced arthritis when injected into experimental animals. They varied however in the production of myositis, endocarditis, myocarditis and pericarditis. This is given as an explanation of variations in the names given above by different workers.

Billings (1913) thinks that foci in this disease may
not be evident at first, but very suddenly becomes increasingly virulent and then has a specific pathogenic affinity with varying degrees of focal tissue reaction. This transmutation of type and pathology certainly occurs in the focus of infection then and makes them apparent. The occurrence of rheumatic fever after the removal of an apparent focus may be due to "secondary systemic latent foci" in lymph nodes approximel to the joints, in the neck or elsewhere. Streptococci of these new foci may take on new virulence and specific pathogenicity from the same causes which induce similar changes in the pathogenic bacteria of the primary foci. All of the lesions resulting from rheumatic fever, are all on the same basis. In chorea, bacterial cerebral emboli have been recovered. Rothstein (Billings 1913) isolated strains of streptococci from the meninges of choreic individuals. The animal inoculation of these streptococci isolated from rheumatic fever and chorea produced joint infection and symptoms characteristic of chorea.

Cecil (1935) states that rheumatic fever is usually preceded by upper respiratory infections in the form of acute tonsilitis, coryza, or a pharyngitis. Dochez and co-workers (1930) showed that although acute respiratory infections are caused by a filterable virus, it may activate the ordinary pathogens of the mouth and thereby increase their virulence.
Goburn (Cecil 1935) found that patients with rheumatic fever carried hemolytic streptococci in their throats which persisted during the active state of the disease. He also noticed the presence of hemolytic streptococci in throats during respiratory infection preceding rheumatic fever.

Hendici (1916) thinks that we are not justified to say that any particular strain of streptococci are specific for rheumatic fever since various rheumatic lesions may be produced by some strains of each variety.

Fowler (1880) reported 20 cases of acute rheumatism which were preceded by tonsilitis and catarrh of the pharynx. Trosseau recognized "a rheumatic sore throat" evanescent in character and preceded by a few hours articular manifestations.

Chronic Infectious Arthritis

Billings (1912) (1913) (1914) thinks that deformities due to streptococci, gonococci, or typhoid bacilli form a fibrin-oplastastic exudate with an attempt to wall off an area of infection. The continued doses of infection from the primary focus continuously add to previous changes i.e. myositis, arthritis, and perineuritis. He lists the following pathological principals:

1) An infection of the joints, muscles and other tissues with a pathogenic organism of a relatively low virulence
2) The hematogenous route of infection by means of emboli which form vascular injury and small hemorrhages.

3) Lessened blood supply and oxygenation leading to relative starvation of the infected tissues.

4) "Retrograde metabolism" due to malnutrition.

As is well known, a chronic tuberculous arthritis is always associated with a focal or generalized tuberculosis. Blum (1918) says that all that is needed is trauma, etc., creating a "locus minoris resistantiae" in a joint so that the bacilli in the primary focus (lung) may then attack.

Poston (1929) cultured 120 surgically removed lymph glands from patients with infectious arthritis and in 60% of the cultures she found bacteria. 93% of these bacteria were streptococci. She also used the tissue crusher devised and used by Rosenow fifteen years previously.

An attempt by Meisser to produce arthritis in dogs failed and was explained by Rosenow as due to the fact that the streptococci from the patients with chronic arthritis was less virulent than other strains, but more probably due to the high natural immunity which a dog possesses against infection of the joint (Cecil 1935).

Cecil and co-workers (1929) showed that the sluggish indolent afebrile type, and the type with swelling, fever and secondary anemia both show increased sedimentation time and agglutination for streptococcus viridens. They are therefore merely active and inactive stages of the same disease. The same is true about muscular rheumatism.
and neuritis. At Bellevue Hospital during some studies on bacteriology, of this disease, they found streptococci morphologically, culturally and biologically identical in the blood, joint, and focus of the same people. In case one it was the blood, joint, and infected tonsils. In case two, it was the blood, tonsil, and erythematous bullae of the skin. In case three it was in the blood, joint, and apical root abscess.

Moon (1931) established chronic foci of infection in the dog by putting cotton soaked with green streptococci in the peritoneal cavity. The dogs developed arthritis and a verrucous endocarditis. Histologically the cells in the heart, heart muscle, and valves suggested Aschoff bodies.

