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# A Review of Methicillin-Resistant *Staphylococcus aureus* (MRSA) on Milk and Milk Products: Public Health Importance

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## ABSTRACT

Methicillin-resistant Staphylococcus aureus (MRSA) is a pathogenic strain of bacteria in humans and animals that can cause anything from mild to severe infections. Detection of MRSA in foodstuffs of animal origin has been widely reported and has raised public concerns about the transmission of MRSA from foodstuffs of animal origin to humans. There have been many reports of MRSA infections originating from dairy cow's milk, milk products, and MRSA transmission between farmers working in dairy pens and people working in the dairy industry. Significant differences in the spread of cases of MRSA infection originating from milk and milk products have been reported among various countries in the world. This difference may be caused by different livestock production management systems in different countries in the world. Milk and milk products contaminated with MRSA will be a potential transmission of MRSA transmission when consumed by humans and can be a problem for public health. The milking process carried out by farmers and the processing of milk for milk products can be risk factors for transmission of MRSA to humans. Contamination of milk and milk products by MRSA is a major cause of food poisoning. Several antibiotics of choice can be used in treating patients who experience poisoning with milk and milk products such as fluoroquinolone, tetracyclines, lincosamide, and trimethoprim-sulfamethoxazole. Adherence to good hygiene practices during milking, processing and handling of dairy cow milk can significantly minimize MRSA contamination of milk and dairy products.

**Keywords:** MRSA, milk, milk products, public health

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## INTRODUCTION

Methicillin-resistant Staphylococcus aureus (MRSA) is a pathogenic strain of bacteria in humans and animals that can cause from mild to severe infections and can even cause death cases worldwide. The epidemiology of the incidence of this infection is also very diverse, considering the possible exchange of MRSA strains between humans and animals or vice versa [1]. Recently this year, the detection of MRSA in foodstuffs of animal origin has been widely reported and has raised public concerns about the transmission of MRSA from foodstuffs of animal origin to humans [2, 3]. Various types of foodstuffs of animal origin have been studied to determine the source of MRSA transmission, such as beef, chicken, pork, dairy cow's milk, sheep's milk, and dairy products [4-10]. It is widely known that Staphylococcus aureus, especially methicillin-resistant Staphylococcus aureus (MRSA) is the main cause of mastitis cases in dairy cows, even MRSA can also be detected in healthy cows [11-14].

During the milking process in dairy cows, especially in dairy cows with subclinical mastitis, this MRSA strain can emerge from the teats of dairy cows to contaminate milk without organoleptic changes in milk, thus allowing this MRSA strain to easily spread to the milk processing process. There have been many reports of MRSA infections originating from dairy milk [11, 13, 15], dairy products [10], and transmission of MRSA between farmers working in dairy pens and people working in the dairy industry [16, 17] .

MRSA transmission can be zoonotic, involving direct animal-to-human contact or vice versa, the processing of dairy products, and contact with environmental contaminants [18]. MRSA transmission disease cases have become a serious problem for dairy farming and the dairy industry [19-21].

Poor management of dairy farms and inappropriate use of antibiotics can increase the incidence of MRSA in cow's milk [22]. Previous studies have reported cases of hospital-related MRSA infection (Hospital acquired Methicillin-resistant Staphylococcus aureus / HA-MRSA) and Community acquired Methicillin-resistant Staphylococcus aureus (CA-MRSA) infections. Recent studies have found another group of MRSA, namely MRSA associated with livestock (Livestock associated Methicillin-resistant Staphylococcus aureus / LA-MRSA). LA-MRSA colonization of dairy cows has been shown to be a risk factor for veterinarians, breeders, employees of the

dairy processing industry, and those in close contact with dairy cows [23].

LA-MRSA infections in humans, originating from milk and milk products, can include skin and soft tissue infections ranging from mild to severe [24]. Expression of methicillin-resistant Staphylococcus aureus may complicate antibiotic treatment [25]. The prevalence of LA-MRSA needs to be done from the beginning before the transmission of food from animal origin to humans can eventually become a threat to human health [26]. Studies on the spread of MRSA that are sourced from foodstuffs of animal origin such as milk and dairy products can limit the threat of MRSA infection cases to human health [23].

