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Atrial Septal Defect: is it a Genetic Problem in Cattle?

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Abstract

This study was designed to determine the time sequence of postnatal changes associated with the atrial septum in the bovine heart, and to assess if atrial septal defect (ASD) is a genetic disorder in stillborn Maine-Anjou calves. The study was divided into three parts: 1) review of the necropsy database; 2) examination of hearts from "normal" Holstein-Friesian calves; and 3) examination of hearts from stillborn beef calves and cattle dying of unknown cause. In the normal Holstein-Friesian calf the opening in the atrial septum is covered completely by a membrane at birth, resulting in an anatomic but not a physiologic opening, and closes completely between seven and 14 days of age. The same time sequence appears true for hearts from beef calves. Of the 27 hearts from beef cattle examined, six bull calves (three purebred Maine-Anjou, two Maine cross, one Shorthorn) and one 18-month-old Maine cross heifer had an ASD, which included both an opening in the atrial septum and an abnormal membrane. ASD is likely a genetic disorder of cattle, which may have a greater gene frequency in the Maine-Anjou breed.

Résumé

Cette étude avait pour but de déterminer l'évolution des changements postnatals du septum atrial dans le cœur des bovins et d'examiner si l'anomalie du septum atrial (ASD) est une maladie congénitale chez les veaux mort-nés de race Maine-Anjou. Cette étude était divisée en trois parties : 1) évaluation des données de nécropsie; 2) examen du cœur chez des veaux de race Holstein-Friesian considérés normaux; et 3) examen du cœur chez des veaux de boucherie mort-nés et chez des bovins morts pour des raisons inconnues. Chez les veaux Holstein-Friesian normaux, l'ouverture dans le septum atrial est complètement recouverte par une membrane à la naissance, créant ainsi une ouverture anatomique plutôt que physiologique, qui se ferme complètement entre sept et 14 jours d'âge. Cette même évolution semble apparente dans le cœur des veaux de boucherie. L'examen de 27 cœurs chez des veaux de boucherie révélait une ASD, incluant une ouverture dans le septum atrial de même qu'une membrane anormale, chez six veaux mâles (trois de race Maine-Anjou pure, deux de race Maine croisée et un de race Shorthorn) de même qu'une taure de race Maine croisée âgée de 18 mois. Il est probable que l'ASD soit une maladie congénitale chez les bovins affligeant plus particulièrement la race Maine-Anjou.

Introduction

In February 1999, a purebred Maine-Anjou cattle producer had a first-calf heifer that delivered a full-term bull calf that was alive at presentation, but died immediately after delivery. The calf did not spontaneously breathe. The producer was present at delivery, did not notice anything unusual and was unable to resuscitate the calf. Necropsy revealed a large atrial septal defect (ASD) with no visible membrane covering the defect. The pathologist concluded that the ASD was the cause of death. Because ASDs are suspected to be genetic defects in other species, the cow was culled. One month later, the same producer had a second bull calf born dead. Necropsy in the field again revealed a large ASD with an abnormal membrane. This cow was also culled. Since ASDs are a common cardiac defect in many species, we asked the question, "Is ASD a problem in Maine-Anjou calves born dead?"

ASD has been recorded in multiple species, including several breeds of cattle. Neither the prevalence nor the genetic basis of ASD in cattle has been determined. Since ASD is believed to have a genetic component in humans and other species, it is reasonable to postulate

that ASD has a genetic component in cattle. Our clinical experience suggests that ASD may be more common in the Maine-Anjou breed of cattle. The purpose of this study was to determine if ASD is a genetic problem in cattle, specifically in full-term, stillborn Maine-Anjou calves.

Methods

This study was divided into three parts: 1) review of necropsy database from the Diagnostic Center for Population and Animal Health (DCPAH) at Michigan State University (MSU); 2) examination of hearts from "normal" Holstein-Friesian calves; and 3) examination of hearts from beef calves and adult cattle.

Review of necropsy database: The MSU DCPAH database from 1990 to 1999 was reviewed. Two searches were done: 1) cases of "congenital heart defects, cattle" and 2) "calves born dead or lived less than 24 hours". Necropsy records for all cases of "congenital heart defects, cattle" and Maine-Anjou cattle "born dead or lived less than 24 hours" were examined.

Holstein-Friesian hearts: To estimate the normal time sequence of perinatal changes in the bovine heart, especially the atrial septum, and to assess what is "normal", we examined 19 hearts from Holstein-Friesians. Specimens included three fetal hearts (five to seven months gestation) and 16 hearts from calves full-term to 150 days of age (14 calves were less than 10 weeks of age; one was 75 days old; one was 150 days old). Holstein-Friesian hearts were provided by the herd veterinarian from a local dairy farm. Hearts were from stillborn calves or animals humanely killed for injury, failure to thrive, diarrhea, or pneumonia.

Results from examination of the Holstein-Friesian hearts, combined with information already available in the literature, allowed determination of the normal time course for closure of the opening in the atrial septum, and what constituted an abnormal septal membrane.

