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REVIEW ARTICLE

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Public Health Significance of Bovine Mastitis

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ABSTRACT

Mastitis is inflammation of the parenchyma of the mammary gland regardless of the cause. The predominant pathogens for the disease throughout the world include staphylococcus species, streptococcus species and coliform species. The principal bacterial infection associated with ingestion of milk and milk products are caused by different bacterial genera. The bacteria that are transmitted through milk and cause disease problems in man are bacteria causing mastitis in cattle and transmissible to human when man uses raw milk from infected udder. Example of such type of bacteria includes Mycobacterium, Brucella, and Staphylococcus and Streptococcus species. Antibiotic residues following treatment of mastitis can be a potential hazard to humans in allergic reaction and possible transfer of resistant to other organisms. Drugs are intended to be toxic to various forms of micro organisms as such may have inherent toxic, mutagenic, teratogenic, drug resistance and carcinogenic effect to humans.

Key words: Drug residues, Mastitis, Mammary Gland, Bacterial Infections and Raw milk.

INTRODUCTION

Mastitis is the inflammation of the parenchyma of the mammary gland regardless of the cause. It is a complex disease, with a number of factors contributing to the level of mastitis in a herd, including environment, management, and udder physiology and cow health. Pathogens causing mastitis in cattle are divided into major pathogens that cause clinical mastitis and minor pathogens that cause subclinical mastitis. Among major pathogen includes *S. agalactiae*, *S. aureus*, and *M. bovis.* Coagulase negative Staphylococcus species such as *Staphylococcus hyicus* and *Staphylococcus chromogen*, which are commonly isolated from milk samples and the teat canal, are from minor pathogens. The most important changes in the milk includes like discoloration, the presence of clots and the presence of large numbers of leukocytes (Wilson *et al*., 1997). Milk is a vehicle of infectious agent and excellent medium for the growth of many pathogenic bacteria. Some of the main reasons why milk is an important transmitter of disease to human are: it is relatively good medium for micro-organisms to grow and is most likely to be contaminated easily during its production. The major bacteria that can be transmitted through milk and produce disease in man include *Mycobacterium bovis* and Brucella species from infected udder. Furthermore, most bacteria causing mastitis like *Staphylococcus aureus* and *Listeria monocytogenes* can also be transmitted through milk and milk products (Heeschen, 1994). With mastitis there is a danger that the bacterial contamination of milk from affected cows may render it unsuitable for human consumption by causing food poisoning, interfere with manufacturing processes or, provide a mechanism of spread of disease to humans. Milk can be contaminated with antibiotics due to a number of reasons including excessive use of antibiotics, failure to identify treated animals, failure to apply antibiotics according the proposed prescription, lack of awareness about withdrawal period, withholding milk only from treated animals and purchase of cows treated with antibiotics (Aielso and Mays, 2005).

Antimicrobial residues in food animals have many implications on public health; there is a possibility of direct reaction to residues or toxic, anaphylaxis. There is also likely hood of developing drug resistance strains of bacteria. Antibiotics which are frequently and commonly applied in veterinary medicine includes: B-lactams (penicilin), Aminoglycosides (streptomycin, neomycin), Tetracycline (doxycycline, minocycline), Macrolides (erythromycin and chloramphenicol) (IDF, 1995). Therefore, the objectives of this seminar paper are:

- To provide highlights about mastitis.
- To provide highlights on public health significance of mastitis due to milk borne disease as well as drug residues in milk following treatment of mastitis.

GENERAL ON BOVINE MASTITIS

Definition and etiology

Mastitis is the inflammation of the parenchyma of the mammary gland regardless of the cause. Bovine mastitis is associated with many different infectious agents. Most commonly, mastitis begins as a result of penetration of teat duct by pathogenic bacteria Although variation exists on the type and isolation rate from country to country, the most commonly incriminated and reported causes of mastitis include *staphylococcus aureus*, *streptococcus agalactiae*, coagulase negative staphylococcal species, *Esherichia*

coli and Bacillus species (Jabb and Kennedy, 1997).