This review describes Methicillin-resistant Staphylococcus aureus in general, MRSA in foodstuffs of animal origin, MRSA in milk, MRSA in milk products, epidemiology of MRSA in milk and milk products, transmission of MRSA transmission from milk and dairy products, risk factors. transmission of MRSA originating from milk and milk products, consequences for public health, treatment of cases of MRSA poisoning originating from milk and milk products, and prevention of MRSA poisoning from milk and milk products.

## Methicillin-resistant *Staphylococcus aureus* (MRSA)

Expression of resistance to penicillinase-stable antibiotics to penicillinase, commonly referred to as "methicillin resistance" or "oxacillin resistance", in staphylococcus aureus bacteria is manifested as bacteria that are resistant to all β-lactam class antibiotic agents including carbapenems and sephalosporins [27].

The start of methicillin-resistant Staphylococcus aureus (MRSA) began in 1961 in the United Kingdom [28], one year after methicillin antibiotics were introduced into clinical practice to treat cases of penicillin-resistant Staphylococcus aureus infection [29]. In the early 90's MRSA began to become a serious health threat in the United Kingdom and the United States [30]. Resistance is encoded by a mobile genetic element, known as staphylococcal chromosomal cassette mec (SCCmec) [31], carrying the genes encoding mecA and mecC, both of which encode penicillin-binding protein 2a (PBP2a) [28, 32]. B-lactam antibiotics bind to PBP, acting in the synthesis of cell wall peptidoglycan, which causes bacterial cells to lysis. But PBP2a has a low affinity for β-lactam antibiotics, so that peptidoglycan synthesis activity continues in MRSA strains [32], despite the presence of various β-lactam inhibitor combinations. The mecA coding gene can be identified in one of eleven SCCmec (I-XI) types, which carry 5 different types of mec-coding gene complexes, such as mecA and their regulatory genes mecR1 and mecI, and eight different types of the ccr gene complex. , which contains two different recombinase CCR genes that play a role in the mobility of the element [33]. MRSA was obtained from the integration of the SCCmec element carrying the mecA gene encoding the methicillin-sensitive Staphylococcus aureus [34]. A new MRSA coding gene named mecC (originally named mecALGA251) by the International Working Group (IWG) was discovered in the SCCmec element classification, which was isolated for the first time from a sample of dairy cow milk in the UK in 2011 [35] and this mecC coding gene was also isolated from human clinical samples in Denmark, Scotland, and the UK in 2014 [36]. This mecC gene is located in the SCCmec type XI element and has 69% similarity in the identity of the nucleotide sequence to the mecA coding gene. Besides MRSA strains have the ability to adapt to the pressure of β-lactam antibiotics, MRSA strains also have the potential to produce enterotoxins that can cause food-borne disease. However, the prevalence of enterotoxigenic MRSA in food and foodstuffs is still low and is usually closely related to milk and milk products. In a previous study conducted in Italy, it was reported that three MRSA strains (1.2%) isolated from milk and dairy products were found to have enterotoxigenic properties [37], and in the United States study 2 MRSA strains (1.33%) were found. those isolated from tank milk had enterotoxins [12].

## Methicillin-resistant *Staphylococcus aureus* (MRSA) in food of animal origin

Many researchers who have reported finding MRSA in foodstuffs of animal origin around the world, have found varying prevalences in beef, lamb, chicken, pork, rabbit, wild boar, eggs, milk, dairy products, and fish [1, 4, 5, 6, 8, 10, 38-43]. In addition, it is important to emphasize that the MRSA strains found in humans have also been found in food, due to contamination of food consumed by humans [44]. It also depends on the epidemiological factors of the geographic area of each country, about 0.7-1.5% of humans in the world have been infected with MRSA [45-47].

Until now it is known that there is a transmission of MRSA clone exchange between humans and animals [48], but it is not clear whether there is a risk of inherited foodstuffs of animal origin associated with MRSA contamination. In 1994 there was a case of food poisoning from food of animal origin at the University of Rotterdam hospital, where out of 27 patients 5 of them died, the incident was caused by an isolated strain of MRSA from a cook contaminating food during food preparation [49]. Also, in 2001 there was a case of food poisoning from food of animal origin caused by MRSA strains contained in Staphylococcus enterotoxin C, which was isolated from roasted pork contaminated by food handlers [50].