Hearts from beef cattle: Producers and veterinarians were contacted to submit hearts from stillborn calves, calves that died shortly after birth and cattle that died of unknown cause or were believed to have heart disease. Information and contact numbers were provided to producers and veterinarians through MSU Extension newsletters, DCPAH newsletters, the American Association of Bovine Practitioners e-mail list and the Michigan Cattlemen's Magazine. In addition, the American Maine-Anjou Association sent information to all adult members.

For all submitted calf hearts, producers provided the following information (when available): date and time of birth; whether the birth was witnessed; calving ease; whether the calf was born dead, or alive at birth and found dead or humanely killed; age at death; gender, weight and color of calf; any obvious gross abnormalities; previous heart problems diagnosed on the farm; breed of sire and dam; any additional information they thought was important. Pedigree information (seven generation) was obtained on all registered Maine-Anjou sires and dams of animals whose hearts were submitted for the study.

Examination of hearts: Producers contacted one of us (LK) by phone or e-mail to determine if we wanted the heart, how to remove it, how to store it and how to ship it. No heart was refused. Hearts were removed, rinsed and placed in water containing table salt, and stored in the refrigerator until shipped. Hearts were transported at no cost to the producer by next-day air, and examined upon arrival. After examination, hearts were placed in formalin.

Hearts were examined and measurements made by a clinician (LK) and a veterinary pathologist (TGB). The examination and measurements were made on two separate occasions in the presence of both individuals. If the measurements were not the same on the two days, they were averaged. Hearts were grossly examined, weighed and measurements made of the thickness of the left ventricular free wall, the right ventricular free wall and the interventricular septum. Measurements were made using a ruler and caliper. Both the LV free wall and RV free wall were measured midway between the base and the apex. Septal wall thickness was measured below the level of the chordae tendineae. The size of the opening between the left and right atria, if present, was measured and the covering membrane and its attachment to the atrial septum were noted and diagramed. The opening was measured at the longest horizontal and longest vertical points. Since the opening was generally circular, this measurement was approximately equivalent to the diameter. The degree of coverage of the opening by the membrane was noted. The area of the opening not covered by membrane was measured using a caliper and ruler. For example, if a 12 cm opening was half-covered by the membrane, the height of the opening would be 12 cm and the width would be 6 cm. Patency of the ductus arteriosus was determined by probing from the aortic side, and the diameter of the aortic opening was measured. The patency was probed with a metal rod of approximately 2 mm diameter. The aortic opening was measured at its widest point with a ruler.

Statistics: Data are expressed as mean +/- standard deviation of the mean, with $p < 0.05$ taken as the criterion of statistical significance. Data were entered and analyzed in Microsoft Excel. Comparisons between

normal hearts and hearts from calves with ASD were made using a non-paired t-test (Tables 3 and 4). To assess the degree of homozygosity present in a purebred individual, the coefficient of inbreeding was calculated using Wright's Formula.[18] Calculations were made only when both the sire and dam were registered purebred animals with a seven-generation pedigree. Because the American Maine-Anjou Association allows upgrading to purebred for a calf that is a product of a purebred Maine-Anjou and a three-quarter blood Maine-Anjou,[2] not all purebred calves had purebred parents. In these cases the coefficient of inbreeding was not calculated.

Results

Review of necropsy database: A search of the DCPAH necropsy database between 1990 and 1999 for cases of "congenital cardiac defects, cattle" revealed 47 animals, aged 0 to 730 days, described as having congenital heart defects. Review of the necropsy records revealed that among the 47 animals, there were 27 Holstein-Friesian, six Simmental, four Maine-Anjou and 10 cattle listed as crossbred, breed undetermined, or other breeds (Table 1). There were nine atrial septal defects, 25 ventricular septal defects and 13 cases described as "other congenital cardiac defects" (Table 1).

Search of the database looking for "calves born dead or less than one day old" revealed 12 Maine-Anjou calves "born dead". Review of these 12 necropsy records revealed that three of 12 were described as having a large atrial septal defect (25%). There were 4,299 calves of other breeds that fit the description "born dead or less than one day old". Of those, five had an atrial septal defect (0.0012%). These five cases were listed as Holstein-Friesian, "bovine, undetermined breed" or crossbred. Of the 4311 animals listed in the search of "calves born dead or less than one day old" most were Holstein-Friesians (72%). Other breeds included crossbreds or breed undetermined (20%), Hereford (2%), Angus (2%) and Simmental (1%). The following breeds represented less than 1% of the database submission: Jerseys, Brown Swiss, Shorthorn, Charolais, Maine-Anjou, Aryshire, Red Poll, Salers, Scotch Highland, Limousin, Guernsey, Gelbvieh, Beefmaster and Texas Longhorn. It should be noted that the predominant bovine breed in Michigan is the Holstein, and that MSU has the Holstein, Angus, Simmental and Hereford breeds in the university herds. MSU farms may utilize the diagnostic laboratory more often than other producers.

