ABSTRACT

The descriptive epidemiology and risk factors were reviewed for six clinical disorders: milk fever, downer cow syndrome, hypomagnesemic tetany, udder edema, left displaced abomasum, and ketosis. Data were included also from preliminary analyses of a data set from ~61,000 Finnish Ayrshire cows. A web of postulated associations among the metabolic disorders and other risk factors (previous lactation diseases and milk yield, calf factors, certain dry period nutritional factors, dystocia, retained placenta, and metritis) was diagrammed.

INTRODUCTION

The objective in this paper is to review the descriptive epidemiology and risk factors for periparturient metabolic disorders of dairy cows. We include six clinical disorders: milk fever, downer cow syndrome, hypomagnesemic tetany, udder edema, left displaced abomasum, and ketosis. Each disorder will be reviewed individually, and then we will diagram the relationships among the disorders. Finally, we will diagram and discuss the risk factors shared by combinations of the disorders.

The material for our review was taken primarily from epidemiologic (observational) field studies, although some feeding trials and other intervention studies were included. It is beyond the scope of this review to include diagnosis, treatment, prevention (except by inference), biochemistry, or pathophysiology. Readers interested in those topics should consult either veterinary textbooks or reviews (1, 2, 9, 11, 38, 43, 46, 48, 73).

Some data have been included from an unpublished, preliminary analysis of a large Finnish data set (Gröhn and Erb, 1987 unpublished). The data are from ~61,000 Finnish Ayrshire cattle (~42,000 multiparous cows) that calved during 1983 and from which data on 23 veterinary diagnoses were collected (under the Finnish national program) from 2 d before calving to the following calving or removal from the herd. All cows had pedigrees, were bred by artificial insemination, and were in herds that recorded milk yields. The herds were from the 76 (out of 461) communities that were judged to have the best record keeping, and included ~30% of all Finnish milk registry herds and ~10% of the entire Finnish dairy herd. Analyses were done using log-linear models that a priori included parity, season of calving, and previous lactation cow and herd milk yield class. Initial screening models also included pairs of diseases. Later models could include multiple diseases as risk factors, based on the screening models, a priori hypotheses, and correctness of time sequences between predictor and dependent disorders (further details are available from the authors). Most analyses excluded the ~19,000 first calf heifers, but they were included (and previous cow yield excluded) for analysis of udder edema. The advantages of this data set are that it is one of the largest (and therefore statistically most powerful) currently available and it includes records of disorders not simultaneously available in other sets. The disadvantages are that the final stages of analyses (which will include control for the 76 communities in the data set) have not yet been completed (so that the findings to date are preliminary), and the breed is Finnish Ayrshire rather than Holstein-Friesian.

MILK FEVER

By milk fever we mean the disorder that also has been termed clinical parturient hypocalcemia or clinical parturient paresis. This review will focus on clinical disease (rather than
on subclinical hypocalcemia), on recumbent cases (rather than on standing cases), and on parturient cases (rather than cases diagnosed later than, e.g., 7 or 30 d in milk). For previous reviews, see Hibbs and Conrad (38), Jørgensen (43), and Littledike et al. (48).

Lactational incidence rate (LIR) of milk fever among Friesian-type cows is 1.2 to 14.1%; most estimates are of <7% (3, 8, 25, 26, 27, 31, 50, 52). Even in studies in which milk fever was not constrained to be a periparturient disorder, it is clear that the disorder is rare at other times. The median day of diagnosis was the day of calving (25) or the day after calving (35), and 140 out of 143 cases were diagnosed within 15 d postpartum (30).

Age, Breed, and Season

All studies found increasing risk with increasing age or parity, regardless of breed (3, 8, 16, 24, 26, 31, 36, 52).

Ayrshires rarely have been compared directly to other breeds regarding risk of milk fever but had average age at first occurrence and average age of (any) occurrence similar to Friesians but older than Channel Island breeds (18). The LIR of Finnish Ayrshires [3.8% to 9.5%; (36, 70)] were similar to those of Friesians in other countries. Where compared within the same studies, Swedish Red and White cattle had higher LIR than did Swedish Friesians (3, 26, 27). The higher risk among Channel Island breeds is well-known (18, 27).

Two Swedish studies found increased risk of milk fever during the pasture season (rather than the stabling season) (3, 27), but Finnish and Canadian studies found no significant seasonal patterns for milk fever (24, 36, 70; Gröhn and Erb, 1987, unpublished). The clearest statement that can be made is that, in contrast to many other disorders, the risk of milk fever is not increased in the winter.

Milk Production

Risk of milk fever increased with increasing herd milk yield (27, 36; Gröhn and Erb, 1987, unpublished). Cows of higher genetic value (estimated transmitting ability for milk or sire's genetic value for milk) had higher risk in some studies (15, 26, 74). The risk increased with increased production in the previous lactation (3; 18 for Holsteins but not for Ayrshires, Jerseys, or Guernseys), even after adjusting for herd production, age, and breed (23, 36; Gröhn and Erb, 1987, unpublished; but not 16). Except for an unconditional analysis (18), in which Jerseys and Guernseys that became cases had lower breed class averages for milk in the previous lactation than their herdmates (without control for earlier age of occurrence in these breeds), there are no suggestions that low milk yield is a risk factor for milk fever. It is likely that higher yielding cows are at increased risk, even after taking herd, age, and breed into consideration. This topic was reviewed recently (29).