## MRSA in milk

The incidence of MRSA infection from cow isolates with mastitis has been widely studied and the prevalence rate is still low [51]. Following the first reports of MRSA from cows with mastitis [52], sporadic cases of MRSA infection in dairy cows have been detected among Staphylococcus aureus isolates from dairy cows with subclinical mastitis and clinical mastitis. In a study conducted in Korea [53], MRSA of cow's milk was found with an isolation ratio of 0.18%. In a report on dairy farming in Belgium, the highest percentage of MRSA identification was found in breastfeeding dairy cows at 15% [51], these cows did have a previous history of MRSA infection. Until now, the prevalence of MRSA identification in dairy cows with mastitis is still low, considering the time period since MRSA was first discovered in dairy cows and close contact with farmers with dairy cows' udders. In a study in Germany, the highest proportion of positive MRSA samples was found in the nose swabs of calves, namely 45% and the lowest proportion of positive samples of MRSA in bulk tank milk was 4.1%, most of the MRSA isolates came from the spa type t011 and t034 belonging to the CC398 clonal complex [4]. The discovery of LA-MRSA CC398 in tank milk proved that MRSA was colonized in dairy cows' udders and a possible cause of subclinical mastitis cases in dairy cows in Germany [4]. Close contact between dairy cows and humans can lead to strain transfer between dairy cows and humans through milk production. In a study in Hungary, identical MRSA isolates were found

from dairy cows with mastitis and a farmer with phenotypic and genotype analysis which indicated that there had been a transfer of MRSA strains between dairy cows and humans [54].

## MRSA in milk products

Staphylococcus aureus and MRSA can contaminate milk either by direct excretion from udders of dairy cows with mastitis or through contamination from the surrounding environment during handling and processing of milk for milk products. It is known that milk is a suitable medium for bacterial development and a means of transmission of bacterial transmission such as MRSA when milk or milk products are consumed by humans, so this is a public health hazard [55].

One of the livestock-based food products that can be a source of MRSA transmission and cause cases of food poisoning by MRSA is milk from dairy cows, then milk from dairy cows that is contaminated with MRSA is processed into milk products. MRSA strains have been identified from a wide variety of dairy products such as cheese [8], yogurt [56], butter [57], ice cream [58], and pasteurized milk [59]. This MRSA strain also possibly carries the Staphylococcal enterotoxin gene which could potentially cause food poisoning [8].

## Epidemiology MRSA in milk and milk products

The cause of transmission of MRSA to humans is obtained from milk cows and milk products contaminated with MRSA [8, 12]. Consumption or handling of milk and dairy products can lead to the spread of the antibiotic resistance gene Staphylococcus aureus to humans [60].

The spread of MRSA infection cases originating from milk and milk products has been reported in various countries around the world. Different livestock production management systems in different countries of the world. Different policies and regulations for the use of antibiotics in each country also contribute to the different spread rates of MRSA infection [61]. Several animal species in an area that cause the transfer of genetic material between MRSA strains can affect the rate of spread of MRSA infection [17]. Reported data explain the wide variety of spread of MRSA infections in milk and dairy products in various parts of the world.

## Europe

In a French study, no MRSA was found among 119 Staphylococcus aureus isolates in the milk of dairy cows with clinical mastitis between 1998 and 2000 [62]. In a similar study in France, only 1 Staphylococcus aureus isolate was classified as MRSA among 139 Staphylococcus aureus isolates in dairy cattle with clinical mastitis between 2007 and 2008 [63]. In a large study conducted in Hungary from January 2002 to December 2004, 139 Staphylococcus aureus isolates (out of 595 samples of cow's milk with subclinical mastitis) detected 27 of them MRSA [54].

Based on a survey conducted in Belgium between 2006 and 2007, out of 118 Staphylococcus aureus isolates obtained from milk samples from dairy cows with clinical mastitis, 11 were confirmed to be MRSA [13].