Dunlap (1934) states that Dr. Olmstead and Boots of the Physicians and Surgeons College of New York reported their bacteriologic studies of blood and synovial fluid as being quite divergent from Cecil's work.

**Gonococcemia and Gonococcic Arthritis**

This condition is undoubtedly the result of a blood stream infection from an existing focus of the microorganism. I doubt if there is any experimenter in the medical world that would not agree to this. This has recently been proven by the recovery of the gonococci from joint tissue, joint exudate, bursae, and tendon sheaths.
Infectious Endocarditis

In malignant endocarditis there appears to be no controversy as to the existence of a focus which causes bacteremia which is always found. Many conditions are known to act as a primary focus of which; pneumonia, typhoid, meningitis, septic wounds, puerperal uteri, and streptococcus foci about the head are the most common.

In 1903 Schottmüller (Billings 1918) reported isolation of the streptococcus viridens from the blood of a patient with chronic endocarditis.

Osler (1909) Horder (1909) Libman (1912) reported patients suffering from what they termed chronic infectious endocarditis, infectious endocarditis, and sub-acute infectious endocarditis.

Billings (1909) Rosenow (1909) (1910) reported cases of "chronic pneumococcus endocarditis". In all cases, streptococci viridens can be isolated from the blood stream and also from the alveolar abscesses and other foci, which when injected into animals produce typical endocardial lesions.

Olawson and Cecil (1935) are strong advocates for the theory that this disease is nothing more than a complication of acute rheumatic fever. As criteria both diseases show high agglutinins with streptococcus, usually streptococcus viridens.

In 1898 Blum (1918) reports a case of an infant in-
fected with proven pyocyaneous enteritis. Patient became quite septic and developed an endocarditis while under observation. He died and on autopsy, the verrucosisites on the heart valves gave up pyocyaneous bacilli.

**Acute Nephritis**

Billings (1912) was a champion of the embolic phenomenon by way of the blood stream as the cause of glomerulo-nephratitis.

In 1914 LeCount and Jackson, inoculated rabbits with a streptococci isolated from patients with "epidemic septic angina". They found the following kidney lesions of the vascular structures when the rabbits died. The glomerular intertubular vessels and the arcuate and interlobar veins contained evidences of perivascular exudate consisting of lymphocytes and plasma cells. The great tendency to repair was considered very important and compared to the tendency of recovery in clinical glomerulo-nephratitis, after the removal of the etiological factor. That a true nephritis existed was considered proven by the clinical findings of bloody urine, albuminuria, and the findings of numerous casts.

**Chronic Infectious Nephritis**

In 1914 LeCount and Jackson gave the following results from their experimentally infected rabbits. Eight or 25% of 33, which died or were killed the first two
weeks, showed chronic changes in the kidneys. Fifteen or 62% of 24 rabbits which lived from 15 to 186 days, showed chronic kidney changes. These figures stress the chronicity of this type of infection and show that it is the repeated attacks of bacteria of low virulence that produce the most lesions.

Klotz (1914) says that a form of acute interstitial nephritis produced in animals by inoculation of strains of streptococci, subsequently give rise to a renal sclerosis of the type known as chronic interstitial nephritis. He therefore doesn't believe in the repeated attacks of the bacteria as being causitive of chronic nephritis.

Ophüls (1912) and Billings (1912) are both champions of the infectious origin from a primary focus.

**Cholecystitis**

Rosenow (1914) isolated the strains of streptococci from operative cases of gall bladder disease, and injected them into experimental animals with the production of cholecystitis. One patient had suffered from tonsilitis on several occasions. He also showed that the affinity of the streptococci for the gall bladder can be obtained, lost or regained by varying methods of culture and by serial animal passage. He agrees with Cannon that typhoid cholecystitis occurs unquestionably via the blood stream.

A peculiarity of the strain of streptococci seeming
to acquire affinity for the gall bladder is that it also has a coincidental affinity for muscles, especially the myocardium. In confirmation, clinicians have noted evidences of myocardial weakness in many patients with chronic cholecystitis.

According to Nickel (1935) cholecystitis is almost invariably an intramural streptococci infection and the theory of selective affinity becomes more than a theory. Branch (1929) agrees with him in every particular.

**Acute Appendicitis**

The French observers Kretz, and Cannon, (Billings 1913) thinks that the infection of the appendix is hemotogenous in origin from foci in the throat, nose, sometimes the jaws, also the cervical lymph glands.