Pathogens causing mastitis in cattle could be environmental or contagious pathogens. Environmental pathogens survive in the cow's environment and enter the udder by propulsion through the teat canal during milking. *Escherichia coli* and *Streptococcus uberis* are the most important environmental pathogens. Contagious pathogens usually live in the udder or teat skin and are transferred to the teat and spread during milking. *Staphylococcus aureus*, *Streptococcus agalactiae* and *Streptococcus dysgalactiae* are the most important (Radostits *et al.,* 2007). Pathogens causing mastitis in cattle are also divided into major pathogens that cause clinical mastitis and minor pathogens that cause subclinical mastitis. Among major pathogen includes *S. agalactiae*, *S. aureus*, and *M. bovis.* Coagulase negative Staphylococcus species such as Staphylococcus *hyicus* and *Staphylococcus chromogen*, which are commonly isolated from milk samples and the teat canal, are from minor pathogens (Bradford, 1996).

Epidemiology

Mastitis is considered to be a typical example of a complex disease, which requires the interaction of the host, agent, and the environment (Radostits *et al*., 1994). Host factors include breed, physiological state of mammary gland, and anatomy of teat canal, sphincter tone and presence of teat lesion. Agent factor includes the ability to survive in the immediate environment of the animal, the ability to colonize the teat duct, the ability to adhere to the mammary epithelium and not to be flushed out with milk flow Environmental factor includes milking practice, housing system and bedding (Quinn *et al*., 1994).

Pathogenesis

Inflammation of the mammary gland predominantly occurs via the teat canal except in the case of tuberculosis, leptospirosis and brucellosis where the method of spread may be haematogenous. The development of mastitis can be explained in terms of three stages as invasion, infection and inflammation. The invasive stage refers to the time in which pathogens move from the teat end to the milk through the teat canal. The infection stage is the stage in which the pathogens multiply rapidly and invade the mammary tissue. The stage of inflammation is the stage with varying degrees of clinical abnormalities of the udder and with systemic effects from mild to per acute as well as gross and subclinical abnormalities of the milk (Radostits *et al*., 2007).

Clinical sign

The clinical findings in mastitis include abnormalities of secretion such as discoloration, clots, flakes, pus in milk, abnormalities in the size of the udder which is larger than normal quarter; firm in consistency and temperature of the mammary glands pyrexic, depressed or has decreased appetite or milk production and, frequently, a systemic reaction (Radostits *et al*., 2007).

Diagnosis

Clinical mastitis is recognized by an abnormal milk, gland swelling and/ or illness. Sub clinical mastitis is characterized by normal milk and requires indirect tests such as Somatic Cell Count (SCC) that includes white blood cells (WBC) and occasionally sloughed epithelial cells. The California mastitis test (CMT) is the commonly used screening test for sub clinical mastitis. Culturing for microbial examination of both individual cow and bulk milk samples are used in the

identification of pathogens. There are also chemicals like potassium hydroxide (10%) for detection of mastitic condition from milk sample (Aielso and Mays, 2005).

Prevention and control

When we speak control, it usually refers to contagious mastitis and environmental mastitis. The primary reservoir of environmental pathogens is an infected mammary quarters. Risk of exposure of uninfected mammary quarters to contagious pathogen is limited in the milking process. In contrast exposure of uninfected quarters to environmental pathogens can occur at any time during the dry period, and prior to first calving in heifers (Smith and Hogan, 1993).

Contagious mastitis is controlled in dairy herds by post milking teat dipping, total dry cow therapy, culling, therapy of clinical cases, and proper maintenance of milking equipment (Radostits *et al*., 1994). Control of environmental mastitis is achieved by reducing exposure of teat ends to environmental pathogens and by maximizing the resistance of the cow to intramammary infection. Significant sources of environmental pathogens are organic bedding materials, manure, and wet or damp areas in barns, or pastures. Milking time hygiene can influence teat end exposure. In general, exposure is minimized when all areas of the environment are clean, cool and dry. Resistance is maximized by providing a stress free environment that minimizes teat injury, and by feeding balanced diets rich in vitamin E and selenium. Antibiotic therapy during lactation or the dry period is of little value in the control of environmental mastitis (Smith and Hogan, 1993).