Research conducted in the Czech Republic between 2006 and 2009, [64] found 18 MRSA strains from cow's bulk tank milk and 4 MRSA strains from goat's milk from a total of 299 Staphylococcus aureus isolates studied. One of the MRSA isolates from the goat farm was detected positive for the gene encoding Staphylococcal enterotoxin (SE) [64]. Moreover, between 2006 and 2008, Stastkova et al. [65] found 5 MRSA strains from 34 isolates of Staphylococcus aureus obtained from 153 milk samples from goat farms, and all these MRSA isolates contained the Staphylococcal enterotoxin B (seb) gene. The lower prevalence of MRSA reported in the Czech Republic is 3%, in this study there were 60 samples of goat's milk, 60 samples of sheep's milk, and 120 samples of dairy cow's milk, only 2 were detected strains of MRSA, 2 of which were dairy cows with mastitis. subclinical from one herd [66].

A study conducted in Italy [8] found 4 MRSA strains carrying staphylococcal enterotoxins from cow's milk samples and dairy products (mozzarella cheese and pecorino cheese), while other researchers [67] did not find MRSA strains from 36 Staphylococcus aureus isolates extracted from cheese sample made from sheep's milk.

A study conducted in Portugal [68] did not find any MRSA among 30 Staphylococcus aureus isolates from milk samples from dairy cows with subclinical mastitis, whereas a study conducted in Ireland [60] did not find MRSA strains with mecA positive in 70 milk samples that were not pasteurized. A study conducted in Slovakia [69] did not find MRSA strains from 79 isolates of Staphylococcus aureus obtained from sheep's milk samples and cheese samples made from sheep's milk.

In Switzerland [70] found only 2 MRSA strains among 142 Staphylococcus aureus isolates obtained from milk samples from dairy cows with mastitis. A survey conducted in Germany on tank milk samples between 2009 and 2010 described an estimated prevalence of MRSA infection cases of 1% to 2% [71] and 5% [72], respectively. According to a study conducted in southwest Germany on three dairy farms, a substantial prevalence of MRSA was found to be 5% - 17% of dairy samples and 1% - 10% of dairy cattle [17]. In a study conducted in the Netherlands [73] detected 62 MRSA strains from 1,839 dairy samples collected from 26 dairy farms.

## America

In the United States, [74] reported a MRSA prevalence of 1% of 846 Staphylococcus aureus isolates obtained from dairy samples on Michigan farms, another study [75] reported a MRSA prevalence of 2% of 2132 Staphylococcus aureus isolates obtained from dairy samples collected from 1994 to 2001 on a Wisconsin farm. No MRSA strains were found among the 357 Staphylococcus aureus isolates obtained from milk samples taken from 24 dairy herds on farms in North Carolina and Virginia [76]. In a survey research conducted by Virgin et al. [77], no MRSA strains were found in 542 bulk tank milk samples. D'amico and Donnelly [78] reported that have isolated 2 MRSA strains among 90 Staphylococcus aureus isolates obtained from raw milk to be used for the production of handmade cheese in Vermont. Haran et al. [12] isolated 2 MRSA strains from 154 Staphylococcus aureus isolates obtained from 150 bulk tank milk samples on a Minnesota farm. They also reported that the two MRSA strains were capable of producing enterotoxins such as SEB, SEC, SED and SEE.

In Brazil, there was a high MRSA prevalence rate of 25% of the 98 milk samples of dairy cows with subclinical mastitis [79], however in a Canadian study, Saini et al. [80] found only one MRSA strain among 1,802 Staphylococcus aureus isolates obtained from milk samples collected from 79 dairy farms.

### Asia

In a study in Japan between 1998 and 2005 [81] found 4 MRSA strains from 363 isolates of Staphylococcus aureus obtained from dairy cows from 260 dairy farms.

In a study in Pakistan [82] revealed an MRSA prevalence of 10%, there were 8 positive MRSA strains out of 77 Staphylococcus aureus isolates obtained from dairy cow's milk.

In a study in Korea between May 2001 and April 2003 [83] revealed an MRSA prevalence of 1.5%, there were 12 MRSA positive strains from 894 samples of dairy milk. Meanwhile, the survey conducted [53] between 1999 and 2003, there was a prevalence of less than 0.5% from examining 9,055 samples of milk from dairy cows. Kwon et al. [53] revealed that all identified MRSA strains carried the Staphylococcal enterotoxin gene (SED, SEI, SEJ). On the other hand, according to two surveys conducted between 2003 and 2009 [84] and between 1997 and 2004 [85], there are estimates of MRSA prevalence of 2.5% and 6% on examinations of 835 and 402 samples of dairy cows with mastitis.

