It’s been a long road from the widespread incidence of dwarfism in the 1950s to the eight carriers of dwarfism identified in 2002-2003. With each turn, the American Angus Association has learned more about the genetic defect, maybe most importantly how much of the terrain is still uncharted. New technologies available today offer potential for faster routes to the desired destination of eliminating genetic defects from the breed, but charting new routes requires caution.

Through research partially funded by the American Angus Association, James Reecy at Iowa State University (ISU) developed and honed a DNA test to identify the specific gene mutation responsible for six calves identified in 2002 as dwarfs. That patented test becomes available this winter.

To make best use of the test and to understand the rationale behind the Association’s rules concerning dwarfism and other genetic defects, it is important to understand the sequence of events that have led to their development. This article provides an overview of the Association’s experience with dwarfism, the development of its policy regarding dwarfism and the availability of the new test.

**The last time**

Keith Evans, former communications director for the American Angus Association, documents the Association’s early encounter with dwarfism in his book *A Historic Angus Journey: The American Angus Association 1883-2000.* In Chapter 22, titled “The Curse of Dwarfism,” he notes that while dwarfism was not a new phenomenon, the number of what were called “snorter dwarfs” became alarming in the early 1950s.

The ensuing panic and controversy nearly caused a split within the Association and between the Association and the publishers of *The Aberdeen-Angus Journal* as the Association took criticism for being too aggressive in trying to identify and eliminate those animals that carried the defect. Also hampering support for the elimination of dwarfism was the appeal of small, compact cattle. The industry-wide preference for this body type was at its peak in the mid- to late 1950s.

Initially, it was accepted as scientific fact that, like many other physical traits, dwarfism was caused by a single recessive gene inherited from both parents. An article by J.L. Lush and L.N. Hazel, scientists at what was then Iowa State College (now ISU), explained this concept in the April 1952 issue of *The Aberdeen-Angus Journal.*

But there were two dwarfism phenotypes observed among Angus cattle in the 1950s. Long-headed dwarfs had a more normal-appearing head with a dwarf-size body. “Snorter dwarfs” ranged from grossly deformed calves that were aborted or died soon after birth to animals that reached nearly normal size and lived to be several years old,” Evans writes. While a Virginia Agricultural Experiment Station research report noted that no one dwarf was likely to exhibit all of the characteristics associated with the snorter dwarf, most had “bulging foreheads, short and wide muzzles, protruding lower jaws, and prominent eyes.”

The fact that some dwarf calves were not identified until after weaning initiated the sequence of events that led to dwarfism being identified in 2002 as the “tablature for charting new routes requires caution.”

**Testing free of genetic defects — the important first steps**

Genetic abnormalities — often called defects — appear in all species, including all breeds of cattle. It is the responsibility of any member who becomes aware of an unusual physical abnormality in an Angus animal to notify the American Angus Association of that finding. The Association Genetic Defects Policy is explained in Rule 300 (see page 76).

There are two classifications of genetic defects recognized by the Association. Class I defects are viewed as lethal, seriously disabling or capable of negatively affecting reproductive performance. Class II defects, while not necessarily fatal or known to affect the reproduction, growth or beef producing ability of an animal, result in abnormal characteristics that are deemed economically undesirable. See Fig. 1 on page 33 of the 2007 Breeder’s Reference Guide for a brief description of each.

**Testing free**

While animals with defects cannot be registered, it may be of importance to a breeder to have other animals tested if they share a common pedigree of a known carrier of a genetic defect. When the appropriate testing procedure is followed and the test results confirm the animal is free (.99 probability level) of any or all defects specified in testing, the animal will be recognized as reported free.

There are designated protocols for members to follow when testing for genetic defects. Some of the important first steps required in the testing process are in common regardless of the defect(s) being tested. These points are highlighted.

► Bull owner(s) must apply to the Association for recognition of test on an official form prior to the beginning of the test.