Rosenow (1915) confirmed the French workers' results by producing appendicitis in animals injected with strains of streptococci, colon bacilli, and others, which had attained elective affinity for the tissues of the appendix. The majority of the animals had demonstrable appendicitis. The invading organism caused small hemorrhages in the walls of the organ, so that the tissue reacted with with the invasion of leucocytes and plasma cells. This in turn caused a tumefaction and obstruction of the canal, thus allowing other bacteria present to become secondary invaders.
Gastric and Duodenal Ulcer

In 1915 Rosenow and Sanford isolated streptococci from the base of ulcers and tissue of the stomach wall of man and inoculated animals with these strains. The streptococcal embolic infection of the submucosa of the stomach with resulting small hemorrhages into the surrounding tissues resulted. As anemic necroses took place, the overlying mucous membrane was weakened and it became digested by gastric juice.

Adami (1899) showed that bacteria can invade the body through the healthy intestinal mucosa and that this fact may play a part in the formation of ulcers.

An attempt to produce ulcer by infecting devitalized teeth in the dog with streptococci obtained from a patient with an ulcer was successfully accomplished by Meisser (O Cecil 1935).

Nephrolithiasis

Rosenow and Meisser (1923) devitalized the teeth of dogs and then infected them with staphlococci from a patient with nephritis. One dog developed pyelitis and cystitis, with marked calcareous deposits in the pelvis. These experimenters also recovered streptococci from the teeth of a patient with nephrolithiasis. They infected the devitalized teeth of dogs with this culture. The teeth became discolored but remained firmly in place in
their sockets. There was rarefaction and absorption of the periapical bone without swelling or tenderness. Renal calculi or lesions in the medulla of the kidney developed in a high percentage of the dogs.

**Herpes Zoster**

Rosenow and Ofterdal (1915) showed that Herpes Zoster was the result of specific infection of the ganglion of posterior roots of spinal nerves and that the etiologic infectious organism can be isolated from infected tonsils and other foci. They did their work on patients of the Mayo Clinic. The typical symptoms were produced in the animals and the streptococci recovered from the posterior root ganglion of the animals.

Davis (1936) reports 250 cases, 90% of which are from a focal infection basis which showed typical pain without the eruption. He thought it to be a subherpetic form of herpes zoster.

**Erythema Nodosum**

Rosenow (1915) has demonstrated the relation of this disease to foci of infection many times. He discovered a strain of bacteria from the streptococci-pneumococci group in surgically removed nodes, and produced erythema nodosum in the skin of animals intravenously injected with the cultures.
At the Presbyterian Hospital, (Billings 1913) the removal of apparent foci has been followed by relief over a long period of time.

**Thyroiditis**

According to Billings (1916) he has observed many cases of thyroid enlargement of the chronic type with evidences of thyroid intoxication in young women with focal infection in the form of alveolar abscesses, tonsillitis and sinusitis.

**Iridocyclitis**

Rosenow (1915) Billings (1916) and other say that infection plays a constant part in the causation of iritis.

Nickels (1935) records a case of iritis in a patient which disappeared after the removal of the tonsils. The culture of these tonsils produced an iritis in a rabbit.

Uveitis, iritis, and iridocyclitis are not rare complications of rheumatic fever and usually are associated with involvement of the ethmoid and sphenoid cells (Cecil 1935).

Evans (1933) is very much in doubt that focal infection plays a part in eye diseases. His experience seems to show that when an eye and a tooth are both infected, unilaterality and ipsilaterality are present. This cannot be explained on the blood borne infectious idea.
He explained it as a reflex set-up by irritations of nerve endings of the second division of the Trigeminal nerve giving rise to neuropathic changes in organs supplied by the first division of the afferent stimulus becomes antidromal.

**Spinal Myelitis**

Billings (1916) cites the case of a man who had suffered for three years from symptoms of "spinal insular sclerosis". For years previous he had suffered from chronic tonsilitis. The tonsils were enucleated and the streptococcus isolated from them injected intravenously into two dogs. In both cases, focal hemorrhages into the cord were formed and the dogs suffered from an ataxic gait and partial loss of power of all four extremities. The streptococcus was recovered.

**Encephalitis**

Evans (1926) showed that Rosenow's concepts of the etiology of encephalitis, or of the ability of organisms to change form were not mere fancy.