Repeatability and Heritability

Milk fever is a repeatable and heritable disease. A cow that has had clinical milk fever in a previous lactation has two to five times greater odds of milk fever than a cow who has not been a case previously (8, 26, 56), even after adjusting for effects of age (3, 23). We include (8, 56) even though those authors disclaimed repeatability, because the rates of repeat cases (19% and 28%, respectively) clearly are higher than the crude incidence rates in their reports. Significant estimates of heritability for Friesian or Ayrshire cattle ranged from .04 to .20 (26, 36, 58, 75), although one study found no significant heritability (24).

Calf Factors and Other Disorders

Calf sex and calf size were not related, but calf mortality was correlated negatively to the occurrence of milk fever (75, 76). Also, the odds of milk fever were not related to twinning or to stillbirth in Israeli cattle (50). These reports seem not to have considered dystocia at the same time. However, Bendixen et al. (3) found that in the absence of dystocia, male calves increased risk and twins decreased risk; neither factor was significant in the presence of dystocia. These findings are inconsistent; there may be calf factors associated with milk fever, but they need further study.

Retained placenta (3) and metritis and clinical ketosis (23) in the previous lactation — independent of milk fever in the previous lactation — increased risk of milk fever. Milk fever, dystocia, and retained placenta tend to occur as a complex of parturient disorders (16, 31, 63, 76; Gröhn and Erb, unpublished, 1987;
but not 23), and milk fever predisposes to ketosis. It is possible that some of the associations of previous lactation ketosis and previous lactation reproductive disorders with current lactation milk fever may be due to subclinical hypocalcemia in the previous lactation. Cows with hypocalcemia in one lactation are at increased risk of milk fever in the next (26); support of this speculation requires evidence that both subclinical and clinical hypocalcemia predispose to reproductive disorders and to ketosis.

Housing

Type of housing has not been studied sufficiently to draw firm conclusions, and no study has compared different types of housing within the same herd; therefore, herd seriously confounds all studies of housing. Most data are from Scandinavia. There was a nonsignificant increase in incidence rates in tied versus loose housing (27) and no difference in short-stalled versus long-stalled cowsheds (70). Opportunity for moderate exercise (5 to 19 h/d versus less or more) seemed to be slightly beneficial, and cows in freestall or loose housing had slightly lower rates than cows in stanchions or tie stalls or exclusively on pasture (15). Incidence rates of milk fever were significantly higher in tied than loose housing in Swedish Red cattle but not Swedish Friesians (3). The trend is toward increased risk when movement is most severely limited by housing. However, if restricted movement truly is detrimental, then milk fever should be a winter disease, but it is not.

Dry Period Nutrition

A detailed review of the effects of nutrition on the risk of milk fever is beyond the scope of this review, especially since good reviews are available [e.g., (38, 43, 48) for review of calcium, phosphorus, and calcium:phosphorus ratio].

Grain feeding cows late in the dry period may predispose them to milk fever, but that interpretation is complicated by differences in experimental rations between studies. Kendall et al. (45) found that grain (an unspecified "typical milking herd mixture") at 1% of body weight reduced incidence, but Emery et al. (28) found that feeding grain (a mixture that included corn, oats, soybean meal, and 1% dicalcium phosphate) ad libitum significantly increased incidence from 0% (no grain) to 16% (ad libitum). Two other studies had nonsignificant increases in milk fever with increased grain but also had very little power to detect significant differences. The 63-cow study found 0/21, 2/21, and 4/21 cases with 0, 2.7, and 6.8 kg grain/d (grain was a mix including oats, corn, wheat bran, corn gluten, soybean meal, and steamed bone meal) (72); the 106-cow study found a rate of 10% on an all-hay diet but rates of 13% for cows eating 1 or 4.1 kg/d of ensiled high moisture shelled corn late in the dry period (42).

Rates of milk fever of 6.1 to 7.5% did not vary among 289 cows on rations of all hay, hay plus corn silage, or limited corn silage plus protein supplement (57). In a multivariate analysis controlling for calcium, phosphorus, and protein, estimated energy intakes late in the dry period did not affect risk of milk fever (16). According to recent research, prepartum diets with high cation (Na+, K+) to-anion (Cl−, S−) ratios may predispose cows to milk fever (6, 34, 60).

Miscellaneous Factors

Miscellaneous factors that have been investigated for association with the occurrence of milk fever include daily barometric pressure \([P > .05; (79)]\) and the hypocalcemic effect of aminoglycoside antibiotics \(\text{[the family of drugs that includes streptomycin and gentamycin; (14)]}\).

Herd size tended to be associated with incidence in Finnish herds: herds of <16 cows had rates of 7%; larger herds (of which there were only 30) had rates of 11 to 13% (70). In the same study, rates were nonsignificantly higher in milk recording herds than in other herds (9% versus 7%; (70)). Because herds that record milk yield tend to be higher producing than herds that do not record yield, the latter trend may reflect the increased risk associated with higher herd production.

DOWNER COW SYNDROME

Downer cow syndrome has no universal definition. Fenwick in Australia (32) defined a downer as any cow with milk fever that did not get up within 10 min of first treatment with intravenous calcium; Björsell et al. from Swe-
den (5) considered a downer cow to be one that had not risen within 24 h after first treatment with calcium for milk fever. We favor the definition used by Cox et al. (12): a downer cow is one down for at least 24 h without apparent reason for being down (that is, no apparent reason prior to development of the sequelae of recumbency). We prefer Cox’s definition because it does not force an association-by-definition to milk fever. For a previous review, we suggest Cox (11).

