RELATIONSHIP BETWEEN BULK TANK MILK SOMATIC CELL COUNT AND ANTIBIOTIC RESIDUES

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Introduction

Most dairy farms occasionally require the use of antibiotics for treatment of sick animals (McEwen, et al., 1991). In a recent survey, 95% of conventional dairy herds (n = 99) reported administering at least 1 dose of antibiotics during the 2 months that preceded the interview (Zwald et al., 2004). Of the surveyed herds, 5% used no antibiotics, 85% administered antibiotics to ≤10% of their animals, 9% administered antibiotics to 11-25% of their animals and <1% administered antibiotics to >25% of their animals (Zwald et al., 2004). In an earlier survey, McEwen *et al*. (1991) estimated usage of selected antibiotics using a mail survey of Canadian dairy herds (<50 cows/herd). In that survey, 1.3-1.9 and 1.3-1.6 cows received intramammary and systemic antibiotics each month, respectfully. Approximately 20% of the herds reported the use of medicated feeds (McEwen et al., 1991). In another study, Danish dairy herds (n = 111) reported a median of 63 drug administrations per 100 calvings (Enevoldsen et al., 1996).

Antibiotics are used to treat a variety of diseases and 80% of conventional dairy herds reported the use of antibiotics for treatment of mastitis (Zwald et al., 2004). Mastitis was the first disease of dairy cattle to be treated with antibiotics and remains their most common disease; consequently, the most common reason for administering antibiotics to dairy cows is for treatment of mastitis (Mitchell, et al., 1998). A study of dairy herds in the Netherlands (n = 201) reported the use of 1.9 antibiotic treatments per case of clinical mastitis (Barkema *et al*., 1998).

Antibiotic residues in milk and milk products are a rare consequence of antibiotic usage on dairy farms. There have been a number of studies looking at reasons for antibiotic residues in milk (Booth and Harding, 1986, McEwen *et al*., 1991; Oliver *et al*., 1990; Wilson *et al*., 1998). The use of intramammary antibiotics and mistakes regarding withholding periods of milk are the most frequently cited reasons for antibiotic residues (McEwen *et al.* 1991, Wilson *et al.*, 1998). In the U. S., public health is protected by regulations that prohibit the presence of antibiotics in milk intended for human consumption (Anonymous, 2001). The purpose of this paper is to review the relationship between the occurrence of antibiotic residues in milk and bulk tank somatic cell count level.

Antibiotic Residues in Milk and Human Health

The occurrence of antibiotic residues in milk intended for human consumption is undesirable for a number of reasons (Allison, 1985). As recently as 30 years ago, the presence of antibiotic residues in milk was considered primarily a manufacturing problem related to inhibition of cheese and yogurt starters (Cogan, 1972). More recently, the presence of antibiotics in milk has been prohibited because of concerns about public health. Initially, public health officials desired to protect hypersensitive individuals from exposure to specific antibiotics. More recently, attention has shifted to the potential for antibiotic residues in milk to contribute to the development and/or transmission of antibiotic resistant bacteria (Allison, 1985, Mitchell, *et al.*, 1995, Mitchell *et al*., 1988)

Hypersensitivity to antibiotic residues in milk. Allergic reactions to antibiotics are well recognized and hypersensitivity to β-lactam compounds is especially prevalent (de Weck, 1983). The literature regarding allergic responses of humans after exposure to drug residues found in milk is sparse and focused primarily on risks associated with exposure to β-lactams (Boonk and van Ketel, 1981; Boonk and van Ketel, 1982; Borrie and Barrett, 1961; Dewdney and Edwards, 1984; Dewdney *et al*., 1991; Ormerod, *et al.,* 1987; Vickers, *et al.*, 1958; and Wicher *et al.*, 1969). The immunological characteristics of most other drug classes (including macrolides, tetracyclines and aminoglycosides) makes the development of allergic responses to minute residues unlikely, although it is considered theoretically possible that exposure could result in clinically relevant immunological events (Dewdney and Edwards, 1984).