► The applicant must identify females used in the test by tattoo or other permanent identification (ID) mark and, if registered, each female’s registration number must be reported.

► The Association may require periodic reports of breeding dates until all females used in the test are considered safe in calf. From the confirmed breeding dates, the Association will require periodic calving status reports.

► Bull owner(s) will be required to maintain accurate records. Aborted fetuses or deaths during or following normal gestation period shall be promptly recorded. Cause of abortions or death losses shall be confirmed in writing by a veterinarian.

► Before calves reach 6 months of age, representatives from the Association will inspect the calves for defect characteristics which are considered harmful or undesirable. The cost of all inspection trip(s) will be borne by the applicant.

► Bull owner(s) must submit a letter to the Association confirming the accuracy and general results of the test.

► A complete or random DNA-marker-typing of females and offspring will be made by the Association with bull owner(s) paying costs involved. An Association representative must be present when DNA samples are taken. Expense of the representative will be borne by the applicant. The Association will issue a letter to the bull owner(s) confirming successful completion of the test.

To start an Association-approved test, contact Member Services to review procedures and obtain appropriate forms for the testing desired.

*CONTINUED ON PAGE 76*
Dwarfism Test Available

Tests involving reactions to insulin injections and X-rays of the vertebral structure were investigated and dismissed. Toward the end of 1957 Nelson reported that “there are no simple, accurate tests to identify dwarf carriers and that there might never be,” Evans records. In its final report to the Association, Nov. 30, 1958, the research committee recommended the Association do six things:

- Compile a file of dwarfism contacts and encourage producers to voluntarily provide information [to the Association] on cows and bulls that had produced dwarf calves.
- Prepare a pamphlet on dwarfism to be mailed to all members.
- Consult with breeders individually on the cause of dwarfism and how to combat it.
- Get permission from owners of dwarf carriers to use the information to benefit all breeders and the breed in general.
- Encourage progeny testing of bulls, which would allow breeders to “clean up and use lines [of breeding] now carrying dwarfism and develop procedures to officially recognize cattle that completed the test and were found to not be dwarf carriers.”
- Encourage further research on dwarfism with grants-in-aid.

Rather than progeny-test, most herds just avoided using lines of cattle known to carry dwarfism, Evans explains. “Dwarfism died out relatively fast. Only five registered Angus bulls born after 1964 were proven dwarf carriers, according to Association records, and they were used very little. The last bull reported to have sired a dwarf calf was born in 1977.”

The breed’s success in stamping out dwarfism during its early experience with discussion among nonscientists that something other than genetics could cause dwarfism, Evans explains. In 1957, The Aberdeen-Angus Journal published an article by an Iowa producer linking dwarfism to nutrition and disputing the scientific evidence. Board Members conducting their first meeting in the Saint Joseph, Mo., headquarters in June 1956, received a letter from “A Committee of Angus Breeders” requesting the Association stop doing research on dwarfism and stop collecting pedigrees of dwarfism carriers. But the Board continued its efforts and in 1956 appointed a research committee to find a practical way to identify dwarfism carriers. That committee consisted of R.H. Nelson, Michigan State University; L.E. Johnson, ISU; and Glenn Bratcher, Oklahoma A&M University; along with Lyle Springer, who served as staff coordinator.

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The 300 series

The 300 series of the American Angus Association Rules pertain to genetic defects.

Rule 300: Genetic Defects: Policy and Related Rules
Rule 300: Genetic Defects: Policy and Related Rules
Rule 301: Notification to the Association
Rule 302: Cooperation with Association
Rule 303: Genetic Determination Process
Rule 304: Notice to the Owner Member(s)
Rule 305: Right to Contest the Determination
Rule 306: Hearing
Rule 307: Publication of Genetic Defect to the Membership

Abnormalities and genetic defects. Abnormalities are present in all species, including all breeds of cattle. Some abnormalities are physical and some are functional. Abnormalities are frequently referred to as defects. Defects can be caused by a number of factors. Some are genetic in origin and some are environmental, caused by such factors as nutrition or sickness. The policy and the rules that follow relate to those abnormalities that are determined to be genetic defects.

