HYDROCEPHALUS, A LETHAL IN CATTLE

By C. L. Cole, research associate in animal husbandry, and L. A. Moore, formerly research assistant in dairy husbandry, Michigan Agricultural Experiment Station

INTRODUCTION

Hydrocephalus has been reported as an inherited lethal in swine (1) and mice (2, 4). Many sporadic cases have been reported in man, cattle, chickens, dogs, and rats. There are two types variously reported: (1) Internal hydrocephalus, a collection of fluid in the cerebral ventricles, and (2) external hydrocephalus, a collection of fluid outside the brain substance.

Houck (7) reported two cases of congenital hydrocephalus, one a grade Durham calf and the other an albino rat. The condition was not lethal in either instance. In the rat, however, blindness was associated with hydrocephalus and the animal eventually died from starvation.

Clark (2) has noted hereditary hydrocephalus in the house mouse which appeared in the F2 and backcross generations of mice with the flexed-tail character. It was apparently due to a single Mendelian factor, the homozygous recessive being lethal. Frequent association with the flexed-tail character suggested linkage or another manifestation of the gene for flexed (2). Later work (3) showed that hydrocephalus was not caused by the same gene as flexed tail. Still further experiments (4) showed no linkage between hydrocephalus and various other characters, including flexed tail.

Blunn and Hughes (1) have recorded a lethal hydrocephalus of the external type in Duroc-Jersey swine, the fluid being found outside the brain in the subarachnoid spaces. Varying degrees of hydrocephalus occurred, but a short tail or no tail always accompanied the defect regardless of its degree. Light coat color also accompanied the defect in all except 3 cases. All the affected pigs were the result of inbred matings. Twenty litters from heterozygous parents produced 178 animals, of which 42 were hydrocéphale and 136 normal. It was suggested that the three associated characters might be the manifold effects of one factor, or they might be caused by very closely linked genes. The goodness of fit between the observed and expected 3 : 1 ratio (χ²=0.187. P=between 0.5 and 0.7) indicates that the hydrocephalus syndrome was caused by a single recessive autosomal gene.

Hyde (8) observed an epidemic of hydrocephalus in experimental rabbits, but was unable to offer any rational explanation for its occurrence or disappearance.

Ely, Hull, and Morrison (6) reported one case of slight hydrocephalus among four cases of agnathia in Jersey calves.

Morrill (10) observed that hydrocephalus occurs in certain breeds of dogs, notably in the German boxer, and he recorded occasional

1 Received for publication February 5, 1942.
2 Italic numbers in parentheses refer to Literature Cited, p. 490.
observations in single individuals of other breeds. He studied several purebreds and various crosses. Among the purebreds, the British bull showed marked external hydrocephalus in four out of five cases examined; one case was practically normal. Among hybrids, the condition was most often seen in the great Dane × St. Bernard crosses, but in varying degrees.

Schlotthauer (11) noted five random cases of internal hydrocephalus in dogs. In only one case was there any evidence that the condition was hereditary.

Eaton (5) summarized 15 known lethals in cattle. None of these corresponds in any way with the lethal reported here.

**EXPERIMENTAL RESULTS AND OBSERVATIONS**

The lethal to be described was discovered in a herd of grade and purebred Holstein-Friesian cattle. Purebred bulls had been used for several generations, but insofar as could be determined, no inbreeding had been practiced before 1938. Early in 1940 the owner interviewed one of the authors relative to a possible nutritional deficiency in his herd. In December 1939, an abnormal calf had been born but no particular significance was attached to the occurrence. However, when another calf with the same abnormalities was born in January 1940, the owner became worried about his ration. A careful check revealed that the herd had been fed legume roughage, mainly alfalfa hay with some sweetclover, and a grain mixture composed of corn and cob meal, oats, and soybean oil meal. The cattle were given free access to a mixture of 1 part bonemeal and 2 parts salt during the winter months, and salt alone during the pasture season. There seemed to be no reason for suspecting a nutritional deficiency and the two cases suggested something other than chance. A check on the breeding program revealed that the two heifers that had given birth to the abnormal calves had been mated to their sire. Previous to these two abnormalities, no unusual calves had been born except that in June 1939 a calf from a similar mating had shown a highly nervous condition, and was unable to stand alone. No improvement of this condition was observed and the calf was later vealed. In December 1939 and January 1940 two calves were born from sire-daughter matings, involving 15 daughters. The breeding program in this herd suggested an inherited condition and so arrangement was made with the owner whereby an additional number of sire-daughter matings would be made. Twenty-seven calves were produced as a result of sire-daughter matings, involving 15 daughters. The results of these matings are given in table 1.