Holstein-Friesian hearts: The three fetal hearts examined displayed cardiac anatomy consistent with fetal hearts of other species, ie, an opening in the atrial septum, covered with a membrane that allowed one-way flow of blood (right to left) and a patent ductus arteriosus (Figure 1). The opening in the atrium measured between nine and 12 mm in diameter. The covering membrane was thin, translucent and pink. The aortic opening of the patent ductus arteriosus was 1- to 8-mm in diameter. The ductus arteriosus in all fetal hearts was patent throughout the entire length.

Table 1. Age (a) and breed (b) distribution of 47 cases of "congenital heart defects, bovine" Data from a DCPAH database search 1990-1999. Cattle were from 0 to 730 days of age. ASD = atrial septal defect; VSD = ventricular septal defect.

Table 1a.

Age	ASD	VSD	Other
Born dead	3	4	3
< 365 days	3	0	3
>365 days	3	21	7
Total	9	25	13

Table 1b.

Breed	ASD	VSD	Other congenital cardiac defects
Maine-Anjou	3	0	1
Crossbred	3	1	0
Holstein-Friesian	2	20	5
Simmental	0	1	5
Angus	0	2	1
Chianina	1	0	0
Hereford	0	0	1
Gelbvieh	0	1	0
Total	9	25	13

Hearts from 16 Holstein-Friesian calves born alive were examined. Of the 16 hearts examined, 13 were considered normal and were from calves less than 10 weeks of age. The 13 normal Holstein-Friesian hearts weighed between 120 and 470 grams. Left ventricular wall thickness ranged from 11 to 18 mm; right ventricular wall thickness was 4 to 14 mm; and interventricular septal thickness was 11 to 20 mm.

Calves less than one week of age had an opening in the atrial septum, covered with a membrane that allowed only one-way flow of blood (right to left). The membrane was thin, translucent and pink. The opening was round-to-oval and ranged from 6 to 11 mm at the point of greatest diameter. When viewed from the left atrium, the membrane completely covered the opening in the atrial septum. The membrane was attached

Figure 1. Schematic of atrial septum, viewed from the left atrium in various conditions. In all diagrams the circle represents the hole between the two atria. A represents the normal atrial septum at birth, with a thin, fibrous, membrane that completely covers the hole between the left and right atrium. This membrane allows blood to flow right to left prior to birth, but prevents left to right flow after birth. In this instance the septum is physiologically closed, although anatomically patent. B represents closure of the hole by fibrotic tissue at 10 to 14 days after birth. C, D and E represent abnormal membranes observed in this study. The membranes varied in size and shape, but none completely covered the hole between the two atria. Thus, the septum is both physiologically and anatomically open.

to the left atrial side of the septum over 75% of the circumference of the opening, from approximately the 12 o'clock to the 9 o'clock positions. When a finger was inserted from the right atrium through the opening, the membrane covered the finger (like a glove) and fenestrations were evident at the tip. All calves less than one week of age also had a ductus arteriosus which was patent along its entire length. The diameter of the aortic opening varied from 7 mm in a calf less than six hours of age, to less than 1 mm in a three-day-old calf.

All hearts from calves over 10 days of age had white scar tissue that filled the opening in the atrial septum. This tissue prevented flow of blood between the atria. The diameter of the aortic opening of the ductus arteriosus was 1 mm or less and the ductus was not patent. It appears that both the foramen ovale and the ductus arteriosus close between seven and 14 days after birth in hearts of normal Holstein-Friesian calves.

Three hearts from Holstein-Friesian calves had significant abnormalities: a three-day-old calf had a high ventricular septal defect; a 75-day-old calf had tricuspid valve lesions of endocarditis; and a 150-day-old heifer calf had a large ASD with a rudimentary, pink membrane that did not cover the opening.

Examination of submitted hearts from beef calves: Twenty-seven bovine hearts were submitted from beef producers in Michigan (19), Ohio (3), Colorado (1), Washington (1), Minnesota (1), Illinois (1) and Nebraska (1). Ten producers in Michigan and two in Ohio submitted hearts. Twenty-four of the 27 hearts were from Maine-Anjou or Maine-cross cattle (Table 2).

Six bull calves and one 18-month-old heifer had atrial septal defects with abnormal membranes (Tables 2 and 4). In these animals the membrane was rudimentary, minimally attached, and when viewed from the left atrium was insufficient to cover the atrial septal opening (Figures 1 and 2). The size of the opening between the atria ranged from 12 to 24 mm in diameter, and was significantly greater in calves with ASD than in non-affected calves (ASD = 17 +/- 4.5 vs normal = 12.8 +/- 3.9 mm; $p<0.05$; Tables 3 and 4). The opening between the atria in ASD calves was both anatomic and functional; because the membrane was rudimentary, blood could pass freely in either direction. In the normal calves, the opening was anatomic, however the presence of the membrane completely covering the opening prevented blood flow from left to right after birth. No significant differences were detected in heart weight, left or right ventricular free wall thickness, interventricular septal thickness, or heart-weight-to-body-weight ratios when comparisons were made between beef calves with ASD and beef calves with normal hearts (Tables 3 and 4).