In a study conducted in Turkey, there was an MRSA prevalence of 17.5%, 18 positive MRSA strains were found among 103 Staphylococcus aureus isolates from milk samples from dairy cows with mastitis [86]. In the latest survey results [87] did not find MRSA strains among 21 Staphylococcus aureus isolates obtained from 857 sheep milk samples and 33 goat milk samples collected from 13 farms in Kirikkale province.

In a study conducted in India between 2007 and 2008 [88] revealed a MRSA prevalence rate of 10% among 128 Staphylococcus aureus isolates obtained from milk samples from Karan Fries (Taurus × Zebu) cows suffering from mastitis. Meanwhile, the same research team [89] has also found a MRSA prevalence rate of 13% among 107 Staphylococcus aureus isolates from a herd of dairy cows on farms in northwest India.

In a survey research conducted in Thailand in 2010 [90] identified 74 MRSA strains out of 375 isolates of Staphylococcus aureus obtained from 598 milk samples from dairy cows with mastitis, 376 bulk tank milk samples, and 46 pasteurized milk samples.

In a study conducted in Iran in 2010 [58] examined 300 samples (100 raw milk, 100 ice cream, 100 pasteurized milk) and found 20 MRSA strains carrying the mecA-coding gene (14 from the raw milk sample and 6 from the ice cream sample). Whereas in a study conducted between 2010 and 2011, examined 348 samples of randomly selected dairy cows and reported an MRSA prevalence rate of 28% [91].

### Africa

In a study conducted in South Africa [92] reported an MRSA prevalence rate of 6% of dairy cow's milk produced on 2 commercial farms, and in a study conducted in Ethiopia [93] found a high MRSA prevalence rate of 60% of 78 Staphylococcus aureus isolates obtained from dairy cows.

In a study conducted in Nigeria, Suleiman et al. [94] examined 339 milk samples from dairy cows and reported an MRSA prevalence rate of 36%, found 26 isolates of Staphylococcus aureus resistant to oxacillin and 2 of them carrying the mecA gene coding.

## Transmission of MRSA

MRSA strains can spread from animals to humans and from humans to animals. MRSA transmission usually occurs through direct contact, often through contact with animals or people who have been infected or colonized with MRSA [83, 95].

The level of spread of MRSA in the general population usually varies depending on the geographical conditions of each country [96]. In the hospital, patients who have been infected and colonized with MRSA will be the main reservoir of transmission of MRSA, which is usually easily spread from patient to patient by hand touch [97]. The route of transmission of MRSA may be similar to that of other strains of Staphylococcus aureus, but there may be differences in the efficiency of host colonization after exposure [98]. There are many other factors in the transmission of MRSA transmission such as through contaminated surrounding air, saliva splashes, and nasal discharge [99- 101].

Animals also act as reservoirs for MRSA transmission and can transmit MRSA to humans and other animals [102-107]. Several types of MRSA exhibit host specificity and are widely spread over certain geographic areas. Therefore, MRSA transmission is more frequently associated with animals than with humans [108-110]. LA-MRSA CC398 is the type of MRSA that is most associated with intensive reared animal-based food-producing livestock, especially dairy cows [97]. Although LA-MRSA CC398 was found to colonize livestock without causing clinical symptoms, it could cause clinical infection with MRSA in animals. LA-MRSA CC398 colonization has been found in many breeders, family members of farmers, employees of the food processing industry, and veterinarians [96, 111, 112]. The spread of MRSA can also occur in personnel and other animals including cats, dogs, horses, between pets, in veterinary hospitals, and in households [44, 113-116]. In some cases, pets can act as a source of MRSA infection in humans [95, 117].

Foodstuffs of animal origin including milk and milk products contaminated with MRSA and the handling process that contaminates MRSA in milk and milk products are also potential transmission transmissions. In the case of patients hospitalized due to food poisoning, MRSA contamination can spread MRSA to other patients or healthcare workers [97]. Reports in the Netherlands, MRSA cases related to contaminated milk infected 27 patients and 14 hospital workers and caused 5 deaths. A person who consumed milk and milk products was found to have colonized the MRSA strains similar to the MRSA strains found in milk and milk product samples. Contaminated milk and milk products may lead to cases of septicemia due to MRSA, which can then be passed on to other patients in the hospital. Airborne transmission that is contaminated with MRSA also plays an important role in the spread of MRSA [49].