There is little documentation of the incidence rate (IR) of downer cow syndrome. A mail survey of 723 Minnesota dairy herds with 34,650 cow-yr at risk found a rate of 21.4/1000 cow-yr at risk (12). Unpublished data from Cornell University [Correa et al., 1987, using data from the study described in (31)] include 28 downer cases in 7767 lactations from 34 herds (>4/1000 cow-yr). In spite of the apparent rarity of the syndrome, it is important because of the devastating prognosis for the cow. Minnesota farmers reported that of cows who were down (and who neither were slaughtered in <1 d nor died in <4 d), 23% were slaughtered, 44% died, and only 33% recovered (12). In a feeding trial, 6 of 8 downer cows failed to respond to treatment (44). In an Ontario case series, 55 out of 82 (67%) downer cows died or were slaughtered (19).

Age, Breed, and Season

There are limited data on these risk factors and none regarding age, although if milk fever and dystocia are indeed risk factors, then heifers (because of dystocia) and older cows (because of milk fever) should be at highest risk.

Similarly, if milk fever is related to a great proportion of downer cases, then the Channel Island breeds should be at highest risk of downer syndrome. The mail survey identified a possible lower risk in Brown Swiss than in Holstein cows (15.7/1000 cow-yr versus 22.2/1000 cow-yr), but the rates in Jerseys (83 herds, rate 17.9/1000 cow-yr) and Guernseys (100 herds, rate 21.8/1000 yr) were intermediate and there were no significant differences (12).

Seventy out of 82 cases occurred from November to April (19), but there was no adjustment for calving rates. However, Cox et al. (12) adjusted for season of calving and still found a significant increase in cases in winter (December to February) and a decrease in the spring (April to June). As with the results for breed, this seasonal pattern argues against downer being simply a sequella of milk fever (for which the season of highest risk might be the summer).

Milk Production

The only evidence regarding milk yield as a risk factor for downer cow syndrome is the reported impression of Minnesota farmers that their downer cows were 48% high producers, 46% average producers, and only 6% low producers (12). The data were recorded by check-off for those terms rather than by indicating an objective measure of yield, so the data only hint at high milk yield being a predisposing factor. There are no data regarding the risk of downer syndrome for cows in high producing rather than low producing herds.

Repeatability and Heritability

There are no data regarding repeatability and heritability of the downer cow syndrome. The case fatality rate is so high that most cows do not have opportunity to repeat in the next lactation.

Calf Factors and Other Disorders

There are no reports relating calf factors to IR of downer syndrome. There is speculation that downer cows could be suffering from vitamin E-selenium deficiency or from other toxicities (e.g., systemic mastitis or metritis) (11)... but a toxic cow would not fit the picture of an alert cow who is down for no reason. The Minnesota survey provided documentation of dystocia as a risk factor; 41% of downer cows that went down within 1 d of calving had dystocia, as did 24% of all downer cows in general (12).

Downer cow syndrome originally was thought to be merely a sequella of milk fever. The incidence rate of downer cows among milk fever cows [4% to 35%; (5, 19, 32)] is at least 10 times higher than the crude rates estimated for the general population of dairy cows. In the Ontario case series, 75 out of 82 downer cows had been treated for milk fever (19). However, it really is not clear whether all 75 cows had
clinical milk fever or whether some cows had been given calcium as a reasonable "best guess" treatment. Unpublished data from 7767 lactations in private herds around Cornell University show that 10 out of 28 downer cows (36%) also had a clinical milk fever diagnosis (odds ratio 12.8) (Correa et al., 1987, unpublished).

**Housing**

Type of housing was unrelated to IR of downer cows, and no trends were suggested by the data (12). Among specified housing types, the lowest rates (20.2/1000) were for the combination stanchions and loose and the highest rate was for stanchions (23.5/1000). Tie stalls, free stalls, and various other combinations were intermediate (12).

**Miscellaneous Factors**

In one Ohio feeding trial, cows fed 15% crude protein while on a corn silage-concentrate ration for the entire dry period (length unspecified but apparently greater than 21 d) had a disastrous downer cow rate of 8/26 cows (44).

Björsell et al. (5) showed (among 283 Swedish Red and White cows who had milk fever) that the serum calcium, glutamic oxaloacetic transaminase, total protein, and albumin:globulin ratios were similar (at first treatment for milk fever) for those cows who recovered and those who became downers. Fenwick (32) found that duration of recumbency prior to treatment for milk fever influenced the occurrence of downer cows. Only 2.3% of cows recumbent <6 h became downer cows, whereas the rate climbed to 38.9% for cows down >18 h prior to treatment. Cox et al. (13) showed that 50% (8/16) of normal cows who were anesthetized and kept in sternal recumbency with one hind leg underneath for 6 to 12 h were unable to stand within 3 h of the end of anesthesia. Duration of anesthesia (6, 9, or 12 h) was unrelated to occurrence of the downer cow syndrome, but all downer cows showed evidence of crush syndrome upon necropsy (13).

**HYPOMAGNESEMIC TETANY**

Hypomagnesemic tetany (clinical hypomagnesemia, grass tetany) was reviewed by Littledike et al. (48), and there is little published epidemiologic work to add to that review.

The LIR of hypomagnesemic tetany is .1 to .3% in Finland (36, 70; Gröhn and Erb, 1987, unpublished), and the fatality rate can approach 30% (48). In unpublished data on ~42,000 Finnish Ayrshire cows, median days postpartum at which tetany was diagnosed were 44 d (outdoor tetany) and 22 d (indoor tetany) (Gröhn and Erb, 1987, unpublished).