Four of six calves with ASD were born dead or lived less than 24 hours. These four Maine-Anjou calves were male and had mean birth weights of 102 lb (46.4 kg), which was heavier than the breed average for bull calves born at this time (91 lb; 41 kg).[2] With the exception of one two-headed calf, all hearts from other calves born dead or that lived less than 24 hours were normal (Table 2).

The six affected calves were sired by six different bulls: four purebred Maine-Anjou, one Red Angus and one Shorthorn (Table 5). Three of the dams were purebred Maine-Anjou; one a three-quarter Maine-Anjou; one a half-blood Maine, one-quarter Simmental, one-quarter Holstein; and the sixth a purebred Shorthorn. In addition, we determined that one of the Maine-Anjou calves identified in the database with ASD was sired by a seventh purebred Maine-Anjou bull and born out of a Chianina cow. Thus, ASD was observed in cattle with percentage of Maine-Anjou ranging from 93 (purebred) to 25%. Since Shorthorn pedigrees often contain Maine-Anjou genetics, and the pedigree of the Shorthorn calf was not available, it is unknown what percent of the Maine-Anjou breed, if any, was present in the Shorthorn calf. Two of the sires of calves with ASD (sire code MA1 and MA4) also sired normal calves (Table 5).

To assess the degree of homozygosity, a seven-generation pedigree was used to determine the coefficient of inbreeding for all calves with registered, purebred Maine-Anjou parents (Table 5). Although there are insufficient numbers to make statistical comparisons, the average coefficient of inbreeding for the ASD group was 2.70%, while the average for calves with normal hearts was 4.69%. If data for one calf with a normal heart and with a high level of homozygosity due to a mistaken

Table 2. Summary of data from all beef cattle hearts submitted.

ID	Age	Breed	Sex	Pathological findings
K1	Stillborn	Maine	M	None
K0	Stillborn	Maine	M	Large ASD with minimal membrane
K23	Stillborn	Maine	M	Large ASD with minimal membrane
T24	Stillborn	Maine	M	Large ASD with minimal membrane
P31	Stillborn	Maine	M	Large VSD with double aorta arising from the RV
W32	Stillborn	Maine	M	None
H33	Stillborn	Chi	M	None
R34	Stillborn	Maine	F	None
P35	Stillborn	Maine X	F	None
P36	Stillborn	Maine X	F	None
T37	Stillborn	Maine X	F	None
K41	Stillborn	Maine	F	None
J42	Stillborn	Maine X	M	None
K43	Stillborn	Maine	F	None
P46	Stillborn	Maine X	F	None
S29	Stillborn	Maine X	M	None
B27	1 day	Maine X	M	Large ASD (24 mm opening) with small, flat membrane covering less than one-half of defect opening
W47	1 day	Maine	M	None
Q25	2 days	Maine X	M	Large ASD (16 mm opening) with minimal membrane
C38	3 days	Maine	M	None
A28	4 days	Shorthorn	M	Large ASD (17 mm opening) with minimal membrane and minimal attachment
F44	7 days	Maine X	F	None
P45	7 days	Maine X	F	None
P30	7 days	Angus	M	None
M39	7 days	Maine	M	Bacterial endocarditis; vegetative lesions on MV and AV
K22	70 days	Maine	F	Large VSD (35 mm opening); large ASD (24 mm opening); common RV and LV outflow tract; cardiac hypertrophy RV>LV
F40	18 mo	Maine	F	Large ASD (30 mm opening) with minimal membrane

ID = case identification; Maine = Maine-Anjou; Maine X = Maine cross. M = bull calf; F = heifer calf; ASD = atrial septal defect; VSD = ventricular septal defect; MV = mitral valve; AV = aortic valve; RV = right ventricle; LV = left ventricle.

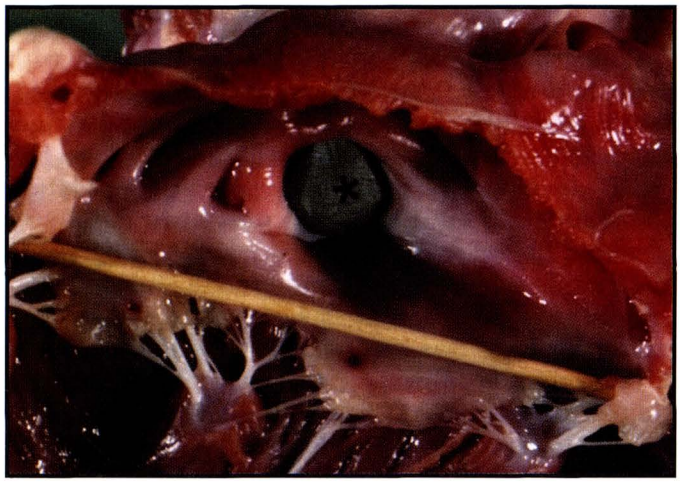

Figure 2. Photograph of atrial septum taken from the left side in a calf with a membrane defect (denoted by the green clay; * indicates the site of the defect).

breeding between half-siblings (W47) is eliminated, the average for the normal hearts is 2.91%, which is still not less than the coefficient of inbreeding for calves whose hearts had ASD. With the possible exception of W47 (which had a normal heart), the coefficient of inbreeding in all purebred animals reported here does not appear to be in the range considered to be problematic.[18] Additional studies on purebred animals could help to clarify the role of inbreeding in ASD in the Maine-Anjou breed.

