The Problem:
Paratuberculosis, or Johne's disease, is a slowly progressive enteric bacterial disease that is commonly present but less commonly recognized in small ruminant flocks. The incubation period is usually at least one year and appearance of clinical disease is hastened by pregnancy/parturition or inadequate nutrition. Clinical signs are nonspecific poor production and ill thrift; intermittent or persistent diarrhea is sometimes noted but not dependable. Preclinical carriers are unlikely to be detected by serologic tests. There is no effective treatment and control by vaccination is not yet an option in the United States.

Etiology:
Paratuberculosis is caused by *Mycobacterium avium* subsp *paratuberculosis*, previously referred to as *M. paratuberculosis*. All strains are closely related genetically and antigenically to each other and to a mycobacterium typically carried by birds (*Mycobacterium avium*). For purposes of this review, the older but shorter name will be used. Strains of *M. paratuberculosis* from cattle and sheep differ in their growth characteristics on primary isolation. Cattle strains will grow in culture after 6-12 weeks of incubation. Sheep strains rarely grow in culture media by standard techniques; when isolated, they require incubation for 3 to 12 months or more to grow. Recently the Australians have developed a method of isolating the sheep strains, but the equipment used is very expensive. The Diagnostic Lab in Ithaca is now using this method. While both types of *M. paratuberculosis* can cause disease in goats and deer, the cattle type is more common in these species.

Transmission:
The primary mode of transmission is ingestion of contaminated feces. To quote Dr. Chris Rossiter at Cornell University, "All manure is guilty until proven otherwise." Young animals are most susceptible; however, older animals can be infected with large doses of *M. paratuberculosis*. In some individuals, the infection becomes systemic with spread to other internal organs via the lymphatics. Transmission in utero (cattle, goats and sheep) and potentially via milk (cattle and goats) has been documented and may also occur in other species. Transmission between species has been documented experimentally and in the field.

Pathogenesis:
Paratuberculosis is characterized by a long subclinical phase of infection during which diagnosis is very difficult. The organism is initially restricted to Peyer's patches in the intestine. As the disease progresses, acid fast bacteria become numerous in the wall of the intestine of some animals but remain few or absent in others.

The age of onset of fecal shedding and clinical disease varies with the dose, age at infection, and herd management factors. Fecal shedding usually precedes clinical signs. The typical range for clinical disease is 2 to 7 years of age; however, in some heavily infected goat and deer herds clinical infection and fecal shedding occur as early as one year of age. Excellent nutrition may delay the appearance of clinical signs until after the animal would be culled for other reasons.

Clinical Signs:
Unlike Johne's disease infected cattle (which typically present with chronic diarrhea and weight loss), sheep, goats and deer present with chronic weight loss as the primary clinical sign. Only 10-20% of clinical cases exhibit diarrhea or clumping of feces in the end stages of the disease. A drop in milk production is a common early sign in dairy goats.

Animals with paratuberculosis often show mild anemia (PCV below 25) and mild to marked hypoproteinemia. [Spin sheep and goat blood samples 10 minutes to get an accurate packed cell volume.] Hypoproteinemia can result in bottle-jaw, which mimics the effects of
endoparasitism. As a heavier than average parasite load often accompanies the terminal stages of paratuberculosis, the two conditions compound each other.

Diagnosis - the Index of Suspicion:
Paratuberculosis must be differentiated from other causes of chronic weight loss including malnutrition, parasitism, and chronic infections. Suspect paratuberculosis when one or more adults become emaciated while most of the group are in good body condition and social hierarchy (inadequate access to feed) or tooth loss will not explain the chronic problem. Check the individual animal and the group for abscesses due to Corynebacterium pseudotuberculosis (CLA), CAE (caprine arthritis-encephalitis) or OPP (ovine progressive pneumonia) virus infections, foot rot and even scrapie. Feel through the cheeks to evaluate molar teeth. Verify that forage was cut early enough to provide nutrients and stored under cover to avoid losses. Verify that the diet has adequate copper, as weight loss, diarrhea, and increased susceptibility to infectious and parasitic diseases occur with copper deficiency.

Suspect paratuberculosis when management systems have animals crowded together when young are present in the herd. Accelerated sheep flocks are increasingly recognizing the problem. Angora goat flocks, rapidly multiplying Pygmy goats, and deer herds on limited, contaminated ground also are at high risk. Fecal contamination of water sources can be a contributing factor.

Suspect paratuberculosis when the thin animals have parasite problems and necropsy yields a report of "starvation and parasitism". Evaluate the parasite control program especially relative to proper dosage of drugs and avoiding re-exposure after deworming. On heavily contaminated ground, animals will die of strongyles even with monthly treatments. Rule out liver flukes by fecal sedimentation tests and necropsy.

Do necropsies on any emaciated animals that die under 8 years of age (tooth problems, neoplasia, kidney disease become more likely in older animals). Sacrifice or home-slaughter several affected younger animals to get a diagnosis. Look for dilated lymphatics on the intestines and mesentery. Sometimes lymph nodes are necrotic or mineralized. Only rarely is there marked thickening of the intestinal mucosa.

Laboratory testing:
Request AGID tests on all small ruminants, fecal culture for goats and deer, and acid-fast stains on fecal smears.