There are two classifications of genetic defects recognized by the Association: Class I defects, which are viewed as lethal, seriously disabling or capable of negatively affecting reproductive performance, and Class II defects, which, while not necessarily fatal or known to affect the reproduction, growth or beef producing ability of an animal, result in abnormal characteristics that are deemed economically undesirable. The Association recognizes the following as Class I genetic defects:

- Dwarfism
- Osteopetrosis (Marble Bone Disease)
- Double Muscling
- Syndactyly (Mule Foot)

Additionally, the Association recognizes Heterochromia Irides (White Eye) as a Class II genetic defect. The Association does not allow registration of animals determined to have any of these genetic defects. A brief description of the symptoms common to these defects is found in the Definition section of these rules.

Genetic factors. The term “genetic factor” refers to the presence of a recessive gene that may or may not produce a certain type of offspring. The Association monitors two genetic factors: the Red Color factor and the Wild Type Color Gene factor. Both are monitored because they may, if present, result in the unintended birth of red calves. While red calves are not eligible for registration under the rules of the Association, they are not defective genetically. The Association permits the registration of animals with either of these factors but it places the designation “R” or “WT” following the animal’s registration number. Additionally, such animals are listed in the annual edition of the Breeder’s Reference Guide and on the Association’s Web site.

Commercial tests are available to determine whether an animal carries one of these genetic factors. For further information, please contact the office of the Director of Member Services.

Policy Overview. This policy is designed to protect and to promote the best interests of the breed and the membership. It has always been and remains the responsibility of every member to make a written report to the Association concerning any unusual abnormality so identified in an animal. The Association shall, in turn, oversee a process by which a scientific determination can be made whether the abnormality is genetic in nature. If a genetic defect determination is reached, the Association shall promptly notify the owner of the impacted animal. Following a brief period of time for the owner to contest such a determination, the animal’s identity shall be published to the membership, in the Angus Journal, on the Association Web site and in the annual spring edition of the Breeder’s Reference Guide.

Future progeny of animals determined to be carriers of genetic defects or the horn gene are not eligible for registration unless owner members of the affected cow or bull are tested in an Association-approved test that can be supervised by the Association. In the event that such progeny are determined to be free of the genetic defect or specific gene in issue, they will be registered. Registration certificates for such progeny will record that the affected animal tested free of a particular defect or gene.
the defect was fostered by the free flow of information encouraged by the Association.

**A policy for handling defects**

The Association developed and adopted a new way of reporting and handling genetic defects in the 1970s. Open artificial insemination (AI) was approved in 1972, allowing broader use of individual bulls and creating concern that this might foster a reoccurrence of dwarfism. Considering this, along with the appearance of osteopetrosis (marble bone disease) as a new genetic defect; and the increasing frequency of red coat color, the Association consulted Keith Huston for guidance in developing a strategy for handling genetic defects, Evans reports.

The Kansas State University (K-State) geneticist recommended “a program of observation, reporting and monitoring,” with both the Association and individual breeders watching for potential genetic problems, Evans documents. Huston recommended breeders report problem calves to the Association, with the Association reporting discoveries of any documented genetic disease found to the industry and making the list of confirmed genetic defect carriers available to Angus breeders.

The Association adopted a policy incorporating Huston’s recommendations in June 1972 and announced the breed would monitor four genetic defects — dwarfism, osteopetrosis, double muscling and red hair color (later classified as a genetic factor). Syndactyly, or mule foot, was added to the list of genetic defects in 1976.

Under the rules, when a breeder applied for an AI service certificate, he was required to certify on the application that the bull was not transmitting any of these four defects. Further, the breeder had to agree that if the bull was ever confirmed to sire animals with these defects, the information would be printed on all AI service certificates issued for the bull.