**Age, Breed, and Season**

The LIR of hypomagnesemic tetany may increase with parity at least through parity 6 ([36]; but this is not the case for indoor tetany (Gröhn and Erb, 1987, unpublished)]. Breed predispositions are undocumented. Tetany is more commonly diagnosed in summer than in winter (36, 70).

**Milk Production**

High milk yield may not be a risk factor for hypomagnesemic tetany, but data are limited. Saloniemi and Roine (70) found a twofold greater (but nonsignificant) increase in risk among milk-recording herds than among herds that were not on milk-recording programs. As in North America, milk-recording herds tend to have higher production than other herds. However, our unpublished multiple log-linear analysis of risk factors for tetany found that neither cow milk yield in the previous lactation nor herd milk yield in the previous lactation was associated with hypomagnesemic tetany (Gröhn and Erb, 1987, unpublished).

**Calf Factors and Other Disorders**

There are no published data on these factors for hypomagnesemic tetany. However, our analysis indicated that milk fever (but not hardware disease) was related to tetany (Gröhn and Erb, 1987, unpublished). Preliminary analyses ruled out associations with dystocia, retained placenta, and prolapsed uterus (Gröhn and Erb, 1987, unpublished).

**Miscellaneous Factors**

The importance of low magnesium and sodium intakes and of heavy fertilization of
forages with nitrogen and potassium have been reviewed (48). That heavy potassium fertilization of forages might increase risk is interesting, because high dietary potassium is a risk factor also for udder edema (65, 71). However, the apparent influence of dietary sodium is in opposite directions for tetany and udder edema (48, 65).

The influence of herd size on the LIR of hypomagnesemic tetany was irregular and nonsignificant (70).

**UDDER EDEMA**

The LIR of severe udder edema (a case diagnosed by a veterinarian or a score >3 on a 1 to 5 scale) ranged from 1.1 to 18% (21; Correa et al., 1987, unpublished). Also, for 73 first lactation Holstein heifers, the mean score (on a 1 to 10 scale) the day before calving was 6 (49), and the mean score (on a 1 to 5 scale) at calving was 1.9 to 2.2 (47). Some degree of udder edema was detected at freshening in 97% of cows (21). Edema typically becomes evident 2 to 4 d before calving, peaks in severity at calving, and declines (but may be evident still) within 1 to 2 wk of calving (21, 47, 49, 72).

**Age, Breed, and Season**

Udder edema is more common and more severe in first lactation heifers than in older cows (21, 28, 80). However, severity increased within first and second (but not later) parities with increased age at calving (21).

There is no documentation of breed as a risk factor for udder edema. Season is not associated with edema (21, 49; Gröhn and Erb, 1987, unpublished).

**Milk Production**

The relationship between udder edema and milk production is unclear. Shanks et al. (74) found that heifers of higher genetic potential for milk yield had 11% greater incidence of udder edema, but we found that edema was not related in our models to cow's previous lactation milk yield (excluding first-calf heifers, of course; Gröhn and Erb, 1987, unpublished). However, when cow's prior yield was not in the model and all parities were included, higher herd milk yield in the previous lactation was associated with higher rates (Gröhn and Erb, 1987, unpublished).

**Repeatability and Heritability**

Dentene and McDaniel (22) found significant correlations of .18 to .20 between the udder edema scores of the first and second calvings. The same authors estimated heritability to be .10 to .13 (21).

**Calf Factors and Other Disorders**

Malven et al. (49) found that increased prepartum (but not postpartum) edema score was related to longer gestation length and also (in the same model) to lighter calf birth weight.

In our unpublished models, milk fever and retained placenta were significant risk factors for incidence of udder edema, but dystocia, uterine prolapse, and hypomagnesemic tetany were not related (Gröhn and Erb, 1987, unpublished). Also, the odds ratios between udder edema and milk fever, left displaced abomasum (LDA), and ketosis were 2.6, 4.0, and 3.6, respectively (Correa et al., 1987, unpublished).

**Dry Period Nutrition**

High dietary sodium and potassium predispose to udder edema (48, 65, 71). Other factors such as energy intake and protein also have been examined in feeding trials; although no associations were significant, sample sizes were quite limited (20 to 24 cows) (7, 80).

Larger feeding trials investigated the effects of prepartum grain feeding on udder edema. Even with the larger numbers of cows (63 to 148), these trials did not necessarily reach statistical significance — but the trends are evident. Schmidt and Schultz (72) fed no grain, 2.7 kg grain/d (mixed oats, corn, wheat bran, soybean meal, and iodized salt), or 6.8 kg/d for 8 wk prepartum to 63 cows; there were two cases of udder edema in each of the grain groups, and only one case in the no-grain animals (with wide confidence intervals, these would correspond to 4 versus 9% IR). Emery et al. (28) fed no grain or ad libitum grain to 50 Holstein cows and 98 Holstein heifers for the last 21 d prepartum. Interaction was significant between parity and grain. There was no effect in cows, but severity of mammary edema was increased in heifers fed grain (mixed corn, oats, soybean meal, and 1% trace-mineralized salt) (28). Johnson and Otterby (42) fed all hay, low grain, or high grain diets such that grain (ensiled high moisture shelled corn; dicalcium phos-
phate continuously available from a bowl) dry matter consumed 30 d prepartum was 0, 1, or 4.1 kg/d. Among the 103 Holstein cows, scores for udder edema increased significantly from 1.4 (on a 1 to 3 scale) in no-grain cows to 2.3 among the high grain group (42). The implications are that grain feeding prepartum increases severity of udder edema, that the effect is easier to detect in heifers than in cows, and that it may be easier to detect an effect on severity than on IR. However, the diets in each study are different, and that confuses the interpretation.

