Susac’s Syndrome (SS) is an autoimmune disease that affects the microvasculature (tiniest arteries and capillaries) of the brain, retina and inner ear---resulting in varying degrees of ischemic injury (injury due to decreased blood flow and oxygen) to these tissues.

By autoimmune, we mean that a person’s own immune system is mistakenly attacking part of that person’s own body. For an explanation of the “immune system” and “autoimmune mistake,” go to the section entitled “The Immune System, Autoimmune Mistakes, and the Concept of Immunological Self-Correction” at the end of this section (pages 4 and 5 of this section).

More specifically, SS results when a person’s own immune system mistakenly attacks the endothelial cells that form the inner lining of the tiny arteries and capillaries in the brain, retina, and inner ear. For more information on autoimmune attack on endothelial cells, click on “Cause” (under “About Susac’s Syndrome”).

In SS the endothelial lining cells become injured, swollen, and pull away from one another. When the endothelial cells become swollen, they threaten to partially or completely swell shut (occlude) the channel (lumen) within the blood vessel. As the channel becomes increasingly swollen shut, less blood flows through the vessel, and, therefore, less oxygen and nutrients can be delivered to the brain, retina, or inner ear. The brain, retina, and inner ear then suffer from lack of oxygen and nutrients, causing ischemic injury and dysfunction. Depending on the severity and duration of the diminished blood flow, the harm (ischemic injury) may be temporary and reversible (either completely or partially) or irreversible (causing permanent damage).

Patients typically develop a triad (a trio) of clinical manifestations (symptoms):
1. **Encephalopathy** (brain disturbance, due to the swelling shut of tiny vessels that feed particular parts of the brain),
2. **Retinal injury** (visual disturbance due to the swelling shut of tiny vessels in the retina), and
3. **Hearing loss** (due to the swelling shut of tiny vessels that feed the cochlea).

The brain disturbance is typically characterized by headaches and cognitive dysfunction (decreased thinking ability---for example, short term memory loss, confusion, slow thought processing, decreased ability to solve problems). These neurological abnormalities are associated with distinctive abnormalities on brain MRI---especially in the corpus callosum (see below).
These brain symptoms and MRI abnormalities are due to ischemic injury to the brain. (For more information about brain disturbance in SS, click on “Brain.”)

The retinal disease is characterized by:
- “Dark spots” (scotoma) in the patient’s field of vision.
- “Cotton wool spots” on routine ophthalmoscopic exam (due to ischemic injury to the retina).
- Branch Retinal Artery Occlusion (BRAO).
- “Leakage” and “staining” on Fluorescein angiography (FA).
- This retinal disease can ultimately result in loss of some vision, primarily peripheral vision.

(For more information about visual disturbance in SS, click on “Eye,” under “About Susac’s Syndrome”)

The hearing loss is usually a low frequency sensorineural hearing loss.

The hearing loss can be to the point of complete deafness. Hearing loss is often accompanied by “ringing in the ears” (tinnitus) and dizziness (whirling vertigo).

(For more information about inner ear disease in SS, click on “Ear,” under “About Susac’s Syndrome”)

The three components of the triad often do not appear at the same time. Any one of the triad can be the first sign of SS. Sometimes visual disturbance is first; sometimes hearing loss is first; sometimes headache and
thinking difficulty are first. It may take weeks, months, or even 2-3 years or more before all three components appear. Sometimes only two of the three ever develop.

The clinical triad is typically accompanied by a triad of MRI findings:
1. White matter lesions, particularly in the central portion of the corpus callosum;
2. Gray matter lesions: in the cortex and deep gray matter
3. Enhancement of the leptomeninges (the covering of the brain).

The MRI abnormalities in the central portion of the corpus callosum are the most important finding, because they are rarely seen in other diseases and are often diagnostic. (For more information about MRI abnormalities in SS, click on “Brain,” under “About Susac’s Syndrome”)

The MRI findings and symptoms of SS are commonly misdiagnosed as “atypical multiple sclerosis (MS).” But, these are two very different and distinguishable diseases, and are treated differently.

SS most commonly affects females who are between the ages of 20 and 40. However, men, children (as young as 8), and adults in their 50s can also be affected.

The clinical course (how the disease behaves over time) and long term outcome of SS differ from patient to patient. Many patients experience an acute “monophasic encephalopathic course” that lasts 1-3 years (sometimes longer) and is not followed by any further encephalopathic disease activity. If the disease during those 1-3 years is relatively mild or is otherwise successfully controlled by immunosuppressive medication, the outcome can be very good—i.e. little or no permanent damage sustained. In more severe cases, more prolonged disease, or both, there is potential for permanent, severe irreversible damage—i.e. varying degrees of dementia, visual loss, and deafness.

In addition to the acute “monophasic encephalopathic course,” there appears to be a somewhat milder and somewhat less worrisome course that is characterized chiefly by recurrent episodes of BRAO and hearing loss (the “recurrent BRAO/HL course”). Other patients appear to have a somewhat mixed course, with a
monophasic encephalopathic course that is either followed by, preceded by, or intermixed with recurrent BRAO/HL.

