

# AMIC Educational Newsletter

## Infectious Diseases and Imaging

### Infections and Nuclear Medicine: How Gallium-67 and Indium-111 WBC studies work

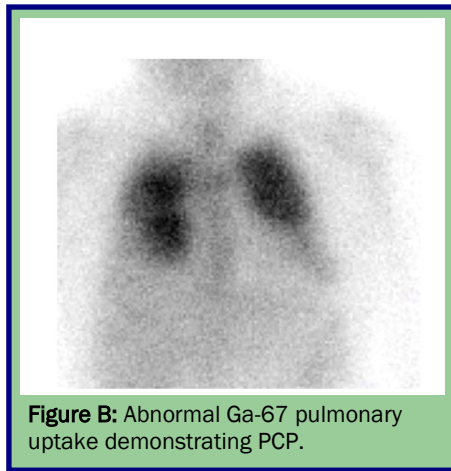
By Michael Rogan, MD

Nuclear medicine is a unique type of imaging that radiologists can use, because images are created by a radiotracer over time. This method creates images that are not static, but instead demonstrate an active physiologic process in the human body. Using two special radiotracers, Gallium-67 and Indium-111 labeled leukocytes, nuclear medicine can diagnose complicated causes of infections.

Gallium-67 is a radiotracer that has been used for more than 40 years. 90% of Ga-67 is in plasma. When there is an infection in the body, the infection causes increased blood flow and increased vascular membrane permeability. These two factors cause increased delivery and accumulation of transferrin-bound Ga-67 at the infectious or inflammatory process.

Ga-67 is an effective radiotracer for diagnosing infections because it binds to lactoferrin, which is present in high concentrations in inflammatory foci. Ga-67 also is directly taken up by bacteria. Siderophores (low molecular weight chelates produced by bacteria) have a high affinity for Ga-67. Even in the absence of circulating leukocytes, Ga-67 accumulates in infections.

There are several clinical situations which Ga-67 is very helpful. Opportunistic infections are a problem with immunocom-



**Figure B:** Abnormal Ga-67 pulmonary uptake demonstrating PCP.

promised patients, which can be detected with Ga-67. In the lungs, a normal Ga-67 scan of the chest excludes infection with a high degree of certainty. Diffuse Ga-67 uptake can represent *Pneumocystis Carinii* Pneumonia. Ga-67 is an extremely sensitive indicator of pulmonary inflammation, and can be seen with sarcoidosis, drug reactions, collagen vascular disease, and pneumoconiosis.

Fever of unknown origin (FUO), can also be evaluated with a Ga-67 scan. The most common cause of FUOs are infection, malignancy, and collagen vascular disease. Nearly 80% of FUOs are caused by an entity other than infection. Ga-67 accumulates in infection, inflammation, and tumor, and is often preferred over imaging with a tagged white blood cell study.

Figures A shows normal Ga-67 distribution, figure B demonstrates increased pulmonary uptake in a patient with *Pneumocystis Carinii* Pneumonia, and figure C shows a patient with sarcoidosis.

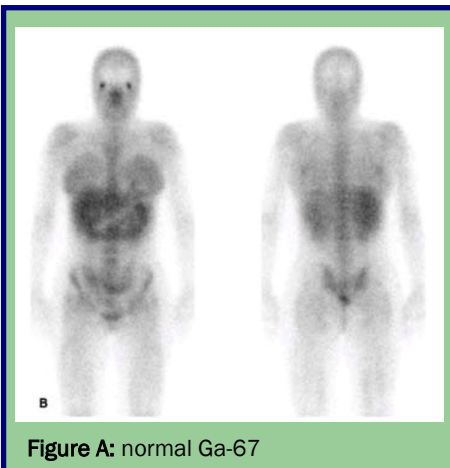
Indium-111-WBC is the other very useful radiotracer used to detect infections. Indium-111 is tagged to white blood cells, mostly neutrophils. Usually images are obtained 24 hours after the injection of radiotracer. Normal distribution is limited to the liver, spleen, and bone-marrow. The procedure is most helpful for identifying neutrophil-mediated inflammatory processes such as

bacterial infections. It is less helpful for those illnesses in which the predominant cellular response is not neutrophilic, such as opportunistic infections, tuberculosis, and sarcoidosis.