Miscellaneous Risk Factors

Forced exercise (walking 5.5 km/h for 1.6 km/d, 5 d/wk for 4 wk prepartum, continuing in some animals for 10 d postpartum) did not affect either edema score at calving or duration of edema postpartum (total n = 42 Holstein heifers) (47). However, prepartum edema was 3.9 to 4.3 d less when compared with that of control heifers housed in similar freestalls but not forced to exercise (47). Interestingly, placentas were released 1.4 to 2.0 h sooner in the exercised heifers (47). Although 2 additional h are probably not of pathologic or practical importance, this supports the association between edema and retained placenta found by Gröhn and Erb (1987, unpublished) and suggests the possibility of a common cause to both disorders.

LEFT DISPLACED ABOMASUM

Most displacements of the abomasum (perhaps 85% to 88%) (78; Correa et al., 1987, unpublished) are to the left. The LIR of LDA was 1.22 to 2.5% (52; Correa et al., 1987, unpublished); the LIR of displaced abomasum without specification as to side was .33% to 4.4% (8, 9, 25, 50, 67). The inclusion of the side-specific range of LIR within the range of the side-unspecified LIR plus the high proportion of displacements that are to the left, suggests that the studies of the epidemiologies can be combined. The expense will be a possible slight loss of power by dilution of some case series with right displacements, rather than any major bias. Displaced abomasum was reviewed by Coppock (9).

Most cases of displaced abomasum are diagnosed soon after calving (55). In Norway, the median day postpartum of diagnosis was 21 to 25 d, in Canada it was 8 d, and in New York it was 1 d to 15 d (25, 30, 78); the mean in another Canadian study was 13 d (51).

Age, Breed, and Season

The LDA is rare in first-calf heifers, increases in LIR through the fourth to sixth calvings (age 6 to 10 y), then decreases (8, 24, 51, 52, 55, 68, 78). Earlier studies indicated that Channel Island breeds were at increased risk (41, 64), and there may have been more Channel Island cows in Martin's 1972 study (51) than expected (10% of the 100 cases but none of the systematically selected control cows were Guernseys or Jerseys). However, the breed distribution in one case series was similar to that of cows of the Pennsylvania DHA (68). After correcting for seasonal calving patterns, authors found either increased risk of LDA in the winter or spring (as opposed to the summer) (41, 51, 53, 55, 64, 68) or no seasonal pattern (24, 78).

Milk Production

The relationship between high milk yield or high milk yield potential and LDA has been examined several times, and the results are inconsistent. In general, the larger studies with multivariate analyses have not found a relationship, whereas associations were suggested by bivariate comparisons.

Of two Pennsylvania studies, the earlier (68) found that herds affected by LDA had higher milk yield than the average for herds on DHI, but the later study (67) found no difference in herd milk yield between high incidence (LIR >6.0) and low incidence (LIR <2.0) herds. Coppock (9) also reported higher herd milk averages in affected herds.

The Iowa high pedigree and low pedigree selection study found nonsignificant doubling of the rate of LDA in the high pedigree animals (total n <400) (74). Coppock (9) reported that DA cows (n = 481) produced 242 kg more milk in the previous lactation than unaffected herdmates [n = 81, (181)]. Martin (using prediagnosis current lactation yield) found a nonsignificant (total n = 82) difference of 1.4 kg/d more milk yield in cows who subsequently developed LDA than in herdmates (51). In a later study comparing 49 cases and 51 herd-parity-matched controls, the same author found...
that the cases had slightly better (+ 1.7 point) breed class averages for milk but poorer (−65.4 kg) previous lactation 305-d mature equivalent milk yield (53).

In multivariate analyses testing deviation from herdmate average in previous lactation mature equivalent milk yield (n = 1374) or in previous lactation breed class average for milk (n = 817) as a risk factor, no associations with LDA were found (16, 23). Our Finnish Ayrshire data set (n ~42,000 multiparous lactations) does not have a separate category for LDA; rather, the category abomasal disease is predominantly (based on experience) LDA but also includes displacements to the right and abomasal ulcers. However, the epidemiology of abomasal disease in preliminary multivariate analysis is consistent with other studies and indicated that high previous lactation herd yield but not high previous lactation cow milk yield was a significant risk factor (Gröhn and Erb, 1987, unpublished). Each of these three multivariate analyses accounted for effects of herd and other likely risk factors such as milk fever, and none can be faulted for low sample size (relative to most of the bivariate analyses). Therefore, it is unlikely that high cow milk yield is a risk factor for LDA.

**Repeatability and Heritability**

Surgically corrected abomasal displacements should not recur, although the abomasopexy can break down. Although two studies that traced sire lines found higher rates of LDA among certain bull lines (54, 68), there is little documentation of heritability.

**Calf Factors and Other Disorders**

There are few epidemiologic analyses of the effects of calf factors on the risk of LDA. However, Markusfeld (50) found that stillbirth was not related to DA, although cows delivered of twins had odds 1.8 times greater than the odds of DA in cows who had single births. This association was present despite control in the analysis for stillbirth, milk fever, and postparturient uterine diseases.