Discussion

The incidence of atrial septal defects in bovine hearts has been described as both "rare"[12] and "common".[11] This confusion is due not only to small and relatively few studies, but also to the lack of complete description of what constitutes an ASD. A patent fora-

Table 3. Summary of data from beef calves with normal hearts.

ID	Age	Sex	BW, lb (kg)	Heart wt, g	ASD opening, mm	LV, mm	RV, mm	IVS, mm	Heart wt /BW (kg) ratio x 100
W32	Stillborn	M	120 (54.5)	360	10	19	12	18	.66
H33	Stillborn	M	95 (43.2)	403	8	18	9	18	.93
R34	Stillborn	F	85 (38.6)	346	12	19	10	19	.90
P35	Stillborn	F	64 (29)	299	12	16	11	15	1.00
P36	Stillborn	F	56 (25.5)	337	12	16	11	16	1.30
T37	Stillborn	F	NA	348	15	13	12	16	NA
K41	Stillborn	F	100 (45.5)	NA	NA	NA	NA	NA	NA
J42	Stillborn	M	NA	286	18	14	10	18	NA
K43	Stillborn	F	100 (45.5)	416	22	18	18	20	.90
P46	Stillborn	F	120 (54.5)	502	15	16	12	23	.0092
S29	Stillborn	M	89 (40.5)	300	10	11	9	11	.74
K1	Stillborn	M	128 (58.2)	440	12	18	9	16	.76
W47	1 day	M	92 (41.8)	401	12	14	11	20	.96
C38	3 days	M	70 (31.8)	254	12	12	8	14	.80
F44	7 days	F	55 (25)	417	8	21	10	17	.0167
P45	7 days	F	80 (36.4)	322	scar	12	8	15	.89
P30	7 days	M	85 (38.6)	342	scar	22	9	19	.89
Mean			89.3	360.8	12.8*	16.2	10.6	17.2	.96
SD			22.5	64.9	3.9	3.3	2.4	2.8	.26

ID = case identification; RV = right ventricle; LV = left ventricle; IVS = interventricular septum. Data are expressed as mean +/- standard deviation. Comparisons made between normal hearts and hearts with ASD (Table 4). * indicates significant difference (< 0.05) in the size of the opening in the normal calves is significantly less than that of those with ASD.

men ovale, although a form of interatrial communication, should not be considered a "defect" and must be distinguished from a true ASD where septal tissue is deficient.[6] Our study concurs with this view from human medicine,[6] as well as the single case report of a Hereford calf.[1] In a newborn calf, an opening in the atrial septum is not a defect if it is completely covered with a membrane that prevents left to right blood flow. It appears that the defect is not only related to the size of the opening, but also the presence or absence of a membrane capable of fully covering it and preventing left to right flow of blood. An opening of 12 cm diameter completely covered by a membrane that prevents left to right blood flow is not a problem, whereas an opening of 12 cm diameter that is incompletely covered by a membrane, thus allowing left to right blood flow, is a problem and would be classified as an ASD.

In the normal bovine heart at birth, the membrane covering the opening in the atrial septum is thin, pink, translucent, redundant and attached approximately 75% around the circumference of the opening. After birth, the normal membrane is capable of preventing left to right blood flow. With age the normal membrane becomes more opaque, white in color and increasingly thick

Table 4. Summary of data from beef calves with atrial septal defect (ASD).

ID	Age	BW, lb (kg)	Heart wt, g	ASD opening, mm	PDA, mm	LV, mm	RV, mm	IVS, mm	Heart wt /BW (kg) ratio x 100
K0	Stillborn	98 (44.6)	NA	20	NA	NA	NA	NA	NA
K23	Stillborn	98 (44.6)	399	13	6	14	11	21	.89
T24	Stillborn	110 (50)	417	12	8	19	12	22	.83
B27	1 day	NA	340	24	10	12	10	15	NA
Q25	2 days	75 (34.1)	228	16	20	17	13	17	1
A28	4 days	91 (41.4)	467	17	6	18	9	24	1.3
Mean		94.4	370.2	17*	10	16	11	19.8	.96
SD		12.8	91.6	4.5	5.8	2.9	1.6	3.7	.13

ID = case identification; ASD = atrial septal defect; PDA = patent ductus arteriosus; RV = right ventricle; LV = left ventricle; IVS = interventricular septum. Data are expressed as mean +/- standard deviation. * indicates significant difference (< 0.05) in the size of the opening in the atrial septum between normal calves (Table 3) and those with ASD.