A report form was developed, and breeders who had a suspect calf were asked to report it to the Association so the Association could launch an investigation. The papers on bulls confirmed to have siredd calves with genetic defects were filed in a special file, which any breeder could access.

**Not all defects genetic**

In a July 1976 article in the *Angus Bulletin*, Horst Leipold cautioned breeders that not all congenital defects were genetic. Most, he said, were the result of nutritional or infectious disease. Leipold, who was professor of...
Dwarfism Test Available (CONTINUED FROM PAGE 77)

pathology and head of the K-State Laboratory for Hereditary Diseases, said the only way to be sure of the cause was proper diagnosis by a veterinarian or the K-State laboratory. He also explained how producers could use sire-daughter matings, and matings to known carrier cows to determine a bull a carrier or free of a recessive genetic defect.

Leipold replaced Huston as the Association’s resident expert on genetic defects and strengthened its genetic defect policy and procedures. In 1977 the Association’s “Suggested Terms and Conditions for Sale of Registered Angus Cattle” were modified, replacing the “dwarfism guarantee” with a “genetic defect guarantee” (see “Under the terms,” page 79). Producers were required to disclose in advertising if a bull was a confirmed carrier of a genetic defect.

The following year, the Association agreed to help defray the cost of shipping a suspect calf to the K-State laboratory for testing, Evans says. And the Association produced and distributed a slide show on genetic defects, their mode of inheritance and their control.

Airing the Laundry

In June 1978 the Board voted to print the complete list of bulls with known genetic defects in the Angus Bulletin, with the first list published in July 1978. That list continues to be published twice a year in the Angus Journal. In the Breeder’s Reference Guide it is accompanied by the form for reporting guidelines, the first steps to proving an animal free of genetic defects (see “Testing free of genetic defects,” page 75), and the rules governing Association policy on genetic defects (see “The 300 series,” page 76).

In October 1978, the Board approved a motion to print genetic defect information — whether a known carrier or tested free — on registration certificates. The Board also established the rule, effective with calves conceived after Jan. 31, 1979, “that members could not register calves sired by a bull they did not own if that bull was confirmed to carry dwarfism, osteopetrosis, syndactyly or double muscling,” Evans documents. Currently, calves sired by a known carrier are not eligible for registration unless they are tested free of the defect.

Along with 16 documented carriers of dwarfism, the 2007 Breeder’s Reference Guide lists 21 Angus sires “tested free of dwarfism (FD)” and another 12 sires “tested free of all defects (GDF).”

A new chapter

After nearly 25 years of monitoring, the Association received a report from a member April 12, 2002, of two calves purchased as embryos that were suspected to be dwarfs. Following protocol, Member Services Director Bryce Schumann encouraged the breeder to provide the Association a written statement along with pedigree information and to send the calves to David Steffen, director of the University of Nebraska Veterinary Diagnostic Center so the Association could begin an investigation into the case. Recognized as a leading authority in bovine congenital birth defects, Steffen is the Board-designated authority the Association consults for technical advice in such matters.

Schumann contacted the original owner of the embryos, who agreed to cooperate in investigating the matter and revealed that four other calves were being examined at Washington State University.

Steffen confirmed that the calves from the original ranch fit the phenotypic characteristics of dwarfism. The next step was parentage verification, a process that ultimately required considerable time and effort.

On Nov. 5, after nearly seven months of investigation, the original owner of the embryos was notified by overnight service of the documented results of the genetic defect investigation and was informed the first bull and cow would be listed as carriers of dwarfism. The other owners of these two animals and the bull stud leasing the bull were notified Nov. 8.

In three successive issues of the Angus Journal (December 2002, January 2003 and February 2003), the Association identified the three sires and five dams that had produced the six calves determined to be dwarfs. Those eight animals were added as carriers of dwarfism to the “Genetic Defects and Factors” listing published in the Breeder’s Reference Guide.