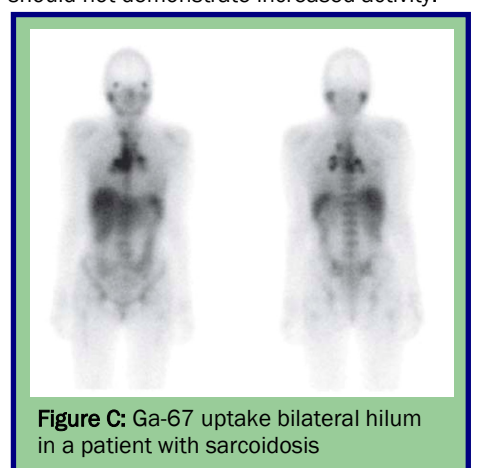
Focal uptake in lungs that is segmental or lobar usually is associated with bacterial pneumonia. Indium-111 does not accumulate in normal bowel. Any radiotracer activity in bowel is always abnormal. A differential diagnosis for activity in bowel is pseudomembranous colitis, infectious colitis, inflammatory bowel disease, ischemic colitis, and GI bleeding.

Postoperative infection is a common clinical question which can be answered using Indium-111 WBC. Indium-111 rarely accumulates in normally healing surgical scar (except for healing tracheostomy sites, which heal by granulation tissue which will normally have radiotracer uptake). An infected surgical incision will be positive, and a non-infected surgical incision will not have radiotracer uptake.

Tagged WBC studies are also the preferred imaging study to evaluate for osteomyelitis. To maximize accuracy, 99mTcSulfur Colloid marrow imaging is also performed. Osteomyelitis is diagnosed with a 3 phase bone scan, with positive findings on all three phase (increased activity is seen during initial hyper-perfusion, blood pool phase, and the delayed phase). The sulfur colloid portion should not demonstrate increased activity.



**Figure A:** normal Ga-67



**Figure C:** Ga-67 uptake bilateral hilum in a patient with sarcoidosis

## Infections and Nuclear Medicine Cont...



**Figure D:** Normal distribution of Indium-111 WBC study

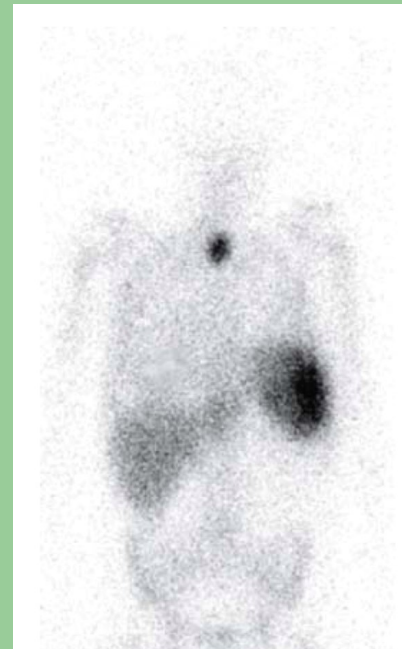
If there is increased activity with sulfur colloid at the suspicious site, then it is not osteomyelitis but rather normal bone marrow uptake. The only time Ga-67 is used for diagnosis osteomyelitis, it is for the interrogation of spinal osteomyelitis.

Figure D shows the normal distribution of Indium-111 WBC scan. Figure E shows abnormal uptake in the colon, in a patient with pseudomembranous colitis. Figure F shows uptake at a tracheostomy site.

When a complicated patient arrives in the hospital with a suspicion of infection, but no clear source, often Nuclear Medicine studies can prove highly valuable. The two most common tests to evaluate the source of infection are Gallium-67 and Indium-111 tagged WBC's. Using these different methods to image for infection, the radiologist and nuclear medicine staff can really help patients find the source of their infection.



**Figure E:** Abnormal uptake in the colon in a patient with Pseudomembranous Colitis.



**Figure F:** Uptake at a new tracheostomy site, which is normal for an Indium-111 WBC study

### Reference:

1. Brant, William E., Helms, Clyde A. Fundamentals of Diagnostic Radiology. Fourth Edition. 2012. Chapter 60. "Scintigraphic Diagnosis of Inflammation and Infection."