(because of increased fibrous tissue), and fuses completely with the atrial septum between seven and 14 days of age. In contrast, the abnormal membrane in calves with true ASD is similar in color and thickness to the normal "immature" membrane, but does not cover the opening in the septum, has minimal attachment and appears rudimentary. In addition, in the two older heifers with ASD, the membrane was pink, suggesting immaturity. This supports the idea that ASD of cattle is a primary abnormality of the membrane.

In stillborn calves with ASD, the cause of death cannot be related to abnormal shunting of blood, since the changes in fetal circulation require respiration. A possible explanation is that the abnormal development of the septum and membrane results in alteration of electrical conduction in the atria. Under these conditions, dystocia, hypoxia and acidosis could predispose the calf to fatal arrhythmia. Conduction abnormalities have been documented in both children and adults with ASD,[3,8,9] suggesting the defect could predispose to altered electrical activity. Birth weights for the Maine-Anjou calves born dead are greater than the breed average for bull calves,[2] further suggesting that dystocia could be involved in exacerbating the condition during birth.

Our finding of ASD in Maine-Anjou calves, coupled with the preponderance of Maine-Anjou calves with ASD in the database, suggested that ASD may be a problem in stillborn Maine-Anjou calves. The fact that ASD was found in Maine, Maine-Red Angus cross and Shorthorn calves, as well as Maine-Angus cross and Holstein-Friesian breeding age heifers, suggests that ASD is not restricted to the Maine-Anjou breed. However, if the defect is inherited, the gene frequency may be higher in the Maine-Anjou breed.

The database represents only those animals presented for necropsy, and some farms may utilize diagnostic laboratory services more often than other producers. As of 2001, there were 990,000 head of cattle in Michigan, including 297,000 dairy cows and 73,000 beef cows.[2] The Holstein-Friesian is by far the predominant breed in the state of Michigan and the database. There were five cases of ASD in the Holstein-Friesian, crossbred, breed unknown group. This group of cattle represented over 90% of the total cattle in our database search.

There were 12 Maine-Anjou animals in the database search (< 1% of total), and three of the 12 (25%) had ASD. Of all the other stillborn calves, only five had an ASD. In 1998, there were 54 producers with registered Maine-Anjou cattle in the state of Michigan. With an average herd size of 13, this represents less than 700 head. Considering the number of Maine-Anjou cattle in Michigan, there seems to be an overrepresentation of animals with ASD, especially when compared to the Holstein-Friesian breed. It appears that ASD may be a cattle problem with a predilection for the Maine-Anjou breed. The genetic relationship of Maine-Anjou cattle to both the Holstein-Friesian and Shorthorn breeds further suggests ASD could be a

Table 5. Pedigree information for calves with normal hearts (a) and hearts with ASD (b).
Each Maine-Anjou sire is listed with a code number, ie, MA1, etc. * next to the sire code indicates calf was a product of artificial insemination. All designations of breed percentage (purebred, three-quarter, one-half, etc.) refer to percentage of Maine-Anjou in the animal listed. Because of upgrading by the American Maine-Anjou Association, a three-quarter bull and a purebred cow can produce a purebred calf. Cattle above 87% are considered purebred. Coefficients of inbreeding were calculated for calves only if both parents were purebred and had seven-generation pedigrees.

Table 5a. Pedigree data for beef calves with normal hearts.

ID	Sire code	Sire breed	Dam breed	Calf breed	Coefficient of inbreeding, %
W32	MA7*	3/4 MA	Purebred	Purebred	-
H33	Chi	Chi	Chi	Chi	-
R34	MA8*	Purebred	Purebred	Purebred	1.46
P35	MA4	Purebred	Unregistered	1/2 MA	-
P36	MA4	Purebred	Unregistered	1/2 MA	-
T37	MA9	Purebred	Shorthorn	1/2 MA	-
K41	MA12*	Purebred	Purebred	Purebred	2.34
J42	MA6*	Purebred	Angus	1/2 MA	-
K43	MA1*	Purebred	Purebred	Purebred	7.91
P46	MA4	Purebred	Unregistered	1/2 MA	-
S29	MA6*	Purebred	1/2 MA	3/4 MA	-
K1	MA2*	Purebred	Purebred	Purebred	1.47
W47	MA13	Purebred	Purebred	Purebred	13.57
C38	MA9*	Purebred	Purebred	Purebred	1.37
F44	MAX	1/2 MA	Commercial	1/4 MA	-
P45	MA4	Purebred	Unregistered	1/2 MA	-
P30	Angus	Angus	Angus	Angus	-

Table 5b. Pedigree data for beef calves with atrial septal defect (ASD).