Allergic reactions to antibiotics develop when an individual is challenged by exposure after a primary sensitization has occurred. Oral administration of antibiotics does not stimulate as rapid or strong of an immunological response as compared to systemic administration and there is no scientific evidence that β-lactam residues present in milk have ever induced primary sensitization in humans (Dewdney and Edwards, 1984). Allergic reactions (dermatitis, pruritis and urticaria) of pre-sensitized individuals caused by β-lactam residues in milk have been documented for a small number of people (Dewdney and Edwards, 1984). Exposure to penicillin residues in milk has been reported as a cause of chronic urticaria (Boonk and van Ketel, 1981, Boonk and van Ketal, 1982, Ormerod, *et al.*, 1987). In one early case report, a highly sensitive individual exhibited a number of generalized symptoms after ingestion of processed milk containing approximately 10 units/ml of penicillin (Wicher *et al.*, 1969). Verified case reports after 1987 are apparently non-existent.

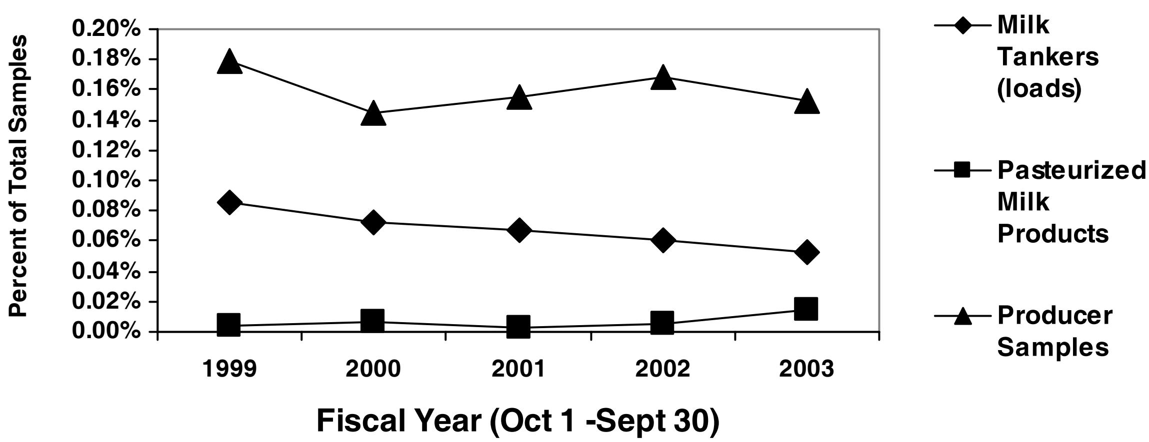
Transfer or development of resistant pathogens. At this point, the relationship between antibiotic residues in milk and the development or transfer of resistant pathogens appears to be hypothetical. There is some indication that mastitis pathogens isolated from dairy cattle with potential exposure to antibiotics may be less susceptible (but not necessarily resistant) than similar pathogens isolated from cattle located on organic dairy farms (Tikofsky *et al.*, 2003). However, mastitis pathogens in general do not appear to be becoming more resistant (Erskine *et al.*, 2002, Erskine, *et al.,* 2004, Makovec and Ruegg, 2003). Direct transfer of resistant organisms to humans through consumption of milk is unlikely because most milk is pasteurized (Teuber and Perreten, 2000). Traditional methods of pasteurization reduce the quantity of bacteria present in milk to negligible levels but will not appreciably reduce the level of antibiotic residues (Moats, 1999). Milk can be contaminated with fecal pathogens that exhibit resistance to antibiotics and raw milk products have been implicated as mechanisms for transferring fecal pathogens from farm environments to humans (Kalman *et al.*, 2000, Villar *et al.*, 1999).

Ingestion of antibiotics present in milk can influence gut flora. Antibiotics present in milk have been shown to increase antibiotic resistance of gut flora in baby calves, but the levels fed were considerably above detection limits of current antibiotic screening tests (Langford *et al.*, 2003). The likelihood of antibiotic residues to create a similar effect on human gut flora is considered extremely remote because of dilution and dairy process mechanization (Allison, 1985).

