

Designing effective calf vaccination programs

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Abstract

Vaccination is an important component for the prevention and control of bovine bacterial and viral diseases. Modified-live vaccines (MLV) have been used because of the good antibody response, longer duration of immunity, fewer doses needed per animal, and lower cost. The selective pressure from an animal's immune response may lead to new viruses that persist and cause problems in the herd. An interesting vaccine will be the live *Pasteurella multocida* and *Mannheimia hemolytica* vaccines. Non-adjuvanted MLV vaccines also fail to booster well vaccinated animals as active vaccine-induced immunity neutralizes vaccine virus preventing the MLV from replicating and preventing a booster immune response. Improved adjuvants have increased the scope and duration of inactivated virus immunity. Inactivated vaccines generate cell-mediated response and can enhance the immune response in well-vaccinated animals. This whole process from vaccination to achieving mature immune response takes at least 3 weeks. This fully developed mature primary response can then be boosted to get a true anamnestic secondary response. There is no "single vaccination program" that will work on most farms or ranches. Each vaccine program needs to be designed based on the actual threats and needs of the farm, and not based on a company's or neighbors suggested program.

Key words: cattle, calf, vaccination, immunity

Résumé

La vaccination est un élément important pour la prévention et le contrôle des maladies bactériennes et virales bovine. Modification-vaccins vivants (MLV) ont été utilisés en raison de la bonne réponse anticorps, plus longue durée de l'immunité, un moins grand nombre de doses nécessaires par animal, et à moindre coût. La pression sélective de la réponse immunitaire d'un animal peut conduire à de nouveaux virus qui persistent et causer des problèmes dans le troupeau. Un intéressant le vaccin sera le live *Pasteurella hemolytica multocida* et *Mannheimia* vaccins. Sans adjuvant MLV vaccins échouent également à bien d'appoint animaux vaccinés que l'immunité induite par le vaccin actif neutralise le virus du vaccin empêchant la réplication du MLV et prévenir un booster de la réponse immunitaire. Adjuvants améliorés ont accru la portée et la durée de l'immunité de virus inactivés. Les vaccins inactivés générer réponse à médiation cellulaire et peuvent accroître la réponse immunitaire dans bien des animaux vaccinés. Tout ce processus de la vaccination pour

atteindre réponse immunitaire mature prend au moins 3 semaines. Cette réponse primaire mature pleinement développé peut ensuite être stimulé pour obtenir une vraie réponse secondaire anamnestic. Il n'y a pas de "programme de vaccination unique" qui fonctionne sur la plupart des exploitations agricoles ou des ranchs. Chaque programme de vaccins doit être conçus sur la base des menaces réelles et des besoins de la ferme, et non pas fondées sur une entreprise ou voisins programme suggéré.

Bovine Vaccine Principles

Vaccination is an important component for the prevention and control of bovine bacterial and viral diseases. Intranasal vaccines have the advantages of inducing mucosal immunity, stimulating good immunity in young animals, and are not being affected by maternal antibody.^{10,20} Maternal antibody interference to bovine viral diarrhea virus (BVDV) or infectious bovine rhinotracheitis (IBR) are less of a problem than it is for bovine respiratory syncytial virus (BRSV),⁸ but animals should receive their first parenteral dose at 1 to 3 months of age with subsequent boosters depending on the type of vaccine (inactivated vs modified live (MLV)) and re-vaccination 30 days prior to breeding.³ Adjuvanted MLV vaccines can overcome maternal interference.^{22,23} Another approach to assess the impact of maternal interference is to collect serum samples from 10 to 20% of the calves (at 3 to 4 months of age), and measure BVDV, IBR and/or BRSV antibody titers to determine if maternal antibody titers are high. If they are high, then retesting could be done 1 to 2 months later to determine if antibody levels are low enough to allow a good vaccine response. Vaccines should contain both CP BVDV 1 and 2. Even though there is some cross protection between Type I and Type II, the best protection comes from CP vaccines containing both Type I and II. NCP BVDV vaccines provide excellent cross protection with just a single type^{1,12} as does the Singer CP BVDV strain.⁵