Given the abundance of evidence for the presence of MRSA strains in dairy cows, it will raise public concern about MRSA contaminants found in milk and dairy products [118]. However, there is no detailed description of the direct association of MRSA in animal and human foodstuffs, although there have been reports of increased MRSA contamination in milk and milk products, as well as the incidence of MRSA infection in the community [97]. Further investigations are needed to determine the true role of milk and dairy products in animal-to-human transmission of MRSA transmission.

Another aspect of MRSA that contaminates milk and dairy products is that MRSA often carries Staphylococcal enterotoxin (SE) genes such as SEA, SEB, SEC, SED which are often the cause of food poisoning (EFSA, 2008).

Different combinations of MRSA clones are associated with the staphylococcal enterotoxin gene, but the reasons for this association have not been widely elucidated [119, 120]. Clinically, cases of food poisoning caused by MRSA are almost the same as cases of food poisoning caused by other strains of Staphylococcus aureus [118]. MRSA strains that contaminate milk and dairy products can also be of human origin, due to less aseptic handling and processing systems for milk and dairy products [50]. The increasing prevalence of MRSA strains among the Staphylococcus aureus strains may lead to an increase in the prevalence of Staphylococcus aureus toxicity [121].

## Risk Factor of MRSA

Studies conducted in the United States, in the human population about 30% of humans are infected with methicillin-susceptible Staphylococcus aureus (MSSA) [122] and about 1.5% of humans are infected with methicillin-resistant Staphylococcus aureus [45, 123] with MSSA colonization sites. and MRSA mostly occurs in the nostrils [124]. While such colonization does not cause clinical symptoms in an infected person, it may be a risk factor for developing subsequent symptomatic infection [122, 125]. Humans infected with MRSA without showing symptoms are categorized as persistent carriages and intermittent carriages that act as MRSA carriers and can transmit MRSA to more susceptible persons [124].

Staphylococcus aureus is a common bacterial agent causing mastitis in dairy cows. A study conducted in Minnesota to estimate the prevalence rate of Staphylococcus aureus in bulk tank milk reported that the MSSA and MRSA prevalence rates were 84% and 4%, respectively [12, 125]. The results of another study estimated that the prevalence rate of Staphylococcus aureus in bulk milk tanks was 35% in samples of dairy cows in Louisiana [12] and 31% in samples of dairy cows in Pennsylvania. Studies from Ireland [126], Turkey [127], Argentina [128], and Brazil [129] have found the presence of the Staphylococcal enterotoxin gene in MRSA derived from cow's milk. Udder of dairy cows with clinical and subclinical mastitis may play a role in the contamination of milk by MRSA via direct excretion of the cow's nipples [130] with large fluctuations in the count of zero to 108 CFU / ml [131]. For example, mastitis cases in dairy cows were the only source of contamination in 1999 in Brazil, then MRSA from cow's milk affected 328 people who consumed unpasteurized dairy cow's milk [132]. Likewise, 293 Staphylococcus aureus isolates were isolated from 127 goat milk samples and sheep milk samples in Switzerland [130]. Recently, MRSA strains were found in the milk of dairy cows with mastitis and bulk tank milk on Hungarian farms which suggest that udders of dairy cows infected with MRSA can contaminate milk and milk products [131]. However, MRSA contamination of milk and milk products can occur in the environment during the processing and handling of milk [124]. Therefore, the milking process carried out by the farmer, the processing and handling of milk for milk products can be a risk factor for the transmission of MRSA to humans [132].

## Public Health Importance

Contamination of milk and milk products by MRSA is a major cause of food poisoning. May be characterized by gastroenteritis symptoms which are clinically manifested as emesis with or without accompanied diarrhea. These cases of poisoning stem from ingestion of one or more Staphylococcal enterotoxins that are formed in milk and milk products that have been contaminated with MRSA. Symptoms of systemic toxicity, such as hypotension and fever are rare cases of MRSA-related food poisoning. Symptoms of systemic toxicity resolve on their own within 24-48 hours after onset. The exact incidence is still not widely known, but MRSA is probably the most common cause of food poisoning in the United States [133].