ID	Sire code	Sire breed	Dam breed	Calf breed	Coefficient of inbreeding, %
KO	MA1*	Purebred	Purebred	Purebred	2.61
K23	MA3*	Purebred	Purebred	Purebred	2.80
T24	MA4	Purebred	3/4 MA	Purebred	-
B27	Red Angus	Red Angus	1/2 MA, 1/4 SM, 1/4 HO	1/4 MA	-
Q25	MA5	Purebred	3/4 MA	Purebred	-
A28	Shorthorn	Shorthorn	Shorthorn	Shorthorn	-

breed-specific problem. However, this interpretation could also be related to selection of both the database sample and our sample.

ASDs have been traditionally viewed as being polygenic. However, recent evidence in humans questions that assumption and suggests either random occurrence or autosomal dominant mode of inheritance, with incomplete penetrance and variable expressivity.[4,9,16] We observed ASD in 25% of calves examined, and one-half of the male beef calves. However, ASD was also found in an 18-month-old Maine heifer, as well as a five-month-old Holstein-Friesian heifer. The finding of ASD in older cattle suggests a continuum; the clinical course of ASD may vary widely. The finding of ASD in both genders tends to rule out the sex-linked recessive mode of inheritance. The inheritance of ASD in Maine-Anjou cattle, if genetic, is unknown. However, important for breeders is the finding that, to date, no single bull currently used is seemingly responsible for this defect in the Maine-Anjou breed, and calves with ASD may not have a greater level of inbreeding than calves with normal hearts.

Unlike in humans, dogs and cats, cardiac disease is not considered a major problem in cattle. This may be because it truly is an uncommon and sporadic event, that even if found there is rarely an economically justi-

fiable treatment, or that we as veterinarians do not often look for cardiac disease in cattle. Ten of 27 hearts from beef cattle submitted for this study had cardiac defects, and we continue to obtain hearts from cattle that have a wide variety of interesting and unusual defects. These defects include single ventricle, coarctation of the aorta, transposition of the great vessels and ventricular septal defect. Because stillborn calves are not often necropsied, the true incidence of congenital cardiac defects in cattle is unknown.

ASDs are common in humans, reported to represent 5-10% of all cardiac defects. They occur singly or with other cardiac defects, and 50% occur with PDA.[5,19] The true incidence of ASD in cattle is unknown. Descriptions of cardiac anomalies in cattle are usually case reports or small studies.[1,7,15] In one relatively large study, Kemler and Martin reported seven cardiac defects among 977 bovine fetuses necropsied.[10] Four ASDs were described: three female fetuses had ostium secundum defects and one male had a complete absence of the atrial septum; thus, 0.4% of fetuses had an ASD, accounting for over half the cardiac defects reported. Priester reported congenital defects in 533 of 16,850 bovines examined, with 20 of 533 cases (4%) having congenital cardiac defects.[14] Gopal *et al*[7] reported 78 cardiac defects from 36 bovine hearts. Hearts were obtained from a long-term study of congenital defects in cattle (n=21) and a perinatal mortality study (n=15). Age of calves was not reported. Two ASDs were reported in conjunction with other cardiac anomalies. Despite the statement by the authors that "patent foramen ovale, an atrial septal defect (ostium secundum type) is common in calves", ASD alone (without other cardiac defects) was not reported in this study. Sandusky and Smith reported only one ASD in seven cases of congenital cardiac defects in a six-month study of approximately 1,000 bovine necropsies,[15] supporting the notion that ASDs are not common in cattle. These studies suggest either a low incidence of congenital ASD, under-reporting of the defect, lack of consistent definition, or perhaps a breed predilection. Just as some congenital cardiac defects are more common in some breeds of dogs,[17] it is plausible that congenital cardiac defects may have a certain predisposition for some breeds of cattle.

Conclusions

Atrial septal defect in cattle appears to be related to abnormal development of the membrane that covers the opening in the atrial septum. The defect has wide-ranging clinical presentation, that can vary from no apparent abnormality to sudden death. In stillborn calves with ASD, we suspect cardiac electrical instability, exacerbated by anoxia and acidosis associated with dystocia, results in fatal arrhythmias. The mode of inheritance has not been determined, but with both genders affected it does not appear to be sex-linked recessive. In addition, no single, currently used sire was implicated in the defect, and coefficients of inbreeding were not greater in calves with ASD when compared to those with normal hearts.

It may be prudent for veterinarians to consider ASD and other congenital cardiac defects in stillborn calves, those that are unthrifty, or do not respond to the usual treatments. It may also be prudent for breeders of Maine-Anjou cattle to consider ASD in stillborn calves, and if documented cull the cow or avoid future mating to the same bull. Although breeding trials could elucidate the inheritance of the defect, time commitment and expense make it unlikely to occur.

Addendum

On February 15, 2005 a 100 lb (45 kg) heifer calf sired by a registered Shorthorn bull out of a Chianina heifer was alive on presentation and died immediately after birth. Necropsy revealed an ASD with a rudimentary membrane.