(For more information about the clinical course of SS, click on “Clinical Course, under “About Susac’s Syndrome”)

SS requires prompt, intensive, aggressive, and sustained immunosuppressive treatment. Treatment options include:

- Prednisone
- Intravenous “pulses” of methylprednisolone
- IVIG (intravenous immune globulin)
- Cyclophosphamide
- Mycophenolate mofetil (MMF)
- Azathioprine
- Newer “biologic therapies” (e.g. rituximab, anti-TNF therapy)
- Plasmapheresis (plasma exchange)

(For more information about treatment of SS, click on “Treatment,” under “About Susac’s Syndrome”)

The Immune System, Autoimmune Mistakes, and the Concept of Immunologic Self-Correction

The Immune System

By the “immune system” we mean that part of our body that is responsible for protecting us from infection. Specifically, we primarily mean the white blood cells (their actions and the actions of the products they produce) that circulate within our blood stream and that also reside in our lymph nodes and other tissues. These white blood cells (WBC) include T lymphocytes, B lymphocytes, macrophages and polymorphonuclear WBC, and the products they produce include cytokines, chemokines, and antibodies.

Autoimmune Mistakes

We want our immune system to go into action and use its WBC and their products to attack invading organisms, like bacteria and viruses. But, we do not want our immune system to attack parts of our own body, as if the immune system thinks (erroneously) that it sees bacteria or virus in those parts, or otherwise thinks these parts are foreign or dangerous. When the immune system does accidentally or inappropriately attack a part or parts of our own body, we call that an “autoimmune” attack.

Rheumatoid arthritis is probably the best known autoimmune disease. In rheumatoid arthritis, the person’s immune system is mistakenly attacking that person’s joints, as if their immune system has decided, quite erroneously, that there is infection in the joint that must be attacked. Their immune system is well-meaning, but is making an unfortunate mistake, and chronically so.

In Susac’s Syndrome the immune system is making the unfortunate mistake of attacking the endothelial cells that line the inner walls of the microvasculature that feeds the retina, inner ear, and certain parts of the brain.
Why does the immune system make such a mistake?
As is the case with rheumatoid arthritis, the mistake is usually a spontaneous one---meaning that it is not triggered by anything specific or determinable. It just happens, out of the blue, for no apparent reason. Most autoimmune diseases (rheumatoid arthritis, lupus, dermatomyositis, Susac's Syndrome, etc.) occur spontaneously.

These spontaneous mistakes probably happen, however, because of an underlying “programming error” in the person's “immune computer.” Our immune systems are, indeed, much like computers. They are “programmed” to know when to go into an attack mode, and when to leave things alone. This “programming” is done by our “immune response genes.” Some people have immune response genes that, unfortunately, mal-programmed their immune computers, such that their immune system is prone to make an autoimmune mistake, like rheumatoid arthritis (a common autoimmune mistake) or Susac’s Syndrome (a rare autoimmune mistake).

Immunologic Self-Correction
Fortunately, our immune systems are often able to correct their mistakes---though it is apparently harder to self-correct some mistakes than others, and children generally have better capacity for self correction than do adults. For example, the immune systems of children usually are eventually able to correct the juvenile rheumatoid arthritis mistake, the juvenile dermatomyositis mistake, and even the lupus mistake; but, the immune system of adults usually has less success in correcting autoimmune mistakes. Fortunately, the immune systems of adults and children seem to be able to self-correct the Susac's Syndrome mistake, often within 1-3 years---though not always.

Limitations of Current Treatments
Unfortunately, we do not currently have treatments that can specifically and directly correct the immune mistake that an immune system is making. If we did, we would have a “cure” for that particular autoimmune disease. However, we do have treatments (immunosuppressive/anti-inflammatory treatments) that either suppress the extent to which the immune system is making the mistake (by suppressing part or all of the immune system), or at least “throw water” on the fires that the immune system is mistakenly setting.

Until we have true “cures” for these autoimmune diseases, the main treatment approach is to use immunosuppressive/anti-inflammatory medications to control the “autoimmune fires” (slow down the fire-setting and throw water on the fires that have already been set) until the person’s immune system is able to self-correct (stop the fire-setting). If it is going to take the individual’s immune system 2 years to self-correct, that individual will need immunosuppressive treatment throughout those 2 years. Usually, self-correction occurs gradually, such that doses of immunosuppressive drugs can gradually be reduced after initial control has been achieved. But, the gradual reduction of immunosuppression needs to be done at a pace that is about equal to the pace of self-correction. If immunosuppressive treatment is reduced at a pace faster than the pace of self correction, a flare-up of disease is likely to occur.

Sometimes a person’s self-correction is interrupted by a return of loss of control (i.e. a relapse). In such an instance, the immunosuppressive doses that were working well, may no longer be sufficient and may need to be increased, at least temporarily.