The risk assessment in milk and milk products relies on detection of classic bacteria and counting the number of coagulase-positive Staphylococcus on selective Baird-Parker media. It is necessary to observe the progression of the disease after consumption of milk and dairy products, the presence of toxic cells, and the production of toxic cells. Therefore, in some countries, low levels of contamination by Staphylococcus aureus and MRSA are tolerated in most food products (e.g. 103 CFU / g of Staphylococcus aureus contamination in French cheese) is not usually considered a public health risk. [131, 133].

## Treatment of food-borne intoxication MRSA from milk and milk products

In cases of poisoning due to consuming milk and milk products contaminated with MRSA, several antibiotics can be used in treating patients who have poisoned milk and milk products. Penicillin is usually still used as the antibiotic of choice as long as Staphylococcus aureus infection is sensitive to it [134]. Semisynthetic penicillins, such as methicillin are indicated for patients infected with β-lactamase-producing Staphylococcus aureus [135, 136]. MRSA-infected patients are treated with a glycopeptide known as the antibiotic vancomycin [136, 137]. Vancomycin is the main antibiotic of choice in the treatment of cases of MRSA infection [136, 137]. Patients who are allergic to vancomycin antibiotics can be given alternative antibiotics such as fluoroquinolone (ciprofloxacin), tetracyclines (minocycline), lincosamide (clindamycin), trimethoprim-sulfamethoxazole also known as cotrimoxazole [135, 136]. Recent quinolones, such as the antibiotic ciprofloxacin which has increased anti-Staphylococcal activity can be used as antibiotics of choice, but their use is still limited because of the rapid development of Staphylococcus aureus resistance during treatment [135, 136]. MRSA infection cases can also be treated with several oral drugs such as rifampicin-fusidic acid, linezolid, rifampicin + fluoroquinolone, cotrimoxazole (trimethoprim-sulphamethoxazole), pristinamycin, doxycycline or minocyline, and clindamycin [138]. Mupirocin (Bactroban) also has the potential to fight MRSA from mucous membrane colonization [139]. A recent antibiotic called platensimycin has also shown success in curing cases of MRSA infection [140].

## Prevention of food-borne intoxication MRSA from milk and milk products

The increasing number of cases of poisoning of milk and milk products due to MRSA strains requires proper precautions. These precautions must be taken to prevent contamination throughout the food processing, production chain and preparation [141]. Adhering to good hygiene practices during milking, processing, and handling of dairy milk can significantly minimize contamination of milk and milk products. Increased vigilance in maintaining cleanliness must be carried out by everyone in the preparation and processing of dairy cow milk so that the safety quality of milk and milk products can be maintained [141, 142]. Milk must also be properly heated to make it

safe for consumption. The results of a recent analysis of growth requirements revealed that Staphylococcus aureus and MRSA can grow at a water activity of 0.867 and at temperatures as low as 8 ° C [143]. Therefore, it is necessary to provide counseling for industrial workers, breeders and the general public regarding the dangers of MRSA contamination in milk and milk products. There are also many cases of milk poisoning by Staphylococcus aureus and MRSA because the milk is left at room temperature for too long, for example during picnics or large banquets, so that the agenda gives Staphylococcus aureus and MRSA to develop and produce Staphylococcal enterotoxin (SE) 143].

The human health risks associated with consumption of unpasteurized milk and milk products [144, 145, 146]. However, Staphylococcal enterotoxin produced from MRSA is very resistant to heating and pasteurization, heating milk for one hour can reduce the amount of toxins, but only autoclave at 15 psi for 20 minutes can completely destroy the toxin. Milk that has been sterilized still requires cooling at a temperature of 0 ° C to 4 ° C so that later the milk can be processed further. Since MRSA is known to grow well on salt media, there is a higher risk of MRSA contamination in home salted cheese [147].

## Conclusion

Milk and milk products are potential vehicles for MRSA transmission when consumed by humans. The association between the multidrug-resistance nature of MRSA and the enterotoxigenic properties presents a serious public health risk, because enterotoxins can be found in milk and milk products contaminated with MRSA. Hygiene monitoring in the processing and handling of milk needs to be done continuously in order to obtain the quality of milk and milk products that are hygienic and safe for consumption. For this reason, the application of good manufacturing practices and hazard analysis critical control point (HACCP) is very important to ensure the quality and safety of milk and milk products.

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