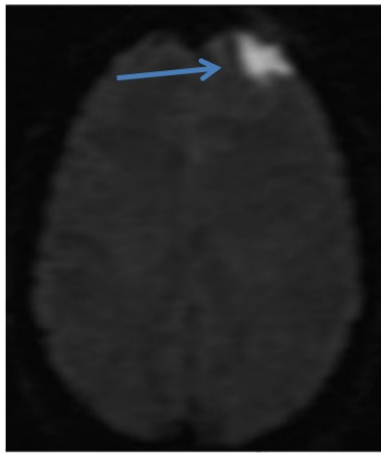
Michael Rogan, M.D.



## Imaging of Intracranial CNS Infection

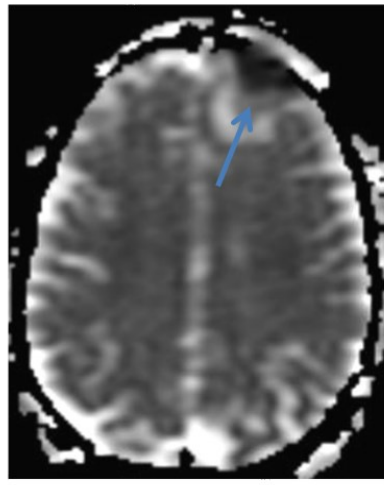
By Nicholas Statkus, MD

Intracranial infection is a relatively uncommon process however when this occurs imaging is often needed to localize the infection as well as to attempt to determine the type of infection. The multitude of infectious pathogens be they bacteria, virus, or parasite will exhibit imaging findings when the infection is active. This review will briefly discuss the imaging findings from a select group of infectious processes including bacterial, viral and parasitic infection where the imaging findings are consistently seen. During this review the MR diffusion sequence and its interpretation are additionally discussed.



**Figure 1A:** MR diffusion sequence through the brain shows high signal in the left frontal extraaxial space (blue arrow) in keeping with an epidural abscess/empyema.

Bacterial intracranial abscesses and epidural/subdural empyema are relatively uncommon. Both of these processes have unique MR imaging features which aid in determining the diagnosis. CT scan will be abnormal in the region of the abscess but MR imaging is needed to seal the deal for diagnosis. The diffusion sequence on MR is based on the micro-motion of water within the tissue being imaged. When water is freely mobile which is the natural state in the tissues within the human body there is no diffusion restriction on the diffusion sequence. When water mobility is reduced this is termed diffusion restriction and results in bright signal on the diffusion sequence. Both brain abscess-

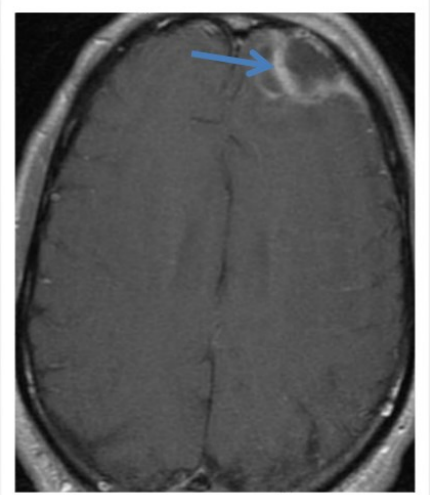
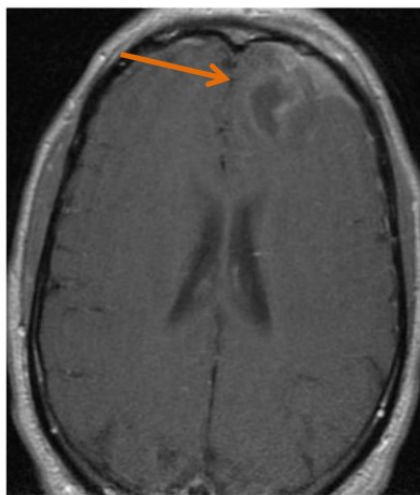


**Figure 1B:** MR ADC map shows low signal (blue arrow) in the left frontal region in the same area of the high signal seen on the diffusion sequence which confirms this represents true diffusion restriction. The ADC map has to be evaluated when interpreting the diffusion sequence. Where there is true diffusion restriction there is high signal on the diffusion sequence and low signal on the ADC map.