**Poliomyelitis**

Rosenow (1924) gives experimental proof that a streptococcus is the cause of the organism in poliomyelitis. According to Nickel (1985) the discovery of Kendall's "K" medium and the now recognized filterable virus
of many heretofore nonfilterable bacteria all tend to show that the streptococci of Rosenow and the virus of poliomyelitis may be manifestations of one organism.

Richardson (1932) verified Rosenow's reports that he could grow his streptococci from filtrates of the virus as well as from filtrates of the culture of streptococci.

Grinker (1934) thinks that Rosenow's work was no good. According to him the clinical studies and pathological picture are neither similar to the disease in man. It is essentially a meningitis. He cites McKinley as culturing material from normal nasopharynges and producing the same degrees in animals by injecting the streptococcus as Rosenow did.

Sampson Hardley (Pern 1934) seems to think that it is the avoidance or efficient treatment of local or general lymphatic infection which produces local areas of lymphstasis, which is the principal means of lessening the incidence of cancer. In this connection dental infection as a secondary infection of the mouth, stomach and bowel arising from it, play a part, the importance of which even now is not fully appreciated. Cancer of a dentally clean mouth is a rarity.

Hardley shows that the lymphatic system doesn't start in the intracellular spaces, but in tufts of closed tubules.
When these are blocked, there is hypertrophy of the papillae they are draining. This forms papillomata which in turn contract the fibrous tissue which strangles the artery and vein. This of course deprives the cells of oxygen and nourishment which causes a reverting to the original type of cell.

There is no cancer in invertebrates where the lymphatic circulation is primary.

**Pathology**

The pathological findings are so varied with different conditions that no attempt to discuss them will be made here.

To quote Adami (1899) "Thus Charrin has shown that bacillus pyocyaneous and its products can produce in one organ, the kidney, pathological conditions so diverse as acute, chronic, parenchymatous, interstitial and thrombotic nephritis within addition cyst formation and amyloid degeneration".

Thus we will give preference to infection as a causative agent in the production of pathological changes, rather than to any particular disturbance.

Rosenow (1915) thinks that the pathological changes seen in cases of focal infection taken as a whole from the chemical as well as the colloidal chemical point of view, are identical with the changes of tissue asphyxiation.
Symptomatology

It is easily discernible without discourse that each separate case of the individual as to the symptoms complained of. Of course the primary focus be it tonsils, teeth, sinuses, or gastro-intestinal tract, will have some symptoms which are characteristic of this region. Other symptoms will depend on the secondary foci and the organs involved. These will not be discussed as they are a part of medicine as a whole and not this subject in particular.

There are general symptoms which are more or less characteristic of the toxic state. According to Wiltsie (1934) they consist namely of: Anemia, Lassitude, loss of weight, anorexia, dizziness, variations in blood pressure, insomnia, headache, physical and mental depression, and the "tendency to take cold".

Pern (1934) lists in addition hyperfunction of the tissue, hypofunction of the tissue and "defense mechanism response", which includes toxic syndrome of increased nervous excitability, tachycardia, and tremor.

A condition often found characteristically in focal infection is segmental neuralgia, called radiculoganglionitis, by Davis (1936). (Post-grippal polyradiculitis of Russetzlsi) He records 250 cases in childhood manifest by segmental pain in the form of cutaneous hyperesthesia and hyperalgesia. In 90% of these cases, there was a preceding or associated infection of the upper respiratory tract. Two girls had a-
brupt cessation and complete relief of these symptoms following the removal of infected tonsils; another after the extraction of several carious teeth. Two boys were likewise immediately relieved following spinal puncture although there was no increased cell count, pressure, or globulin.

Ogilvie (1935) divides the symptoms into classes:

1) Under general manifestations he includes: loss of energy and of the "feeling of health", loss of weight, insomnia, headache, and anemia.

2) As to manifestations in fibrous tissues, he includes: sciatica; lumbago; cervical myositis; painful heels; nodules on tendons, fascia, and periosteum; and ankylosing periarthritis.

3) Articular manifestations include acute or chronic arthritis.

4) Cardiovascular manifestations consisting of: endocarditis, degeneration of the heart muscles, Buerger's disease, arterial degeneration, venous thrombosis, purpura, and hemorrhage from the mucous membrane.