PUBLIC HEALTH SIGNIFICANCE

With mastitis there is a danger that the bacterial contamination of milk from affected cows may render it unsuitable for human consumption by causing food poisoning and provides a mechanism of spread of disease to humans through consumption of raw milk. Many farm families simply consume raw milk because it is a traditional practice and it is less expensive to take milk from the bulk tank than buying pasteurized retail milk. Some believe that raw milk has a higher nutritional value than pasteurized milk. The bacteria that are transmitted through milk and cause disease problems in man are bacteria causing mastitis in cattle and transmissible to man when man uses raw milk from infected udder**.** Example of such type of bacteria includes Mycobacterium, Brucella, Staphylococcus, streptococcus, Campylobacter and Listeria species (Heeschen, 1996).

The presence of residue in milk following treatment of mastitis is a major public health concerns that adversely affects the dairy industry, the practicing veterinarian and the safety of milk for human consumption (Hagsted and Hubbert, 1986).

Milk borne infection

Raw (unpasteurized) milk has been found to participate in spreading out of illnesses caused by *Mycobacterium bovis*, *Brucella abortus*, *Staphylococcus aureus*, *Listeria Monocytogenes, Campylobacter jejuni, Salmonella, Staphylococci species,* and *E. coli.* With severe clinical mastitis, abnormalities of milk are easily observed and milk is discarded by the producer. Such milk normally would not enter the food chain. But when milk of cows with sub-clinical mastitis, which is with no visible changes, is accidentally mixed into bulk milk, it enters into food chain and can be dangerous to humans. Although pasteurization is likely to destroy most of human pathogens, there is concern when

raw milk is consumed or when pasteurization is incomplete or faulty (Jayarao *et al.*, 2006).

The principal bacterial infection associated with ingestion of milk and milk products are caused by different bacterial genera. The reservoir of these bacteria may be milk producing mammals, humans or contamination from environmental reservoirs. In diseases such as brucellosis, salmonellosis or tuberculosis milk may be contaminated with the causative bacteria before it leaves the infected udder. The selection of milk borne pathogen is difficult because of the different importance in different countries. However, in general Brucella species, Mycobacterium species, *Listeria monocytogenes*, *Campylobacter jejuni* and *Staphylococcus aureus* seem worth to be as milk borne zoonosis (Heeschen, 1994).

Brucellosis

Brucella species are mainly parasite and pathogens of domestic animals. However, *B. abortus* can cause brucellosis in humans, who acquire the disease from the animals (Michael *et al*., 1986). Brucella is small bacilli which show some variation in size, measuring from 0.6 -2.0 micro meters in length and 0.3-0.5 micro meter width (Buxton and Fraser, 1997). Growth in laboratory media is slow and often not visible until after 48 hours incubation at 37 centigrade. *B. abortus* grows particularly in 5-10 percent. Brucella is killed by heating to 60 centigrade for 10 minute and in milk by pasteurization. They are susceptible to an acid pH, to disinfectants and to direct sun light. The organism remains viable for long periods at low temperature (less than 8 centigrade). For optimum growth rate and for primary culture a variety of solid media including serum agar, liver infusion and tryptose agar have been recommended (Sharman and Adlakha, 2003).

Mode of transmission, pathogenesis and clinical symptoms in human: Human infections rise primarily from ingestion and contact, infected milk and milk products, meat and meat products constitute important source of disease for human. The risk of infection is particularly severe for veterinarians, farmers and other concerned with handling of infected animals fetuses after birth, discharges and laboratory cultures which precaution for laboratory workers to manipulate infective material and cultures with great caution under protective hoods of proved efficiency (Buxton and Fraser, 1997).

The organism initially multiplies within lymph nodes and then passes to the blood stream. Here antibodies formed by the patient act in conjunction with complement to cause bacteriolysis and liberation of endotoxin, which causes the fever response and other generalized symptoms. In human the disease characterized by generalized aches pains of muscle and joints, headaches and prolonged irregular (undulant) fevers which continuous into chronic form (Michael *et al.,* 1986).

Bovine tuberculosis

Tuberculosis (TB) is a serious disease caused when bacteria attack the respiratory system. There are three type of TB: human, avian and bovine TB. Avian TB typically restricted to birds, and bovine TB is the most infectious one and capable of infecting most mammals (Banner, 2007).

Bovine TB results from infection by *Mycobacterium bovis,* a gram positive, acid fast bacterium in the Mycobacterium tuberculosis complex of the family Mycobacteriacea*e* (Cousins and Florisson, 2005). Mycobacterium tuberculosis is more adapted to humans and may have initially

developed from strain of *M. bovis*, many years ago; that humans were exposed to after they started herding cattle (Copeland, 2007).