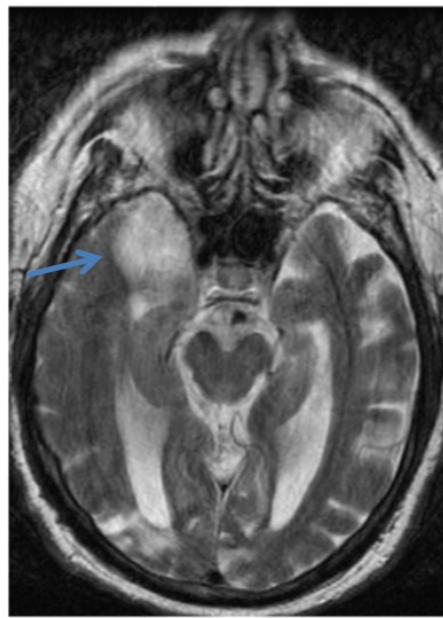
**Figure 1C:** Head CT in the same patient shows a cystic collection in the left anterior frontal region in keeping with an epidural abscess.

es and epidural/subdural empyemas will exhibit diffusion restriction on MR in the majority of cases (figure 1). Brain abscesses and empyemas will additionally show rim enhancement (figure 2). The early phase of a brain parenchymal infection is termed cerebritis and will show parenchymal edema



**Figure 2:** Postcontrast MR images in same patient as figure 1 show rim-enhancing fluid collections in the left frontal extraaxial space (blue arrow) as well as within the adjacent left frontal lobe parenchyma (orange arrow) in keeping with epidural and parenchymal abscesses. Of note in this case the brain abscess exhibits no diffusion restriction. Diffusion restriction usually, but not always, will be seen with brain abscesses/epidural abscesses.

## Imaging of Intracranial CNS Infection Cont...



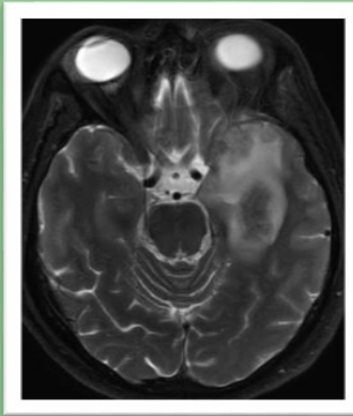
**Figure 3:** Axial T2 brain MR sequence shows parenchymal swelling and high signal within the right temporal lobe and right insula (blue arrows) in keeping with HSV infection. Post-contrast images, not shown, revealed no contrast enhancement in this area.

with or without minor enhancement and will often not show diffusion restriction. It is when the infection liquefies that the diffusion sequence shows the characteristic finding of high signal (diffusion restriction). It is important to note that an epidural/subdural empyema is a neurosurgical emergency as the empyema needs to be evacuated urgently to prevent significant complications from the infection such as development of parenchymal abscesses or venous sinus thrombosis.

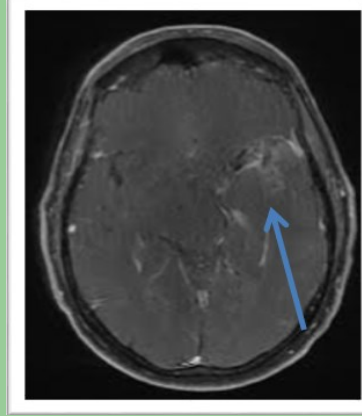
Herpes encephalitis is a brain parenchymal infection caused by HSV1 in immunocompetent patients in 95% of cases. The herpes virus remains dormant in many patients who are exposed to the virus residing in the trigeminal ganglion with acute infection occurring secondary to reactivation of the virus. Herpes infection in the brain characteristically affects the medial temporal lobes, insula and inferior frontal lobes where the parenchyma will appear enlarged and will exhibit edema on CT and MR (figures 3 and 5). The literature describes bilateral



**Figure 5A:** Head CT in patient with HSV infection shows non-specific edema in the left temporal lobe. This could represent a tumor, infarct of HSV infection. The clinical history should be helpful in differentiating tumor from HSV infection as symptoms related to tumor should be progressive over weeks to months as opposed to HSV infection which will have acute symptomology. When temporal lobe edema is seen HSV must be considered in the differential diagnosis as early treatment with acyclovir is essential.