Vaccine Types

Modified live vaccines are used because of the good antibody response, longer duration of immunity, fewer doses needed/animal, and lower cost. These vaccines are administered intramuscular, intranasally or subcutaneously. MLV vaccines have drawbacks because they can contain adventitious agents and the MLV BVDV and IBR vaccines are immunosuppressive. Although the return to virulence in MLV viruses has been minimal, mutations will occur and there is some risk of new strains arising. The selective pressure from

an animal's immune response may lead to new phenotypes. MLV vaccines also fail to booster well vaccinated animals as active vaccine induced immunity neutralizes vaccine virus, thereby preventing the MLV from replicating and preventing a booster immune response.^{7,17} One of the more interesting developments has been the development of intranasal live-bacterial vaccine containing *Mannheimia hemolytica* and *Pasteurella multocida*.⁶

Inactivated vaccines contain chemically or physically treated bacteria, toxins and/or viruses so there is no danger of replication of the pathogen in the vaccinated animal or adventitious agents that maybe present in a MLV. Improved adjuvants have increased the scope and duration of inactivated virus immunity. They have several disadvantages including cost and more doses required/animal. Inactivated vaccines generate cell-mediated responses.^{18,19} Hypersensitivity reactions (allergic) also occur more often with inactivated vaccines. Interestingly there is ample evidence that inactivated vaccines can effectively boost MLV vaccines.^{9,13,17}

Timing of Vaccination

Vaccination at the Time of Arrival (and/or Weaning)

Vaccination programs are a routine practice in beef and dairy operations to protect cattle against bovine respiratory diseases (BRD). Numerous commercial vaccines for the prevention of BRD have been available since the 1950s. Current vaccine protocols recommend that calves be vaccinated prior to weaning or commingling to provide protection against BRD. Unfortunately, many calves are not vaccinated prior to weaning or commingling into backgrounding lots, feedlots or pasture operations. These animals are at increased risk of viral infection and are predisposed to secondary bacterial pneumonia.¹⁶ However, the highly-stressed calf presents a unique problem—the vaccines may sometimes actually predispose the calves to more severe disease while on other occasions providing protection.

The time from vaccination to onset of protection can play an important role in subsequent health management of newly arrived cattle, in particular protection against BRD viral agents such as bovine herpesvirus 1 (BHV-1; IBR) BRSV, and BVDV. Commercially available MLV vaccines administered to non-vaccinated, low-stress calves at weaning or at arrival to feedyards will provide increased weight gain and protection to animals as early as 48 hours prior to an IBR exposure,⁴ at 5 to 7 days prior to a BVDV² exposure, and 8 days prior to BRSV exposure. This protection is due to the innate immune response, which is activated within hours after exposure to MLV vaccines or infectious virus.

Frequency of Vaccination

No more than 1 to 2 doses of MLV or 2 to 3 doses of inactivated vaccine should be administered to young calves less than 4 months of age to develop good herd immunity against respiratory diseases.

Interval between Doses of Vaccine

In all animals there is expansion in the populations of responding T- and B-cells following vaccination¹⁴ (Figure 1). However, to have a complete and mature immune response, this T- and B-cell expansion must not only stop but also an active process of cell death (apoptosis) must also occur. This “waning process” allows “culling” T- or B-cells that may be poor responders or even cause autoimmunity to be removed by apoptosis (Figure 1). This whole process from vaccination to achieving mature immune response homeostasis takes at least 3 weeks. This fully developed mature primary response can then be boosted to get a true anamnestic secondary response. In many cases, cattle vaccine primary and booster doses are administered at 2-week intervals. In young calves, this is done to provide an opportunity to make sure that the calves develop a primary response in the face of maternal immunity. The adjuvants that are used with most commercial vaccines provide superior immune development over older generation adjuvants like alum. Therefore, in most instances, if primary vaccination occurs after 3 weeks of age, booster vaccination beyond 3 weeks and even longer will be efficacious. The dogma that revaccination must occur within 2 weeks of the primary vaccination is not true, and the anamnestic response will be better if we wait longer

The Special Case of Young Calves and their Immune Response

Active Immunity in the Calf

While all the essential immune components are present in the neonate at birth, they do not seem fairly functional until at least 2 to 4 weeks of age. The developing and newborn calf is subject to a number of immunomodulatory effects. The