Mode of transmission and clinical signs in humans: Cattle shed *M. bovis* in respiratory secretion, feces and milk, and sometimes in urine, vaginal secretions or semen. *M. bovis* can infect humans, primarily by the ingestion of unpasteurized dairy products but also in aerosols and through breaks in the skin. Raw or under cooked meat can also be a source of the organism. Person to person transmission is rare in immunocompetent individuals. But *M. bovis* has occasionally been transmitted within small clusters of people, particularly HIV infected individuals (Cousins, 2001).

Some human infections are asymptomatic. In other case, localized or disseminated disease can develop either soon after infection, or many years later when waning immunity allows the infection to reactive. Localized disease can affect the lymph node, skin, bones and joints, genitourinary system, respiratory system. The symptoms may include fever, cough, chest pain, cavitations and hemoptysis. Genitourinary disease can result in kidney failure (Cousins, 2001).

Campylobacteriosis

Campylobacter is small, gram negative microaerophilic, slender, curved, motile bacterium with a polar flagellum (Aielso and Mays, 2005). *Campylobacter jejuni is* found in the intestinal tract, udder, and feces of cattle, in poultry and wild birds, and in contaminated water sources. Gastrointestinal campylobacteriosis caused by *C*. *jejuni* and *C*. *coli* is associated with diarrhea in various animal hosts including humans. In human it is a leading cause of diarrhea *Campylobacter jejuni is* destroyed by pasteurization. *Campylobacter jejuni* is one of the most common bacterial causes of diarrheal illness in human. Illness can often occur as sporadic events and in larger outbreaks. *C. jejuni* and *C. coli* are thermophilic being able to grow at 37 centigrade to 42 centigrade, but incapable of grow below 30 centigrade (Hirsh and Zee, 1999). *C.jejuni* can be distinguished from other species by its ability to hydrolyze benzoic acid, glycine indoxyl and acetate (WHO, 2001).

Mode of transmission, pathogenesis and clinical symptoms in human: Transmission to humans mainly occurs by ingestion of food or water containing fecal matter, consumption of raw or unpasteurized milk from infected animals (Blaster, 1997). Animals carry this organism as normal gut flora and act as reservoir for humans. It is usually self limiting and last up to 10 days. Symptoms of campylobacteriosis include diarrhea which is bloody, abdominal pain, cramping, nausea, vomiting, and fever. Patients with Campylobacteriosis usually recover without specific treatment other than fluid and electrolyte replacement (Pal, 2007).

Staphylococcal infection

The staphylococci are gram-positive cocci that tend to be arranged in irregular clusters or bunch of grapes formation. They are facultative anaerobic (fermentative), catalase positive, oxidase negative, non-motile. The pathogenic staphylococci are: *S. aureus*, *S. intermedius* and *S. hyicus* (Quinn *et al*., 2002).

They are preferred to grow aerobic environment but can grow in the absence of oxygen, they can grow at temperature of 6-44 centigrade (optimum 37 centigrade) (Rajesh and Rattan, 1994). *Staphylococcus aureus* is very sensitive to aniline dyes and a concentration of 1:500,000 of crystal violate

can inhibit their growth, fatty acids are also active against them (Quinn *et al*., 2002).

Mode of transmission pathogenesis and clinical symptoms in man: The pathogenesis of staphylococcal disease relates to the resistance of phagocytosis, the action of several staphylococcal enzymes, the development of delayed hypersensitivity and activities of toxins. Man is constantly exposed to staphylococcus from birth until death, but susceptibility is greatest young and elders (Rajesh and Rattan, 1994). The usual symptoms of staphylococcal infection develop within 1 to 6 hours; headache, muscular cramping and marked prostration are observed in more severe cases. Usually the infection is self limiting and symptoms persist for more than 24 hours (Varnam and Evans, 1991).