In a memo posted to the Association web site, the Association explained that the 845 progeny and grand progeny of the eight animals were permitted to remain in the registry; however, all prospective three-generation pedigrees related to the animals identify the specific carriers by the special “D” designation (denoting a carrier of dwarfism) behind the registration number. Future progeny of the eight identified dwarfism carriers were to be ineligible for registration with two exceptions:

(1) calves conceived by AI to a non-owned sire within 60 days of the date the bull’s identity was initially published in the Angus Journal; and

(2) animals that have been successfully progeny-tested under specific guidelines and tests approved by the Association.

A new test: Round 1

Prompted by these six dwarf calves, in late 2002 ISU proposed the Association partially fund a project, using DNA, to identify microsatellite markers that could indicate whether a descendent of a known carrier was also a carrier of that gene. ISU informed the Association that molecular markers were available for genotyping both Japanese Brown and Dexter cattle for certain strains of dwarfism discovered in those breeds.

Based on the possibility of recognizing an alternative test as reliable, but potentially less time-consuming than progeny testing, the Board voted to partially fund the ISU proposal. Working in cooperation with ISU, the Association provided relevant pedigree information and facilitated the collection of DNA samples from 26 animals in the affected pedigree.

In late February 2004, James Reecy, assistant professor in the Department of Animal Science at ISU, made a presentation to a committee of the Association’s Board of Directors regarding the status of the dwarfism study. In his report, Reecy presented the preliminary, nonvalidated and nonpeer-reviewed results of the research project.

He reported that ISU had performed a whole-genome scan in order to identify markers associated with the strain of dwarfism in the questioned pedigree. Statistical analysis was performed to predict the probability that a given animal in the pedigree was or wasn’t a carrier. The result produced a wide range of statistical probabilities, measured in percentages, that ranged from a low of 1% to a high of 99%.

In March 2004, the Association asked ISU to further clarify what exactly had been done and what remained to be done with the study. With that information received from ISU, the Association next sought and obtained the university’s permission to have an independent expert evaluate the study, the science it utilized and what the Association believed to be the clear limitations of the study.

Upon the conclusion of the independent review, the Association deemed that the test’s benefits were outweighed by its limitations, namely:

► The ISU test was pedigree-specific. It was determined that the marker test had no applicability to Angus cattle outside the affected pedigree. Viewed in terms of registration numbers, the pedigree
of the eight identified carriers at issue numbered 388 registered progeny and 457 registered grand progeny, contrasted to the 2,791,450 animals that, at that time, had been registered by the Association since 1993, the year the oldest of the eight animals was registered.

- The study was limited to a particular strain of dwarfism that had been identified from the eight animals designated as carriers.
- The test was not designed to test for a specific gene. The causal mutation for this strain of dwarfism had not been identified.
- The test for this specific pedigree did not provide the degree of reliability and certainty attainable by using the "progeny test" approved by the Association.

Though this time taking criticism for not being aggressive enough, for the reasons noted above the Board of Directors voted unanimously at its June 2004 meeting not to approve or endorse the ISU DNA marker process as an alternative to progeny testing as a means to determine whether progeny in this pedigree could become eligible for registration.

In January 2004, Bishnu Mishra of ISU presented a poster authored with Julie Cavanagh of the University of Sydney and Reecy at the Plant & Animal Genomes XII Conference in San Diego, Calif., that reported the mutation in the Angus line was not the same as the known mutations causing dwarfism in Japanese Brown and Australian Dexter cattle. According to the abstract, "this does not preclude the possibility that novel mutations may have arisen in American Angus cattle."

A New Test: Round 2

Two years after the first test was presented, and after conducting additional fine-mapping, Reecy came back to the Board with further research indicating a mutation in the PRKG2 gene as the likely mutation that caused the dwarfism in the Angus calves and a DNA test that could be conducted to determine whether an animal was a carrier of the mutation.