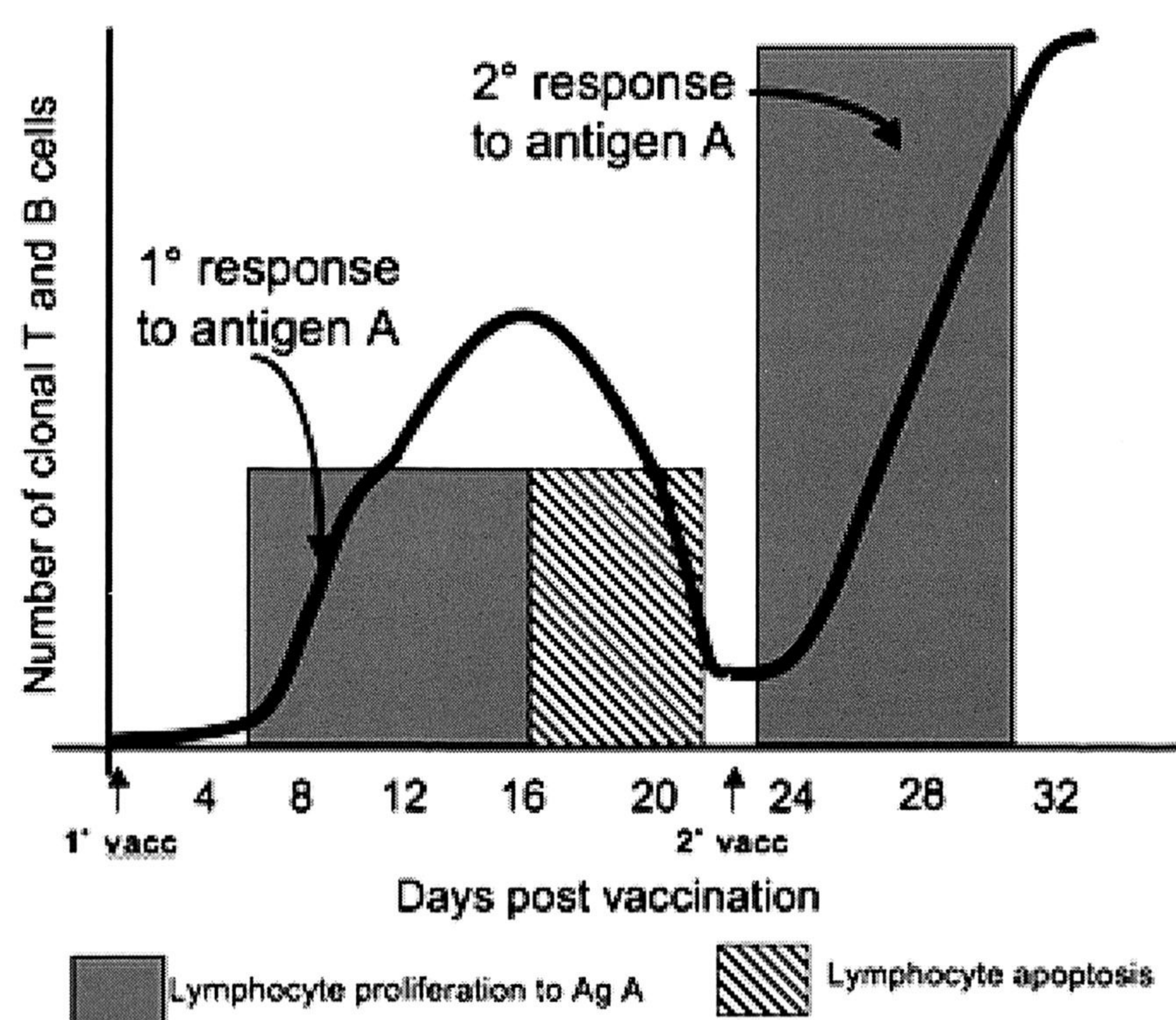


Figure 1. Interval between vaccinations.

placenta produces hormones and cytokines, such as IL-4 and IL-10, that affect both the fetus and the dam and suppress immunity. In addition, the cow produces estrogen and cortisol prior to parturition that all also have immunosuppressive effects. Finally the calf, as part of the parturition process produces high levels of cortisol that remain elevated for the first week of life. The cumulative effect of these hormones is to suppress the immune system and to direct the immune response away from the long-term memory response to the short-term antibody immune.³