Milk fever has been identified as a risk factor for LDA both in a bivariate analysis (Correa et al., 1987, unpublished) and in a multivariate analysis (Gröhn and Erb, 1987, unpublished). In other multivariate analyses (which included other potential risk factors such as retained placenta), milk fever and LDA were not related (16, 23, 50). Thirty percent of Norwegian cows with LDA had been treated for milk fever, which probably was higher than the expected rate (78). Also, studies of the intravenous infusion of a calcium-chelating agent showed that abomasal hypotony resulted from the induced hypocalcemia (20, 39), and natural hypocalcemia was associated with DA (40). Milk fever is a risk factor for retained placenta (31, 70; Gröhn and Erb, 1987, unpublished). Retained placenta is a risk factor for LDA in bivariate analyses (10, 66) and in some (including the statistically most powerful) multivariate analyses (50; Gröhn and Erb, 1987, unpublished) but not all (16, 23). All multivariate analyses of the milk fever-LDA association controlled for retained placenta. Our interpretation is that milk fever is a risk factor for LDA and that much of the association is mediated by retained placenta.

Association between metritis and LDA was not tested by Curtis et al. (16) or Dohoo and Martin (23) in their path analyses. Association was found by Gröhn and Erb (1987, unpublished), by Markusfeld (50), and also in bivariate analyses (10, 66). Robertson (68) reported that 52% of cows with LDA also had concurrent metritis and 24% had metritis previously; these rates probably were higher than expected (although no control data were available). In our model (Gröhn and Erb, 1987, unpublished), metritis was in the model simultaneously (as was also clinical ketosis) with both milk fever and retained placenta, and each had independent direct effects on LDA.

Clinical ketosis diagnosed prior to LDA diagnosis was related strongly to LDA [odds ratios 12 to 39; (16, 66)]. There also was a strong bivariate association between the diagnoses (time order was uncertain) in Correa’s data set (Correa et al., 1987, unpublished), and 30 of 53 LDA cows had a diagnosis of ketosis in the week prior to their diagnosis of displaced abomasum (78). Therefore, it seems likely that ketosis is indeed a risk factor for — and not merely a consequence of — LDA.

Retained placenta and the outdoor syndrome of hypomagnesemic tetany were related to LDA in our preliminary data; rumen acidosis, hardware disease, and mastitis had been
ruled out as risk factors (Gröhn and Erb, 1987, unpublished). In preliminary bivariate data, the significant odds ratio between udder edema and LDA was 4.0 (Correa et al., 1987, unpublished).

**Housing**

Robertson’s survey included questions on housing, but he made no explicit statement regarding the responses (68). Apparently, housing was among the husbandry factors surveyed, most of which did not differ between affected and unaffected herds (68). Martin’s questionnaire (51) also failed to elicit any significant differences between affected and control cows, although twice as many case cows as control cows (19% versus 8%) calved in tie stalls and twice as many affected herds as unaffected herds (28/66 versus 4/26) used loose housing (as opposed to tie stalls or a mixture).

**Dry Period Nutrition**

Nutritional factors were reviewed by Coppock (9), who concluded that diets high in grain or corn silage predisposed cows to displaced abomasum. Not all of the feeding practices reviewed were necessarily for prepam cows, Coppock made no distinction between cow and herd feeding practices, and of course, a few new studies now are available.

Although it is thought that dry period corn silage and grain predispose cows to LDA, in fact, the data are mildly inconclusive. The experimental studies suggest trends, but there are no large field studies of cow data, and results of the herd studies disagree.

Robertson (68) found that herds unaffected for over 3 yr by DA fed more nutrients in the form of roughage than did affected herds. However, he found no correlation between amount of grain feeding and incidence of LDA within herds. Affected herds fed 1.25 kg (presumably per day) more grain to cows in the last month of the dry period (68). In a much later study (also in Pennsylvania), high incidence and low incidence herds did not differ regarding prepam feeding of corn silage and hay, and there was a nonsignificant trend for more dry period grain feeding in the low incidence herds (LIR <2.0%) (67). Curtis et al. (16) asked farmers to estimate the energy content of their late dry period rations. Compared with the lowest tercile of energy, the higher energy intakes were preventive of LDA. Similarly, higher terciles of late dry period protein also were protective (indirectly).

In a feeding trial, Coppock et al. (10) fed four different forage to grain ratios prepam, and LDA incidences were 2/22 and 8/21 in the >50:50 and <50:50 groups, respectively. Johnson and Otterby (42) fed three diets: all hay; corn silage, alfalfa silage, and 1 kg grain/d; or silages plus 4.1 kg grain/d for the last 30 d postpartum. There was no DA in any treatment group (total n = 106), although the grain and silage diets predisposed cows to milk fever and udder edema and protected cows from ketosis. Nocek et al. (57) assigned 289 cows to all hay, 50:50 hay:corn silage, or limited corn silage plus liquid protein supplement at drying-off. The nonsignificant trend was for more displaced abomasums as the diet got further from all hay: 3, 4.3, and 6.3% LIR, respectively.

**Miscellaneous Factors**

There are two inconsistent reports of the relationship between body weight or body condition and LDA. Robb et al. (67) reported that cows in low incidence herds had lower weights but higher condition scores than cows in high incidence herds. However, Coppock (9) reported that cows with displaced abomasums were 50 kg heavier on the average than their herdmates in the lactation preceding the displaced abomasum (the association may have been confounded by age).

Miscellaneous factors that apparently did not differ between affected and unaffected herds include increasing or decreasing herd size, pasture type and quality, pasture water supply, milking method (hand/machine), farm topography (flat/hilly), soil type and acreage, fertilizers, insecticides, and method of heat detection (68).