Prevalence of Antibiotic Residues in Bulk Tank Milk

Antibiotic residues occur in milk supplies throughout the world. In some relatively unregulated markets, antibiotic residues may exist in 8-15% of total bulk tank loads (Shitandi, and Sternesjo, 2004; Baynes *et al*., 1999). In the U. S., the dairy industry bears the primary responsibility for ensuring the safety of milk and milk products (Talley, 1999). The Food and Drug Administration (FDA) is responsible for verifying that the industry is complying with regulations and initiates regulatory action when necessary. The FDA has accepted appendix N of the Grade A Pasteurized Milk Ordinance (PMO) as the official reference regarding testing for drug residues in milk. Appendix N requires that every tanker of milk must be screened for β-lactam residues prior to unloading. Individual bulk milk samples from every farm are tested once monthly 4 times in every 6 month period. Additional random testing for other drug classes is also performed and individual state regulatory agencies or individual milk processors may test more frequently. Results of official drug testing are compiled annually in the National Milk Drug Residue Database (http://www.cfsan.fda.gov/~ear/milkrp03.html). The prevalence of positive test results for bulk milk tankers has been steadily declining (Fig 1) and 30% less milk was discarded in fiscal year 2003 as compared to FY 1999 (76,370,000 lbs (34,640,848 kg) versus 107,744,000 lbs (48,871,856 kg)).

Figure 1. Prevalence of Positive Antibiotic Test Results



In 2003 the value of milk discarded because of positive antibiotic test results exceeded $7.6 million USD (@ $10.00/cwt). Additionally, 8 of 54,932 antibiotic tests performed on pasteurized fluid milk and milk products were positive resulting in disposal of 64,000 lbs (29,030 kg) of finished products.

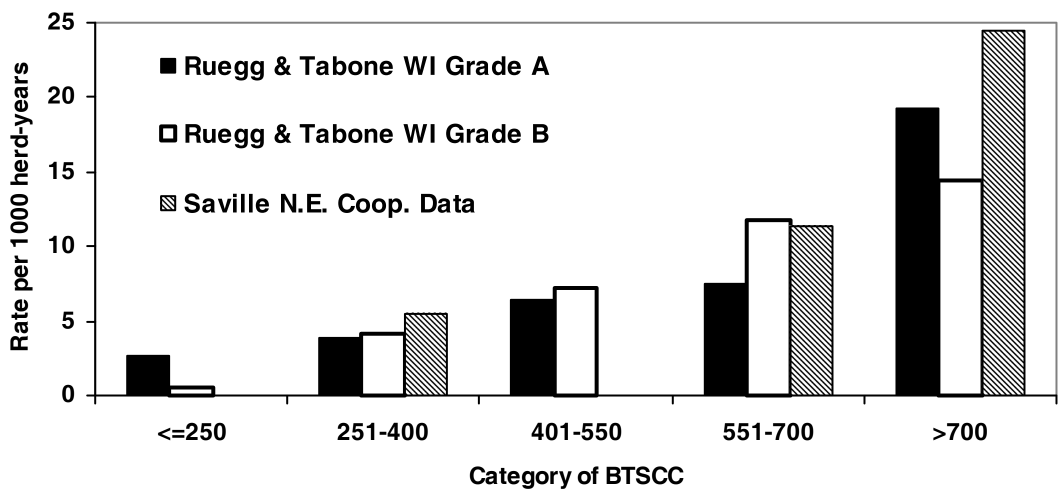
Relationship Between Antibiotic Residues and SCC

The bulk tank somatic cell count (BTSCC) is used as a key indicator of milk quality and reflects the prevalence of subclinical mastitis in a dairy herd. The BTSCC is an indirect measure of the overall amount of mastitis that a herd is experiencing and herds with high BTSCC have been reported to have higher rates of clinical mastitis and to cull more mastitic cows (Rodrigues *et al*., 2004). In many regions, the BTSCC is used to define financial incentives paid for high quality milk and herds shipping milk containing high levels of somatic cells may have a significant financial disadvantage (Rodrigues, *et al*., 2004). Under regulations contained in the PMO, BTSCC values are monitored for all farms. The current U.S. regulatory limit for SCC is 750,000 cells/ml (anonymous, 2001). Repeated violations of this limit result in significant financial penalties and potential loss of grade A status.