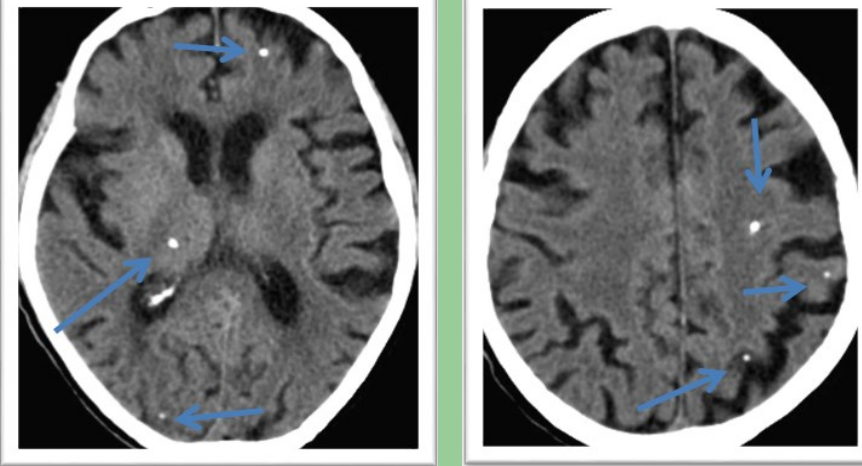


**Figure 5B:** Axial T2 brain MR image shows edema in the left temporal lobe in keeping with HSV infection.



**Figure 5C:** Axial contrast enhanced brain MR shows ill-defined enhancement in the left anterior temporal lobe. The enhancement is non-specific and thus the differential considerations are tumor, subacute infarct and HSV infection. Because of the temporal lobe location HSV infection must be a consideration.

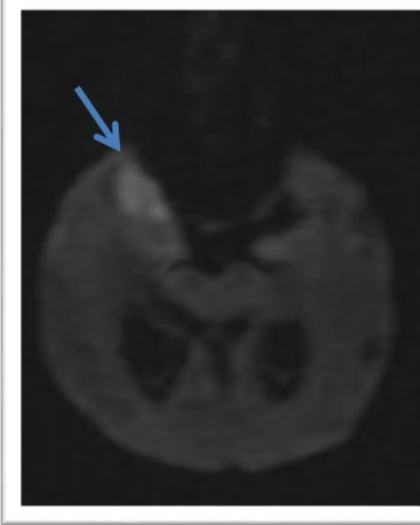
## Imaging of Intracranial CNS Infection Cont...



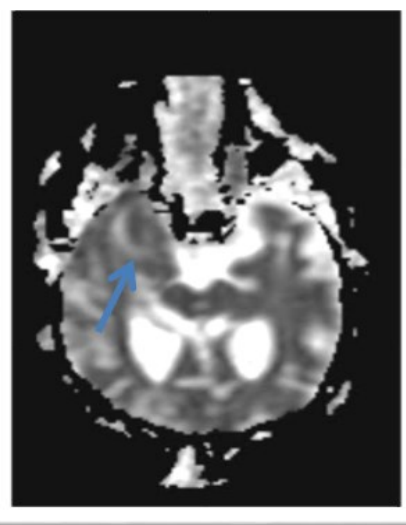
**Figure 6:** Head CT images show multi-focal parenchymal and CSF space calcifications in keeping with residua of distant neurocystocercosis infection. These calcifications are the most commonly seen finding in these patients.

involvement as a common finding however in my experience the infection is more often seen to be unilateral. No contrast enhancement will be present in the early stage of the infection. Gyriform enhancement can be

seen up to one week following infection. The MR diffusion sequence will show bright signal but does not will not always exhibit diffusion restriction (figure 4). When interpreting the diffusion sequence one must evaluate the



**Figure 4A:** MR diffusion sequence in same patient as figure 3 shows bright signal in the right anterior temporal lobe.



**Figure 4B:** MR ADC map of same patient as figure 3 shows no definite low signal in the region of diffusion bright signal therefore this represents T2 shine through and not diffusion restriction. This is an important distinction as the high signal on the diffusion sequence may be erroneously interpreted as an acute to subacute infarct (diffusion high signal is seen with brain infarcts) and HSV infection may thus not be included in the differential diagnosis.

ADC (Apparent Diffusion Coefficient) map. When the signal is high on diffusion sequence and low on the ADC map this is true diffusion restriction. When the signal is high on diffusion sequence and bright or neutral in signal on the ADC map this is termed T2 shine through and does not represent true diffusion restriction.