Listeriosis

The genes Listeria contain seven species, but only two are of interest in human and animal and animal pathology. *L. monocytogenes* and *L. invanovii*. A notable difference between the two pathogenic species is their hemolytic ability. *L. monocytogene* is beta hemolytic in blood agar and forms a narrow band of hemolytic around the colonies, but *L. invanovii* which forms a wide band (Pedro and Boris, 2001). The organism produces acid in glucose, rhamnose and salicin within 24 hours of inoculation, produces acid in sucrose, maltose, lactose, glycerol, and starch in 7-12 day of inoculation. The organism is destroyed at 58 centigrade in 10 minutes. Moreover, it is killed by usual disinfectants (Sharman and Adalkha, 2003).

Mode of transmission pathogenesis and clinical symptoms in man: Transmission to humans mainly occurs by ingestion of food or water containing fecal matter, consumption of raw or unpasteurized milk from infected animals. Listeriosis in human is not characterized by set of symptoms. However, after incubation period of 4-21 days, disease occurs in various form; meningitis septicemia, abortion, pneumonia, conjunctivitis and endocarditis (Pal, 2007).

Drug residue

The presence of residue in milk following treatment of mastitis is a major public health concerns that adversely affects the dairy industry and the safety of milk for human consumption. Milk can be contaminated with antibiotics due to a number of reasons including excessive use of antibiotics, failure to identify treated animals, failure to apply antibiotics according the proposed prescription, lack of awareness about with drawal period, withholding milk only from treated animals and purchase of cows treated with antibiotics. Antibiotics which are frequently and commonly applied in veterinary medicine include B-lactams (e.g. penicillin), Amino-glycosides (e.g. streptomycin, neomycin), Tetracycline (e.g. doxycycline, minocycline), Macrolides (e.g. erythromycin) and chloramphenicols (Nicholas *et al*., 1992).

Drug are intended to be toxic to various forms of micro organisms as such may have inherent toxic, mutagenic, teratogenic and carcinogenic effect to humans. The principal consumer concerns are drug resistance, toxicity and potential allergy. Drug resistance has been postulated as a problem both from the effect that trace residues may have in stimulating resistance, or transferring resistance from non pathogenic bacteria to pathogenic bacteria within the human digestive system (WHO, 2001). The public health significance due to drug residues includes the following points.

Development of drug resistance

Human health can either affected through residues of drugs in food of animal origin, which may cause direct side effects, or indirectly, through selection of antibiotic resistance determinant that may spread human pathogen. Resistant microorganism can get access to human either through direct contact or indirectly via milk, meat, and or egg. As the bacteria of animal origin, they may either colonize human endogenous flora or superimpose and additional load to the reservoir of resistance genes already present in man. The potential for animal to human transfer of resistance is existed. Clearly, the use of antibiotic in livestock production has been associated with development of human antibiotic resistance. Animal fed with low level of antibiotic may develop bacteria evolving resistance to these bacteria during the preparation or consumption of food of animal origin. It has been documented that human develop drug resistant salmonellosis from food of animal origin. Examples of drugs which have been shown to cause the growth of resistant bacteria in food of animal are fluoroquinolones and avaoparin. The resistance of microorganisms, arising from sub-therapeutic uses of penicillin, tetracycline's, and sulfa drugs; in agriculture is suggested by the WHO to be a high priority issue (NRC, 1991; Nicholas *et al*., 1992).

Allergy or hypersensitivity

Drug hypersensitivity is defined as an immune mediated response to a drug agent in a sensitized patient, and drug allergy is restricted to a reaction mediated by IgE. An allergic or hypersensitive effect following administration of a drug (that is drug allergy is quite similar to that typified by allergic response to protein, carbohydrate, and lipid macromolecules. Allergic reactions to drugs may includes anaphylaxis, serum sickness, coetaneous reaction, a delayed hypersensitive response to drugs appear to be more commonly associated with the antibiotics, especially of penicillin. About 10% of the human population is considered hypersensitive to a number of substances including penicillin, but in animals the extent of hypersensitive to, drug is not well known (Jerry, 1992).

Carcinogenic effect

Carcinogenic effect refers to an effect produced by a drug having carcinogenic or cancer producing activity. Among the carcinogenic veterinary drugs in the current use in many countries are nitrofurans, nitroimidazols, quinoxaline and griseofulvin. These drugs are acquired through food of animal origin as antibiotic residues. The potential hazard of a carcinogenic residues is related to their interaction or covalently binding with various intracellular components such as proteins, DNA, RNA, glycogen, phospholipids, and glutathione (Aielso and Mays 2005).