Fecal culture will detect 40-60% of infected animals in goat and deer herds with clinical infection. In sheep flocks, the standard fecal culture is very insensitive and so rarely yields a positive result that it is an impractical diagnostic test. Paratuberculosis diagnosis in sheep is based on compatible clinical signs, and typical gross or histopathologic lesions with acid-fast organisms. Acid-fast smears of feces will identify approximately 55% of histopathologically positive sheep with clinical signs of paratuberculosis. The Australian culture system now being used at Cornell does detect infection in sheep in just a few weeks.

The best tissues for postmortem diagnosis are the ileocecal junction and ileocecal and mesenteric lymph nodes in all species. These should be submitted for culture and histology. Acid fast stains of impression smears are often diagnostic, if the owner finds histology too expensive.

Mycobacterium paratuberculosis infection must be differentiated from infections caused by M. bovis, the cause of bovine tuberculosis, and M. avium. All three mycobacterial infections can cause granulomatous lesions with acid-fast staining organisms in the intestinal tract. The organisms can be distinguished by culture and genetic probes on fresh or frozen tissue. These tests are done at the National Animal Disease Laboratory in Ames, Iowa.

Serologic tests used to screen for paratuberculosis include the enzyme-linked immunoassay (ELISA), agar-gel immunodiffusion (AGID), and the complement fixation (CF) tests. Cell mediated immunity and fecal shedding typically precede humoral immunity; thus serological assays detect animals progressing to the later stages of infection. The sensitivity (per cent of truly infected animals that show a positive test) of the AGID, CF, and ELISA has been
reported to be 87-100% for animals showing clinical signs; however, the sensitivity of these tests may be less than 20% in herds or flocks with little disease.

Given the difficulty in culturing sheep-type strains, the AGID test appears to be the most specific test with good sensitivity for identifying sheep in the later stages of disease. This test can be used to screen animals over 1 year of age to identify individuals most likely shedding organisms to herdmates and offspring.

The AGID test and fecal culture can be used together to detect infected animals in goat and deer herds. Believe the positive! To decrease expense, screen the herd with the AGID and then do fecal cultures on AGID negative animals over 1 year of age to identify subclinical animals that are light shedders. The frequency of testing depends on the herd owner's goals (control vs eradication and time line) and economics (labor of sample collection and test costs).

Control Programs:

There is no treatment for Johne's disease. Improved nutrition and supportive care of a clinically affected pet or breeding animal can certainly prolong its life but will also greatly increase the contamination of the barn, yards, and pastures. As the organism persists in the soil, keeping one animal alive may eventually lead to the premature death of many others. Also, the risk of in utero transmission in clinically affected animals and our inability to detect these infections in a timely fashion should together discourage the rebreeding of any known infected animals except for the production of slaughter animals.

Animals with clinical disease are more likely to transmit organisms in milk and in utero than are subclinically infected animals, and thus their offspring are apt to develop clinical signs at an early age. Lowered age of onset goes hand in hand with increased prevalence. On a herd basis, the problem (once recognized) gets worse before it gets better, even if the cycle of transmission is broken.

Once the disease has been diagnosed in a herd or flock, test and cull if feasible. Culling on the basis of a positive AGID result should be helpful for flock control as the heavy shedders are usually AGID positive. (The test sensitivity for this group is close to 95%). Test negative animals showing clinical signs consistent with paratuberculosis should also be segregated or culled. [When in doubt, cull it out!] Offspring of these animals should be culled or at least taken from the dams at birth, reared on colostrum and milk from test negative, healthy animals and monitored in a suspect group.

Whether or not a test and cull program is implemented, stress control by management. Body condition score regularly and cull to slaughter any animal without a good excuse for being thin. Some of these animals may have a different problem, such as caseous lymphadenitis or CAE/OPP, but culling for the wrong reason is still the right choice. Cull all offspring of suspect animals. Care should be taken to avoid fecal build up in birthing areas to limit fecal-oral transmission of \textit{M. paratuberculosis} to offspring. Shear or crutch ewes prelambing. Do not overcrowd. Use elevated feeders to prevent fecal-oral transmission. As \textit{M. paratuberculosis} can survive for a year or more in the environment, overgrazing and spreading of infected manure on pasture must also be avoided to prevent transmission. Manage all home reared replacements to minimize risk of infection. Do not house the thin or sick animals in the lambing/kidding area just for the convenience of easy access. Thin animals with or without nursing young should be housed away from the main flock and the area cleaned thoroughly afterwards.

Don't introduce the disease with rescued animals or colostrum or milk from infected dairy herds. Manger sweepings from cow dairies are an important source of infection for heifers and presumably can also infect small ruminants. Also avoid buying replacements from herds or flocks with a history of paratuberculosis or from herds with naive owners.

Vaccination programs using either killed or modified live organisms have been used with success to prevent herd losses in Europe. Ideally replacements are vaccinated while quite young, but vaccination of adults appears to limit future losses from clinical paratuberculosis. No vaccine is yet available for small ruminants in the United States.
Selected References:

Websites:
Johne’s Information Center <http://johnes.org/>
PARA - Paratuberculosis Awareness and Research Association (dedicated to Crohn’s disease) <http://crohns.org/>