5) Nervous manifestations including peripheral neuritis and degenerations of the tracts of the spinal cord.

Diagnosis

Speaking in general terms, focal infection must be thought of in all chronic cases of general undifferentiat-
ing symptoms. There will usually be according to Ogilvie (1935) a slight rise in temperature usually along towards evening. The white blood count usually runs between nine and twelve thousand with a definite shift to the left. The sedimentation rate may be slightly increased. Of course bacterial cultures lead to a definite diagnosis if positive.

Such common syndromes, as discussed under separate headings previously in this thesis, should always suggest a search for a focus of infection. For example, atrophic arthritis, peptic ulcer, segmental neuritis, iridocyclitis, etc.

Tonsils are considered a focus if they are buried, bound down by adhesions and have congested faucial pillars. A tonsillar stump may be a focus if pus can be expressed. A normal tonsil with an interior abscess can be diagnosed according to V. Schmidt (Cecil 1935), by an examination of the blood when an infected tonsil is massaged. There is an increase in polymorphonuclear leucocytes of from 100 to 6000 caused by the forcing into the circulation of certain toxins. Normally there is no increase or a temporary leucopenia. Suction has also been used to cause this phenomena. (Worms & LeMee as in Cecil 1935).

Richards (1932) diagnosed foci of infection in the tonsils or teeth by the bacteremia demonstrable after massage or other trauma to the foci.
Sinuses are diagnosed as a foci by physical examination, transillumination, and X-ray. Post-nasal gripping is suggestive according to Cecil (1935) and Byfield (1918).

Middle ear is diagnosed by routine otoscopic and hearing examinations. Caloric tests are seldom of benefit here.

Teeth are diagnosed as a source of infection by X-ray and inspection as a rule. However, many cases require conduction tests to be certain.

Gynecological and urological examinations are confined to their field and are usually picked up on complete examination, or from history. No special measures are necessary as a rule.

**Treatment**

Billings (1916) divides the treatment into preventative and the treatment of the disease itself. Under prevention he includes cleansing of the mouth, teeth and throat of all particles of food after eating. Both this and removal of all persistent overgrowths of lymphoid tissues in the nasopharynx and throat are of special importance in childhood.

In pyorrhea dentalis and alveolar abscess, it was found that in conjunction with routine treatment the endamoebia buccalis must be destroyed. This was accomplished with emetin in ten day periods so as to get rid of the cysts.
He also recommends surgery in appendicitis and cholecystitis to "relieve the patient of the local menace to life, of reflex dyspepsia, and remove etiological factors of systemic disease". Surgery of morbid rectal conditions, pelvic organs in the female, prostate in the male, and pyogenic infections of the kidney, is also indicated.

As to treatment of the disease itself, the immediate removal of foci in chronic diseases and the removal of foci in acute diseases during late convalescence is of primary importance. Importance of the removal of all foci, both primary and secondary is apparent, for if any focus is left the symptom remains.

Natural defenses must be built up through mental and physical rest, nourishing food, restorative tonics, cheerful environment, good air and sunshine, and in some cases bacterial antigens. The antisera according to Billings are without notable good effects. Autogenous vaccine were not beneficial as far as can be determined, but nonspecific protein therapy and typhoid or albdmose antigens gave astonishing results in some cases. Wiltsie (1932) uses autogenous vaccines as a means of desensatization in arthritic and other allergic conditions. He never uses them otherwise.

Nickel (1935) finds much more success with autogenous vaccine and practically none with foreign protein therapy.
Cecil (1935) cleans up sinuses with suction and argyrol packs. Byfield (1918) agrees with this conservative treatment in these cases. A dry hot climate is also suggested, while surgery is controversial. If tonsils are the foci he suggests immediate removal with as little trauma as possible.

Wiltsie (1934) thinks that drainage of the focus is of primary importance, and that if it is adequate, the focus will clear up unless fed from some other source behind it. If the latter is true, then complete eradication of the source will cause complete cure. As an example, he cites many clinical cases of pyelitis which promptly clear up following the correction of a colon infection.