**CLINICAL KETOSIS**

Epidemiologic studies of clinical ketosis have used a wide variety of definitions, including lack of appetite for concentrates within 5 wk of calving (4, 27); primary ketosis (veterinary diagnoses) (36, 61, 70; Gröhn and Erb, 1987, Journal of Dairy Science Vol. 71, No. 9, 1988
unpublished); primary ketosis without concurrent disease on the same day (veterinary diagnoses) (37); no specification (8, 17; Correa et al., 1987, unpublished); no concurrent or previous case of metritis, retained placenta, LDA, milk fever, or metritis (16); and both primary and secondary (52). Previous reviews include those of Baird (2), Kronfeld (46), Littledike et al. (48), and Schultz (73).

The LIR of clinical ketosis among Friesian-type cows is 1.1 to 9.2% (4, 8, 16, 25, 27, 52). There is no particular trend in incidence according to liberalness of definition, which suggests that most studies are of essentially the same disease. The median day postpartum at diagnosis was 10 d (25) and 28 d (35; Gröhn and Erb, 1987, unpublished). The median postpartum week at diagnosis was 4 wk (61), and 51% and 55% of cases occurred 3 wk to 5 wk postpartum (36, 37).

Age, Breed, and Season

The relationship between age or parity and ketosis is a little confusing. There was no linear association found by Curtis et al. (16), but peaks were found at 8 to <10 yr (52), 9 yr (24), and at >9 to <7 yr (8). By parity rather than age, the peaks were at fourth to seventh (4), third to fourth (36), and > seventh (37). Apparently, there is a peak in risk as cows become mature and then an increased risk again in very old cows.

Comparisons among breed-specific risk are confounded by herd and usually also by study and country. The range of LIR for Finnish Ayrshire cattle is 5.8 to 7.1% (36, 37, 70) and is in the upper part of the range for Friesians. There was no pattern of differences among Swedish Friesian, Swedish Red, or Ayrshire breeds in one study (27), but in a recent study the IR among Swedish Red cattle (4.4%) was higher than the IR among Friesians (1.8%) (4).

After adjusting for calving patterns, one author (27) found no seasonal pattern of risk for clinical ketosis, but several other authors found significantly decreased risk in the summer months (4, 24, 36, 37, 61, 70). However, the risk associated with milk yield of individual cows is not clear. Without correction for herd, Ekesbo (27) found no clear association (although risk in tied cows was highest in the highest yielding cows among cows tied in bedded housing but not in tied cows in unbedded housing), and Gröhn et al. (37) found no association between cow's latest 12-mo milk yield and ketosis. Norman and Van Vleck (58) found significant small positive phenotypic correlations between first lactation yield and ketosis but could not estimate genetic correlations. Shanks et al. (74) found no difference in rate of ketosis between high milk and low milk pedigree lines, all within one university herd. Pehrson (62) had small sample size (>74 cows), and found that the advantage in milk yield of .8 kg/d prior to ketosis (in cases compared with controls) was not significant. Correcting for herd yield, no association between previous lactation yield and clinical ketosis was found by Curtis et al. (16) or by Dohoo et al. (23), but Gröhn et al. (36) and our multivariate analysis indicated that higher previous yield was associated with higher risk (Gröhn and Erb, 1987, unpublished). In the data of Overby et al. (61), risk was lowest for cows and herds in the lowest yield groups, but it is not clear that the groups were based on yield prior to ketosis. The significant associations were found mostly in the Scandinavian data and, generally, in the largest (statistically most powerful) studies. This suggests that there may not be an important effect of cow's production in previous lactation on risk of ketosis in North America.

Repeatability and Heritability

Depending on parity and breed, Swedish cows that had ketosis in previous lacies were at 4.4 to 12.3 times greater risk of ketosis than cows with no previous history of clinical ketosis (4). Ketosis in the previous lactation predisposed cows to ketosis in current lactation (23). Heritability of ketosis has been estimated as .06 to .09 (59), .08 (37), .3 (77), and .31 (24).

Calf Factors and Other Disorders

No data relate calf factors to incidence of ketosis. Ketosis, lameness, and retained placenta in the previous lactation predisposed to
ketosis (23). Milk fever in the current lactation was associated with increased odds of ketosis (4, 16; Gröhn and Erb, 1987, unpublished; but not 23). Retained placenta was a risk factor in three studies (16, 23; Gröhn and Erb, 1987, unpublished) but only nonsignificantly increased risk among Swedish Friesians (and not at all among Swedish Reds) if milk fever was absent (4). If both retained placenta and milk fever were present, IR were highest (4). Other diseases related to ketosis include udder edema (Correa et al., 1987, unpublished; but not Gröhn and Erb, 1987, unpublished), metritis (36; Gröhn and Erb, 1987, unpublished), acute mastitis (36), and displaced abomasum (although this probably is secondary ketosis) (16, 23; Gröhn and Erb, 1987, unpublished). Hypomagnesemic tetany and ketosis were not related (Gröhn and Erb, 1987, unpublished).

**Housing**

All of the housing data are from Scandinavia. Cows in short-stalled cowsheds had rates similar to those in long-stalled cowsheds (70). Friesian and Swedish Red but not Swedish Ayrshire cows in loose housing were at lower risk than those in tied housing during the housing season, but the rates were without pattern during the pasture period (27). In that same study, herds in open housing (access available to an open-air exercise and resting yard) had lower rates than herds in closed housing (27). In the very powerful study of Bendixen et al. (4), loose-housed cows had less than 40% the risk of ketosis of tied cows. Among tied Swedish Red (but not Swedish Friesian) cows, those in housing systems with pasture periods had slightly lower risk than cows in zero-grazing herds (4). The trends are for confinement and restricted movement to increase risk of ketosis.