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Abstracts

Postpartum Manual Examination of the Vagina Does Not Cause Uterine Bacterial Contamination in Cattle

Sheldon I.M., Noakes D.E., Rycroft A.N., Dobson H.
Cattle Practice (2004) 11(2):65-68

Manual examination of the vagina is used to diagnose postpartum endometritis in cattle. The present study examined the risk that vaginal examination of cattle could cause uterine bacterial contamination or inflammation. On day 21 postpartum, the vagina of cows were examined using a clean gloved hand (n=34) or were unexamined controls (n=26). Swabs were collected from the uterine body lumen of cattle on day 21 and 28 postpartum, and bacteria were identified by aerobic and anaerobic culture. Manual vaginal examination did not cause uterine bacterial contamination. Furthermore, vaginal examination did not provoke an acute phase protein response or affect uterine horn diameter. Thus, manual vaginal examination is a suitable technique for the diagnosis of endometritis in postpartum cattle.

Management of the Dairy Heifer

Dawson L.E.R., Carson A.F.
Cattle Practice (2004) 12(3):181-192

Nutritional and management regimens imposed during the rearing of dairy heifers can have a significant effect on subsequent lactational performance. The purpose of this paper is to review research undertaken at the Agricultural Research Institute of Northern Ireland and elsewhere on the effect of nutrition and management throughout all phases of the rearing process on fertility, production and health. Heifers reared to calve at 620 kg produced 11% more milk in their first lactation compared to those calving at 540 kg, lost more weight in early lactation and had longer calving intervals. In second and third lactations, live weight at first calving had no effect on milk yield. These effects, coupled with higher rearing costs associated with calving at heavier weights, indicate that it is more economic to rear heifers to calve at 540 kg. Diet offered during the rearing period has been shown to have smaller effects on subsequent performance, although the results reported indicate that grazed grass has beneficial effects on mammary development and incidence of lameness. Management of heifers throughout the rearing period is as important as nutrition and the effect of housing system, training of heifers to the parlour prior to calving and introduction of heifers into the main herd are also discussed.

BRIEF SUMMARY
(For full Prescribing Information, see package insert.)

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INDICATIONS: NUFLOR Injectable Solution is indicated for treatment of bovine respiratory disease (BRD) associated with *Mannheimia (Pasteurella) haemolytica, Pasteurella multocida,* and *Haemophilus somnus,* and for the treatment of bovine interdigital phlegmon (foot rot, acute interdigital necrobacillosis, infectious pododermatitis) associated with *Fusobacterium necrophorum* and *Bacteroides melaninogenicus.* Also, it is indicated for the control of respiratory disease in cattle at high risk of developing BRD associated with *Mannheimia (Pasteurella) haemolytica, Pasteurella multocida,* and *Haemophilus somnus.*

RESIDUE WARNINGS: Animals intended for human consumption must not be slaughtered within 28 days of the last intramuscular treatment. Animals intended for human consumption must not be slaughtered within 38 days of subcutaneous treatment. Do not use in female dairy cattle 20 months of age or older. Use of florfenicol in this class of cattle may cause milk residues. A withdrawal period has not been established in preruminating calves. Do not use in calves to be processed for veal.

WARNINGS: NOT FOR HUMAN USE. KEEP OUT OF REACH OF CHILDREN. This product contains materials that can be irritating to skin and eyes. Avoid direct contact with skin, eyes, and clothing. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. Consult a physician if irritation persists. Accidental injection of this product may cause local irritation. Consult a physician immediately. The Material Safety Data Sheet (MSDS) contains more detailed occupational safety information.

For customer service, adverse effects reporting, and/or a copy of the MSDS, call 1-800-211-3573.

CAUTION: Not for use in cattle of breeding age. The effects of florfenicol on bovine reproductive performance, pregnancy, and lactation have not been determined. Intramuscular injection may result in local tissue reaction that persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.

ADVERSE EFFECTS: Inappetence, decreased water consumption, or diarrhea may occur transiently following treatment.

DOSAGE AND ADMINISTRATION: For treatment of bovine respiratory disease (BRD) and bovine interdigital phlegmon (foot rot): NUFLOR Injectable Solution should be administered by intramuscular injection to cattle at a dose rate of 20 mg/kg body weight (3 mL/100 lbs). A second dose should be administered 48 hours later. Alternatively, NUFLOR Injectable Solution can be administered by a single subcutaneous injection to cattle at a dose rate of 40 mg/kg body weight (6mL/100 lbs). Do not administer more than 10 mL at each site. **The injection should be given only in the neck.**

NOTE: Intramuscular injection may result in local tissue reaction that persists beyond 28 days. This may result in trim loss of edible tissue at slaughter. Tissue reaction at injection sites other than the neck is likely to be more severe.

For control of respiratory disease in cattle at high-risk of developing BRD: NUFLOR Injectable Solution should be administered by a single subcutaneous injection to cattle at a dose rate of 40 mg/kg body weight (6 mL/100 lbs). Do not administer more than 10 mL at each site. **The injection should be given only in the neck.**

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*As reported by independent diagnostic laboratories, data on file.

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