In addition to rest, diet, psychic analysis, and surgical removal of primary sites of infection, Wiltsie thinks that treatment of focal infection per se can never be successful without the combating of "chronic intestinal toxemia". Wiltsie (1928) through the intravenous injection of sodium iodide with a few brilliant results, brought to light many unsuspected foci. A local reaction which was followed sometime later by a general reaction and an increase in the leucocyte count was the usual result. Wiltsie (1931) confirmed his results by a series of 60 cases and some controls. In some cases of hay fever and asthma, there resulted a decrease in the existing leucocytosis, and a relief of symptoms. Wiltsie explained this action at that time
by the theory that the iodides acting on a focus, promoted a lysis of exudates which in turn released antigenic bodies causing a stimulation of the immunity mechanism with a reaction at the focus.

Retan (1932) while studying the effects of hypertonic solutions for the relief of intracranial pressure, conceived the idea of reversing this process for the treatment of spinal syphilis, encephalitis lethargica, and other inflammatory conditions of the brain and cord. The intravenous injection of hypotonic sodium chloride and the simultaneously performed continuous spinal drainage caused no cerebral edema, but if drainage was not continuously present, cerebral edema appeared. He also observed edema in other diseased tissue, but never in healthy tissue. His reason for this fact was that the capillary permeability was increased in damaged tissues, and they therefore showed edema first.

Wiltsie (1934) found curiously enough that hypertonic sodium iodide influences osmotic pressure in the same way large amount of hypotonic solution does. The mechanism is caused by the iodide reducing the viscosity of the blood by dehydration of its colloid particles. Thus the osmotic pressure is reduced and there is increased fluid into the perivascular spaces about the foci. If lymph drainage is free, cure takes place; if it is impeded, there is an increased local edema, pressure, and pain.
After 24 to 36 hours, the direction of the flow may be reversed due to the reestablishment of the normal osmotic pressure in the capillaries. On the other hand the extension of the inflammatory process may take place due to the breaking down of the barriers.

Wiltsie (1929)(1932)(1933) suggests that high colonic irrigations are definitely beneficial in all cases of focal infection. He begins at once and says that sometimes other foci will clear spontaneously. He also uses periodic duodenal drainage and abdominal diathermy as an aid to drainage.

According to Sollis-Oohen (1921)(1930) successful treatment requires the production of bacteriocidins and other anti-bodies to destroy the invading bacteria and render their toxins harmless. He thinks that autogenous vaccines are no good, but that specific vaccine is necessary. He uses the pathogen-selective method which is based on the assumption that organisms capable of growing in the fresh whole coagulable blood of the patient are those which are most pathogenic for that individual, to find the specific one. The vaccine should contain as many antigens as possible, the soluble exotoxins as well as the endotoxins.

Davis (1936) uses counter-irritation and common analgesics to relieve segmental neuralgia whenever present.

Herrick (1902) thinks that malignant endocarditis can recover. He suggests as treatment; iron and arsenic,
antitoxic serums and perhaps the use of colloidal silver preparations, as advocated by Credé.

Conclusions

1) Focal infection implies the following points:
   a) The presence of a principal focus of pathologic bacteria
   b) The invasion of the circulation by the toxins or bacteria themselves
   c) Sequential effect from the above.

2) Focal infection must be considered as a possibility in numerous diseases of man, especially in childhood.

3) Much more experimental work must be done to disprove the possibility of transmutation of bacteria and elective localization, although these theories cannot be accepted entirely as yet.

4) There are various factors determining the invasion of a tissue by bacteria from a focus. They are; dilatations of the capillaries and sluggish circulation leading to thrombi formation, the virulence of the bacteria, the resisting powers of the host, the amount of drainage possible, and a relative quiescence or movement of the tissues.

5) Any and all tissues of the body may be involved in focal infection, the serous and synovial membrane being especially susceptible.
6) The usual primary foci are in the tonsils, teeth, sinuses, middle ear, and genito-urinary tracts, but any part of the body may be the primary offender.

7) The symptoms of focal infection consist of general toxic manifestations, those referable to the primary focus, and those referable to specific tissue infected secondarily.

8) The diagnosis requires recognition of the morbid process as secondary and tracing it to its source. The various possibilities of secondary foci and the inadequate methods of diagnosis of the teeth, sinuses, tonsils, etc., make this very difficult.

9) The treatment consists essentially of systemic and local attack of both the primary and secondary state. Because of extreme complexities it is successful in only a small percentage of cases.

10) There is much room for improvement in all divisions of focal infection and a large amount of work must be done before the diagnosis and treatment of the condition can be systematized as successful.
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