**Dry Period Nutrition**

The effect on ketosis of feeding high energy grain-corn silage during the (late) dry period is unclear. Two feeding trials suggested non-significant trends toward more clinical ketosis among cows fed all hay diets during the dry period than among cows who received some corn silage and perhaps grain or a protein supplement (42, 57). However, three trials suggested no effect of adding grain to diets that already contained corn silage in addition to hay (28, 33, 72). In one trial of each set, IR of ketosis were quite high (~29% and 64%) (28, 42). In another of these studies, there were no cases at all, in spite of the fact that ~179 cows and heifers were on what was thought to have been an energy deficient diet (115% of maintenance) (33). Nöcck et al. (57) reported that all of their diets were slightly energy deficient, yet they had ordinary rates of ketosis (6.3 to 9.1%), and the trend was not consistent with the differences in energy deficiency.

In a questionnaire study in which farmers estimated nutrient intakes for the last 3 wk of the dry period (median estimated dietary protein and energy were above requirements in all terciles), on a bivariate basis, the trend seemed to be toward lower rates of uncomplicated ketosis as tercile of energy increased (17). However, multivariate analysis indicated that higher protein was protective but energy was unrelated (16). A problem with both this study (16) and Pehrson's (62), which suggested that low energy led to ketosis, is that both used herd (not cow) data.

These several studies suggest it was the presence of corn silage in the dry period diet that was protective rather than the presence of grain or amount of energy.

**Miscellaneous Factors**

In Finnish Ayrshires, incidence of ketosis was greater in milk-recording (than non-milk-recording) herds, but herd size had no effect (70). Swedish data also showed no trend in LIR relative to herd size in loose-housed cows or in cows in tied, zero-grazing housing, except that highest rates were with modest herd size (26 to 50 cows) (4). However, there was a pattern of lower rates with increasing herd size for tied cows with pasture periods and for tied, zero-grazing Friesians (4).

**ASSOCIATIONS BETWEEN THE METABOLIC DISORDERS**

We caution that the time sequences we have assumed are subject to great individual variability, and some associations are based on a single study (Gröhn and Erb, 1987, unpublished: dotted lines, Figure 1). Also, arrows imply merely "associations" not cause-and-effect; associations could be causal in nature.
but also could reflect underlying etiologies held in common by both disorders. In the latter instance, the disorder that is the risk factor for another disease is an indicator variable for the underlying common cause.

None of the six periparturient metabolic disorders occurs in isolation from the others (Figure 1). In our interpretation, milk fever plays a central role linking to all of the other disorders. The only metabolic disorder that is a risk factor for multiple disorders in the subsequent lactation is ketosis. However, milk fever and udder edema are repeatable; there may be too few survivors of downer syndrome to allow detection of effects in subsequent lactations; and LDA and hypomagnesemic tetany have not been investigated well enough to rule out effects on disorders in subsequent lactations.

Both downer cow and udder edema appear to be “dead ends” in our scheme of interrelationships, even though they occur early in the periparturient period. The suggested association between hypomagnesemic tetany and LDA is only for outdoor tetany (not the indoor syndrome). The relationship between LDA and ketosis has been represented with a double-headed arrow (Figure 1), because ketosis can be both a risk factor for and a consequence of LDA.

**RISK FACTORS FOR MULTIPLE METABOLIC DISORDERS**

Figure 2 is an elaboration of Figure 1 and includes our interpretation of associations between the metabolic disorders and other risk factors. We have included only those risk factors related to more than one of the metabolic disorders. The same caution must be used in interpreting Figure 2 as in Figure 1. In addition, we caution that Figure 2 has not yet been tested as a path diagram (even though it looks like one); the relative significance and importance of the direct and indirect pathways implied by Figure 2 are unknown.

The arrows from previous lactation cow and herd yields imply higher risks of several disorders among higher producing cows and herds. Interestingly, although reproductive disorders form links between metabolic disorders, the reproductive disorders are not predisposed to by high previous lactation cow milk yield according to studies published to date (29). However, high herd milk yield may predispose to the reproductive disorders (69; Gröhn and Erb, 1987, unpublished).

Calf factors is a very nonspecific term, and inclusion in Figure 2 implies merely that a variety of calf factors have been related to disorders. Specific effects of calf sex, calf size, calf survivorship, and twinning need to be evaluated simultaneously for effects on multiple disorders in a series of data sets.

Dry period grain and dry period corn silage both are represented in Figure 2. Increases in both feedstuffs may have protective effects (symbolized by the negative signs) on ketosis (the only protective effects in the scheme). Otherwise, grain and corn silage have been related to different sets of disorders.
Age and parity, breed, and season of calving were left off our summary diagram. Risk by age or parity is highest for milk fever in older cows, is unknown for downer syndrome, and is highest for udder edema in first-calf heifers. For hypomagnesemic tetany, LDA, and ketosis, risk increases to middle ages, then decreases. Channel Island cows are at higher risk of milk fever and may be at higher risk for LDA; otherwise, breed risks are not well-documented. Summer is the season of highest risk for tetany and perhaps for milk fever; there is no known seasonal predisposition for udder edema; and winter is the season of high risk calvings for downer cow syndrome, LDA, and ketosis.

REFERENCES