Herpes infection can be a difficult diagnosis to make as the imaging findings may be confused for an acute to subacute infarct or a brain tumor when the findings are unilateral therefore based on location alone this diagnosis must be considered when imaging findings occur in the temporal lobes, insula and inferior frontal lobes. HSV infection is a rapidly progressive infection and early treatment with acyclovir is essential to diminish morbidity/mortality.

Neurocystocercosis, caused by the pork tapeworm *taenia solium*, is the most common parasitic infection. CNS infection occurs in 60-90% infected with this parasite. The parasite is endemic in Latin America therefore in the U.S. the most commonly affected individuals are from Latin America. Neurocystocercosis is the most common cause of seizures in this patient population. There are 4 stages of intracranial infection with this parasite. The exact stage of infection may not be able to be determined based on imaging however the main pertinent findings included multi-spacial intracranial cysts in the brain, CSF space or ventricles in the earlier stages of the disease with variable degrees of parenchymal edema and enhancement depending on the stage of infection. The end stage of the disease is multifocal parenchymal or CSF space calcifications which represent the residua of the prior infection. The most common imaging finding seen related to this infection is the end stage multi-focal small intracranial calcifications which are visible both by MR or CT but are best appreciated on CT (figure 6).

Reference source:

1. Diagnostic Imaging Brain second edition. Osborn, Anne. Amirsy 2010.

Nicholas  
Statkus, MD



# Portal Hypertension

By Kenneth Cicuto, MD

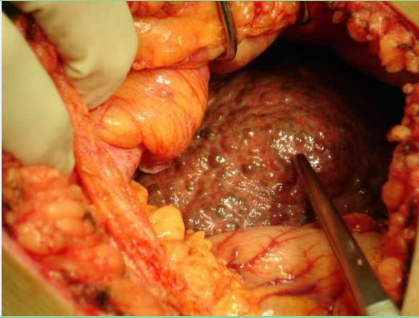


Figure 1

Portal Hypertension is defined as a portal systemic gradient as  $>5\text{mmHg}$ . Portal Hypertension is major cause of morbidity and mortality in US and worldwide. The most common cause in the US is cirrhosis, usually secondary to Hepatitis C or chronic alcohol abuse. Non-alcoholic steatohepatitis (NASH) will soon take over as the number one cause of cirrhosis in the Western Hemisphere. Figure one (pathologic cirrhotic liver).

Although we think of Hepatitis C as the most common cause of liver failure and cirrhosis, the number one cause is actually a fresh water parasite carried by snails! Schistosomiasis, also known as snail fever, is a disease caused by a parasitic flatworm. Infected individuals release eggs into fresh water and the larvae infect certain snail populations. The parasite matures and are released back into the body of water. Once ingested via a human host, the larvae make their way through the human vascular net-

work eventually dwelling within the GI or GU track. Figure 2 (page 6).

Schistosomiasis affects almost 210 million people worldwide with an estimated up to 200,000 human fatalities annually. The disease is most commonly found in Africa, as well as Asia and South America. Around 700 million people, in more than 70 countries, live in high

risk areas with children being the most susceptible host. In tropical countries, schistosomiasis is second only to malaria among parasitic diseases with the greatest impact.

Due to involvement of the mature worm and subsequent ova, the acute signs/symptoms of disease are rash, abdominal pain, diarrhea, bloody stool or urine. Figure 3 The more chronic sequelae include cirrhosis, renal failure, failure to thrive in children, and bladder cancer. In reference to cirrhosis, the ova of the mature worms become lodged in the small intrahepatic portal radicles causing obstructions. Additionally, the worms secrete soluble antigen and induce granulomatous reaction and subsequent scarring. Clinical signs and symptoms of cirrhosis with portal hypertension can include splenomegaly ( $>13\text{cm}$ ), gastroesophageal varices, ascites, right hepatohydrothorax, encephalopathy and much more. Figure 4a /4b

As interventionalists, our involvement with portal hypertension is extensive including diagnosis with trans-venous liver biopsy with pressure measurements to common minimally invasive procedure such as paracenteses and thoracentesis. More complex interventions such as transjugular portal

systemic shunt, (TIPS) and balloon retrograde transvenous obliterations (BROTO) are proven therapies which can be lifesaving and life prolonging in the patients with this unfortunate pathology. Figure 5a/5b