Innate Immunity

The humoral components of the innate system are suppressed. Complement activity at birth in the newborn calf is about 50% of the cows and quickly decreases to <20% of the cows activity at 1 day of age. They gradually increase and by 1 month of age are back to 50%. Interferon production by leukocytes is lower. The cellular component is also affected. Neutrophils numbers in the newborn calf are 4X higher than 3-week-old calves.^{11,21} The neonatal neutrophils and macrophages have reduced phagocytic ability that increases following the ingestion of colostrum. By 1 week of age, neutrophils are functional and able to mount an effective response. Neutrophil function gradually improves to adult levels by 5 months of age. The number of dendritic cells is lower and their ability to present antigen to the acquired immune system is also decreased.^{11,21} Natural killer cells are also low at 1 week of age (3% of total lymphocytes) and increases to 10% by 6 to 8 weeks of age.^{11,21}

Acquired Immunity

The neonatal calf is born without any antibody and is totally dependent on colostrum intake for immunoglobulins. The number of B cells is greatly reduced in the neonate at 4% of the total lymphocytes at a week of age, and increase gradually to 20% of total lymphocytes at 6 to 8 weeks of age (normal is 20 to 30%).^{11,21} This low number of B cells coupled with the immune suppression induced by the calves endogenous corticosteroids, maternal, and placenta hormones results in a lack of an antibody response until at least 3 weeks of age against parenterally administered viral and bacterial antigens.¹⁵ Activation of T-lymphocytes is slightly less depressed at birth and remains constant through 28 days after birth. The take home message of active immune response in young calves is that cell mediated responses to vaccines can be induced very early, however animals must be 3 to 4 weeks of age before vaccines will induce robust antibody responses that will develop in 10 to 14 days following vaccination. The management of the calf's immune response requires understanding of the immaturity and development of the calf immune system. Vaccine timing needs to be managed to take advantage of the biology of the immune system and not haphazardly.

Calf Vaccination Programs

There is no "single vaccination program" that will work on most farms or ranches (Table 1). Each vaccine program needs to be designed and based on the actual threats and needs of the farm, and not based on a company's or neighbors suggested program. The generic disease syndromes (respiratory, reproductive or enteric) included in this sample vaccination program are provided as examples, and vaccines for specific diseases should be those that are either present (and/or have been a problem in the past) and/or a new disease that is a real threat to the farm. Any calf disease control program begins with a good vaccination program in the cow prior to calving, particularly for calf diarrheal diseases. Colostrum is essential for beef calf immune development and protection.

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Table 1. Vaccination programs for calf immunity.

Beef

Heifers (prebreeding) need to receive at least 1 dose of MLV prior to addition to the breeding herd

Respiratory and Reproductive Diseases

MLV-2 doses
 >6 months of age and repeated 2 months before breeding

Inactivated-2 doses
 5 weeks and 2 weeks before breeding

Enteric Diseases

MLV-2 doses
 5 weeks and 2 weeks before calving

Inactivated-2 doses
 10-12 weeks and 4 weeks before calving

Cow Herd

Respiratory and Reproductive Diseases

Inactivated
 3-4 weeks before breeding is ideal

MLV
 3-4 weeks prior to breeding is ideal. Do not vaccinate pregnant cows - no efficacy demonstrated for preventing PI in subsequent pregnancy. Problems with IBR abortion in animals poorly vaccinated

Enteric Diseases

MLV-1 doses
 2-4 weeks before calving

Inactivated-1 dose
 4-6 weeks before calving

Calves (<4 months)

MLV - viral and bacterial respiratory (*M. hemolytica* and *P. multocida*) vaccines
 Calves on vaccinated cows - MLV intranasal vaccines (depends on maternal antibody levels. MANY MLV IM or SC **NOT EFFECTIVE**
 - ONLY adjuvanted MLV IM or SC)

Inactivated Respiratory - well adjuvanted, not affected by maternal antibody

Bacterial respiratory *M. hemolytica*, *P. multocida*, *H. somni* - (live or bacterins, subunit vaccines intranasal)

Clostridials

Leptospirosis???

Calves (>4 months)

2-3 weeks prior weaning

 MLV respiratory virals - 1 dose

 Inactivated respiratory virals - 2 doses

 Bacterial respiratory *M. hemolytica*, *P. multocida*, *H. somni* - (live or bacterins, subunit vaccines)

 Clostridials

At weaning (worse time to give vaccines)

 MLV respiratory - immunosuppressive

 Inactivated respiratory virals - 2 doses - least stressful

2-3 weeks post weaning

 MLV - 1 dose

 Inactivated virals - 2 doses

 Bacterials *M. hemolytica*, *P. multocida*, *H. somni* - (live or bacterins, subunit vaccines)

 Clostridials

Brucellosis

Leptospirosis

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