In February 2006, following confirmation by an independent reviewer, the Board determined it was satisfied the test could determine if Angus cattle are carriers of this particular strain of dwarfism and announced it would enter into discussions with the ISU Research Foundation (ISURF) to negotiate an exclusive license to market the test.

The final licensing agreement with ISURF was reviewed at the June 2007 Board Meeting, with discussion pertaining to the rules on genetic defects, as well as how to offer the DNA test to the industry.

At the September 2007 Board Meeting, the Board reviewed the testing procedures and set a test price of $75, which includes parentage results. It also discussed differences in identifying carriers of dwarfism in the past with identifying carriers of dwarfism with the new test, namely:

a) In the past, any animal listed as being a carrier of dwarfism had in fact produced progeny documented to be genetic dwarfs. The new test would allow the identification of animals carrying the PRKG2 mutation that have not yet produced progeny with the genetic defect.

b) It is unclear whether all animals previously listed carried the PRKG2 mutation. The Association cannot rule out the possibility that other gene mutations could also cause dwarfism in cattle.

Recognizing those significant differences, the Board adopted a policy that animals DNA-tested and found to be carriers of this gene mutation would be designated with a D2, determined a carrier of dwarfism by DNA test. Those found to be free of this gene mutation would be designated FD2, denoting they have been found free of this form of dwarfism.

In early January, the Association was finalizing a contract with MMI Genomics to offer the test to cattlemen in hopes the test would be available by publication of this article in the February issue of the Angus Journal.

For information on how to submit a potential genetic defect, see "Submitting a Potential Defect" on page 80. For information about the test available through MMI, contact Bryce Schumann, director of member services at the Association, at 816-383-5100 or bschumann@angus.org.

Under the terms

The "Suggested Sale Terms and Conditions" put forth by the American Angus Association contains the following section pertaining to genetic defects.

Genetic defect guarantee

1. All animals are guaranteed by the seller not to produce a calf with the following defects for a period of two years after the date of sale: Dwarfism, Osteopetrosis (marble-bone disease), Double Muscling, Syndactyly (mule foot) and Heterochromia Irides (white eye).

2. The buyer must notify the seller in writing immediately upon the birth of a calf suspected of being defective or immediately after determination is made that such calf is defective.

3. The seller at his expense will be permitted, and provided with reasonable opportunity, to obtain DNA material of an alleged defective calf and its sire and dam for the purpose of DNA-marker analysis to establish parentage.

4. The animals will be returned by the buyer to the seller at the buyer’s expense (unless prohibited by the health requirements of the seller’s state). The buyer will pay transportation expenses immediately after determination is made.

5. The return of the purchase price in connection with a defect-producing animal will be deemed full satisfaction and settlement.

6. The buyer and seller agree to fully and promptly comply with all rules of the American Angus Association relating to genetic defects.

7. If there is a dispute as to whether a calf is defective, the American Angus Association will make the final determination.

8. Registration certificates issued after Jan. 30, 1979, for animals that, prior to issuance of the certificate, had been reported and verified as carriers of recessive genetic defects or genetic factor or had tested free of certain genetic defects or genetic factors contain the following codes relative to such defect.

\[
\begin{array}{ll}
S & — Syndactyly \\
H & — Double muscling \\
D & — Dwarfism \\
M & — Osteopetrosis \\
HI & — Heterochromia Irides \\
HG & — Horn gene \\
R & — Red \\
X & — Multiple defects, check list for kind \\
F & — Tested for defect printed without producing abnormal calves \\
GDF & — Produced 35 or more calves from daughters without a genetic defect or genetic factor \\
WT & — Wild Type Color Gene
\end{array}
\]

The absence of any such notation on a pedigree of an animal, in a sale book, does not establish that the animal in question is not a carrier of any such genetic defect or genetic factor.

*For voluntary consideration and use by sellers in their independent business judgment.

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