Figure 4A



Figure 4B

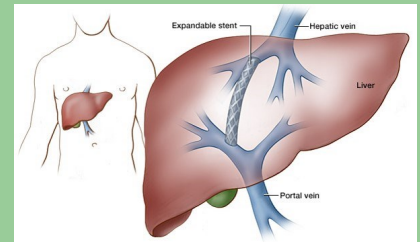


Figure 5A

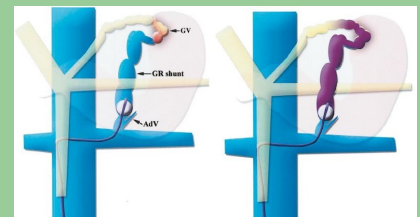


Figure 5B

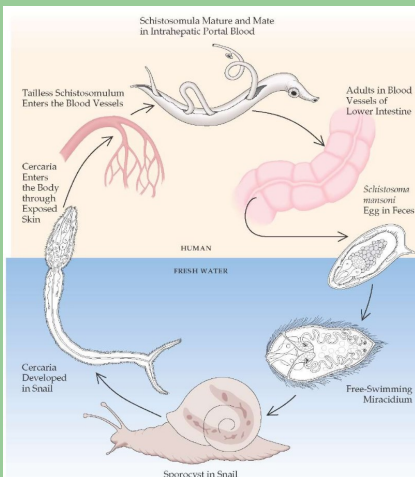


Figure 2



Figure 3

Kenneth Cicuto, MD



# Plain Film and MRI Imaging in the Diagnosis of Osteomyelitis

By Amy Hayes, MD

Osteomyelitis is infection of bone. It is a difficult to treat condition characterized by progressive inflammatory distraction and apposition of new bone.

## Pathogenesis

Bone is normally resistant to infection but trauma, surgery, bacteremia or foreign bodies may disrupt and lead to the onset of osteomyelitis. Infection can enter the bone by hematogenous seeding (i.e from bacteremia), by direct introduction from a contiguous focus of infection (adjacent diabetic ulcer for example), or by direct inoculation from penetrating trauma.

In adults, the vertebra are the most common site for hematogenous spread, lumbar spine is most common. In children the most common site for hematogenous spread is the metaphyses of the long bones.

## The disease process involves 5 stages:

1. Inflammation: This stage represents initial inflammation with vascular congestion and increased intraosseous pressure; obstruction to blood flow occurs with intravascular thrombosis.
2. Suppuration: Pus within the bones forces its way through the haversian system and forms a subperiosteal abscess in 2-3 days.
3. Sequestrum: Increased pressure, vascular obstruction, and infective thrombus

compromise the periosteal and endosteal blood supply, causing bone necrosis and sequestrum formation in approximately 7 days.

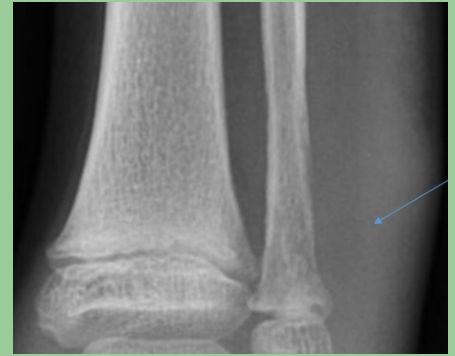
4. Involucrum: This is new bone formation from the stripped surface of periosteum.
5. Resolution or progression to complications: With antibiotics and surgical treatment early in the course of disease, osteomyelitis resolves without any complications.

## Organisms

The most common organism causing osteomyelitis is Staph aureus followed by Pseudomonas and Enterobacteriaceae. Less common organisms include anaerobic gram-negative bacilli and streptococcal viridans which is associated with dental extractions.



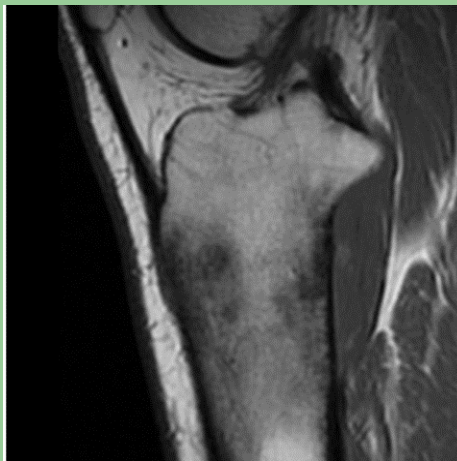
Soft tissue swelling with osteopenia indicative of osteomyelitis.