Mutagenic effect

The term mutagenic is used to describe chemical agents that damage the genetic component of a cell or organism. Several chemicals including alkylating agents and analogs of DNA bases have been shown to elicit mutagenic activities. There has been an increasing concern that drug as well as environmental chemicals may pose a potential hazard to human population by production of gene mutation or chromosome aberration. Either the germinal or somatic cell may be affected. Understandingly; injury to either cell group may lead to serious consequences. However public health stand point of view, mutation in germinal cells is more immediate importance, because of the hazard to further generation (Jerry, 1992).

Teratogenic effect

The term teratogenic applies to a drug or a chemical agent that produces a toxic effect on the embryo of fetus during a critical phase of gestation. As a consequence, a congenital malformation that affects structural and functional integrity of the organism is produced. The well known thalidomide incident involving a number of children in Europe was a direct testimony to hazard that may occur when such an agent is administered during pregnancy. Of the anthelmentics, benzimidazol are embryo toxic and teratogenic when given during early stage of pregnancy as a result of the antibiotic activity of the drug (Joes, 1993).

Disruption of normal intestinal flora

The bacteria that usually live in the intestine acts as a barrier to prevent in coming pathogen from getting established and causing diseases. Antibiotics may reduce total number of the bacteria or selectively kill some important species. The broad spectrum antimicrobials may adversely affect wide range of intestinal flora and as a consequence cause gastro intestinal disturbance. For example, drug like, flunixin and streptomycin are known for this effect (Jackson, 1980)

Milk borne intoxication

Milk may serve not only as a potential vehicle of transmission of disease causing organisms, but it can also allow these pathogens to grow, multiply and produce certain toxic metabolites, thereby making itself an extremely vulnerable commodity from the public health point of view. (Kluytmans, 1998).

A variety of pathogenic organisms may gain access into milk and milk products from different sources and cause different types of food-borne illnesses. Milk and milk products may carry organisms as such or their toxic metabolites (poisons) called **t**oxins to the susceptible consumers. Ingestion of toxins already synthesized in the food which is, pre-formed brings about poisoning syndromes in the consumers. This is called 'food intoxication' and the toxins affecting the gastro-intestinal tract are called enterotoxins. Whereas the ingestion of viable pathogenic bacteria along with the food leads to their implantation and establishment in internal organs. This is called food infection. There are yet other types of organisms, which can infect intestine when ingested along with the food and produce toxins *in situ* to bring about symptoms of poisoning. This situation is called toxi-infection (NMC, 1996).

The bovine mammary gland can be a significant reservoir of enterotoxigenic strains of *Staph. aureus.* Milk and other dairy products are frequently infected with *S. aureus.* Milk of infected animals is the main source of enterotoxigenic *S. aureus* of animal origin. For example certain *S. aureus* strains produce heat-resistant enterotoxins, which cause nausea; vomiting and abdominal cramps when ingested by humans and are responsible for staphylococcal food poisoning outbreaks (Kluytmans*,* 1998). Toxins are produced due to improper cooling of milk, during cheese manufacture from raw milk and also due to post-processing contamination. These toxins cannot be destroyed by heating or drying (NMC, 1996).

CONCLUSION AND RECOMMENDATIONS

Generally, mastitis is usually considered as the most important disease in dairy cattle and human beings and hence remained a concern of most dairy farmers and veterinarians. The bacteria that are transmitted through milk and cause disease problems in man are bacteria causing mastitis in cattle. The major bacteria that

can be transmitted through milk and produce disease in man include *mycobacterium bovis, Brucella abortus, staphylococcus aureus, Listeria monocytogenes* and *Campylobacter jejuni* from affected udder due to localization from their septicemic phase. Antibiotic residues following treatment of mastitis can be a potential hazard to humans in allergic reaction and possible transfer of resistant to other organisms.

Based on the above facts the following points are recommended:

- Mastitis control measures should be largely under taken to reduce bacterial contamination of milk from the udder.
- Education of public at large about hazard of raw milk consumption and the possible control and preventive measures through heat treatment should always be encouraged before milk is consumed.

Milk producers should be educated about risks associated with antimicrobial residues as result of failure to respect the with drawl period.

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