Farms experiencing consistently high BTSCC have considerable motivation to reduce the number of infected quarters. Treatment of infected quarters using antibiotics is one tactic used to control mastitis. The use of antibiotics introduces the risk of having an antibiotic residue. Farmers don't intentionally adulterate milk. Antibiotic residue violations occur primarily because of mistakes regarding withholding periods or identification of treated cows (Booth and Harding, 1986, McEwen *et al*., 1991). Investigators have consistently identified a relationship between BTSCC and the rate of antibiotic residue violations (Ruegg and Tabone, 2000; Sargeant, *et al*., 1998; Saville *et al*., 2000; van Schaik, 2002).

In data obtained from both Wisconsin and Ohio, the rate of violative residues per 1000 herd years is clearly associated with BTSCC (Fig. 2).

Figure 2. Antibiotic Violation Rates per 1000 Herd Years



In Wisconsin, data were analyzed for the period of Jan. 1995 through November 1998 and consisted of results of tests performed on 805,772 grade A and 176,763 grade B milk samples (Ruegg and Tabone, 2000). Herd-year SCC averages were used to classify herds ($\leq$250,000; 251,000 to 400,000, 401,000 to 550,000, 551,000 to 700,000, >700,000) and the relative risk of antibiotic residue by SCC class was determined. The arithmetic mean SCC values were 334,634 and 480,029 for grade A and grade B milk respectively. SCC values were significantly higher for samples with positive antibiotic residue tests for Grade A milk during all 4 years tested. SCC values were significantly higher for samples with positive antibiotic residue tests for Grade B milk for 3 of 4 years. The rate of antibiotic residue violation per 1000 herd-years increased with SCC class for both grade A and grade B milk. The relative risk of antibiotic residue violation by SCC class was 1.0, 1.43, 2.38, 2.78 and 7.10 for Grade A milk and 1.0, 1.11, 2.67, 4.33 and 5.43 for Grade B milk.

In Ohio, information was analyzed for 1994 through 1997 (Saville *et al.*, 2000). Two separate data sets were assessed: 1) 16,831 herd-years of data obtained from a large milk marketing cooperative and 2) 12,042 herd-years of data obtained from the Ohio Dept. of Agriculture. In the milk marketing dataset, violative antibiotic residues occurred in 153 of 8441 (1.8%) farms included in the study. In the Ohio Dept. of Agriculture dataset, violative antibiotic residues occurred in 482 of 4,022 (12.0%) farms. The large difference in the violative rate was attributed to the regulatory function of the Ohio Dept. of Agriculture and perhaps to intervention by field personnel of the milk marketing cooperative. In both datasets, herds were classified into strata based on BTSCC (<400,000; 400,000 to 750,000; ≥750,000). The rate of antibiotic residue violation per 1000 herd-years increased for both datasets. The relative risk of antibiotic residue violation by SCC class was 1.0, 2.3 and 5.1 for milk cooperative data and 1.0, 1.3 and 2.2 for data from the Ohio Dept. of Agriculture.

Other researchers have reported similar results. Data obtained from all herds in Ontario was analyzed for the period between March 1985 and July 1994 (Sargeant *et al.,* 1998). The rate of antibiotic residue violations by SCC category was: 1.6% (<150,000); 1.6% (150,000-299,000); 3.4% (300,000-499,000); 3.7% (450,000-599,000) and 5.7% (>600,000). In data analyzed from five large milk plants operating in New York State, farms with SCC levels >750,000 had a much greater rate of antibiotic residue violations as compared to herd producing higher quality milk (van Schaik, *et al*., 2002).

Conclusion

Adulteration of milk supplies with antibiotics is clearly undesirable and the regulation of milk supplies to prohibit antibiotic residues is useful to protect public health. Researchers have identified a consistent relationship between BTSCC and the occurrence of violative antibiotic residues. Interventions that reduce the prevalence of subclinical mastitis and therefore reduce the need for antibiotics may have an added benefit of further reducing the risk of violative residues.

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