Osteopenia, loss of normal trabecular pattern and appositional bone growth consistent with osteomyelitis.

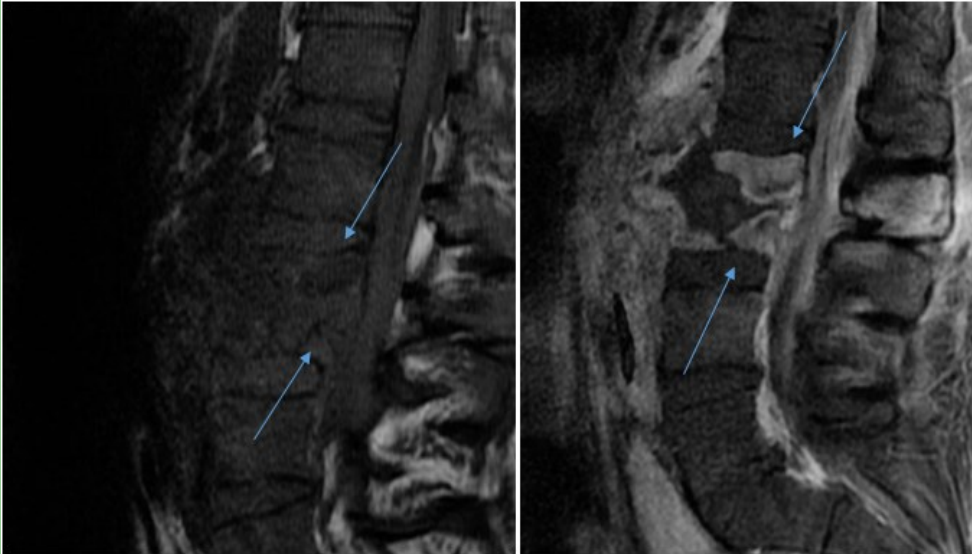


Soft tissue swelling, osteopenia, loss of cortex consistent with osteomyelitis



Osteomyelitis of the proximal tibia. Low signal in the marrow on T1 weighted images (left) and high signal on STIR images (right).

## Plain Film and MRI Imaging in the Diagnosis of Osteomyelitis Continued...



Vertebral osteomyelitis with enhancement of the affected vertebral bodies post-gadolinium.

be obvious until the infection has been present for 5-7 days in children and 10-14 days in adults. Findings include periosteal thickening, lytic lesions, endosteal scalloping, osteopenia, loss of trabecular architecture and new bone apposition. Specificity of plain films for osteomyelitis is higher than the sensitivity and thus additional, more sensitive imaging studies are important for early detection.

MRI allows early detection of osteomyelitis and assessment of the extent of involvement. It is considered the most useful imaging technique to evaluate suspected osteomyelitis because of its ability to demonstrate changes in the water content of bone marrow and has excellent spatial resolution. MRI is highly sensitive for detecting osteomyelitis as early as 3-5 days after the onset of infection. The earliest finding of acute osteomyelitis on

### Diagnosis

Osteomyelitis is primarily a clinical diagnosis but the clinical picture can be confusing. Symptoms are non specific and include pain, swelling and fever. Imaging can help distinguish between osteomyelitis and other diagnoses.

### Imaging

Current imaging recommendations include plain radiographs followed by MRI or 3 phase bone scan.

Evaluation typically starts with plain radiographs. Changes may be subtle but may not

MRI is an alteration of bone marrow signal intensity, which can be seen as early as 1-2 days after the onset of infection. Edema and exudate so in the medullary cavity produce an ill defined low signal intensity on the T1 weighted images and high signal on T2 weighted and STIR images. Gadolinium can cause peripheral enhancement of abscess or necrosis which can aid in the diagnosis.



16 year old stepped on a splinter two weeks prior. She presented with foot pain and swelling. Plain radiographs demonstrate periosteal reaction along the distal 2nd and 3rd metatarsals. STIR images from MRI demonstrates increased signal in the 3rd metatarsal consistent with osteomyelitis.

Amy Hayes, MD



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