<table>
<thead>
<tr>
<th>Cow No.</th>
<th>Date of calving</th>
<th>Condition of calf</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dec. 30, 1940.</td>
<td>do.</td>
<td>Do.</td>
</tr>
<tr>
<td></td>
<td>June 1, 1939.</td>
<td>Jumpy.</td>
<td>Female.</td>
</tr>
<tr>
<td></td>
<td>Apr. 21, 1941.</td>
<td>do.</td>
<td>Male.</td>
</tr>
</tbody>
</table>

Table 1.—Date of calving, and condition and sex of calf from sire-daughter matings involving 15 daughters
The lethal was manifested by an internal hydrocephalus accompanied by a marked papilledema. The lateral ventricles were greatly distended so that only a thin layer of cerebral tissue remained between the cavity of the ventricles and the cranial bones. On dissection, no abnormalities were found which might suggest a lack of embryological development of the arachnoid villi, nor were there any apparent points of blockage in the various foramina so far as could be determined. As a result of the pressure developed, the cranial cavity of the skull was enlarged from two to three times the normal size, as shown in figures 1 and 2.

Ventrally the position and angle of the foramen magnum was markedly altered from that of a normal animal, as shown in figure 3. It is possible that this abnormality might partly or completely block the foramina of Magendie and Luschka, thereby causing the hydrocephalus as a secondary manifestation of a gene for bony abnormalities. Figure 3 shows also a marked widening of the space between the mandibles as compared to the normal.

Both the humeri and femurs of these animals showed marked malformation. The shaft of these bones was considerably shortened, but larger in diameter than the normal, as shown in figure 4.

The condyles and heads of both bones had the appearance of having had pressure applied against the articulating surfaces so that they were bent down toward the shaft and twisted to one side. Previous to dissection, the twisted condition of the femur resulted in extreme width through the hips, causing difficult parturition. The abnormal humerus also resulted in a twisted appearance of the forelegs (fig. 5).
Figure 1.—Frontal view of hydrocephalus calf, showing marked enlargement of the skull; note twisted condition of forelegs.
Figure 2.—Side view (A) and frontal view (B) of hydrocephalus skulls; B shows asymmetrical condition.

Figure 3.—View of skulls showing position of foramen magnum and also abnormal condition of mandibles: A, normal; B, lethal.
Figure 4.—Humerus and femur from an abnormal (A) and a normal calf (B).

Figure 5.—View of abnormal calf showing extreme width of hips and twisted forelegs.
The asymmetry of the skull and face was shown most distinctly in the living animal by a twisting of the face to one side. When the head was cleaned of surrounding tissues, asymmetry of the lower jaw and facial bones was quite apparent. In addition, the bony structures of the cranium were unequally developed and displaced to one side of the midline. In the specimen photographed in figure 2, which is typical of these individuals, the unequal development of the cranial bones is well shown, as is the twisted appearance of the face. In addition, the left mandible was considerably shorter than the right. This was also true for the maxillae.

The condition designated as "jumpy" was suggestive of cerebellar or thalamic dysfunction. Marked lack of muscular coordination and control was at all times evident. These calves were unable to rise or stand unaided. When placed on their feet, the weight was supported reasonably well for a short time at least. In this position, however, the animal tended to sway from side to side or backward and forward and unless supported was unable to remain standing. Tremor was present in both the upright and lying positions. In the lying position, in addition to the tremor, there was almost constant movement of the limbs. Resistance to flexion of the limbs was present irregularly.

Possibly the lethal trait, the asymmetry, and "jumpy" are due to three recessive autosomal genes.

A genetic analysis based on the above hypothesis may now be attempted. The three pairs of alleles would be as follows:

- \( L \) — normal
- \( A \) — symmetrical
- \( J \) — normal nervous reaction
- \( l \) — lethal
- \( a \) — asymmetrical
- \( j \) — "jumpy"

The sire should have the genotype \( LlAaJj \).

The daughters from normal dams would have eight different genotypes, as follows: \( LlAAJJ \), \( LLAAJj \), \( LLAaJJ \), \( LLAaJj \), \( LlAAJj \), \( LlAaJJ \), \( LlAaJj \), and \( LlAaJj \). These daughters backcrossed to their sire would then produce the following percentages of phenotypes in their offspring: \( LAJ \), 66.992; \( LAj \), 9.570; \( LaJ \), 9.570; \( lAJ \), 9.570; \( lAj \), 9.570; \( lAj \), 9.570; \( laJ \), 1.367; \( laj \), 1.367; \( Laj \), 1.367; and \( laj \), 0.195.

The expected and observed distribution of the 27 calves by phenotype would, therefore, be as shown in table 2. In this table \( LAJ \) and \( LAJ \) are combined as are also \( laJ \) and \( laj \). These combinations must be made because of the impossibility of observing the "jumpy" condition in the "l" calves which are born dead. The goodness of fit between the observed and expected values (\( \chi^2 = 2.92; P = between 0.7 and 0.8) suggests the action of three recessive nonlinked genes.

<table>
<thead>
<tr>
<th>Distribution</th>
<th>( LAJ )</th>
<th>( LAj )</th>
<th>( LaJ )</th>
<th>( lAJ—lA j )</th>
<th>( Laj )</th>
<th>( lAJ—laj )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expected</td>
<td>18.09</td>
<td>2.58</td>
<td>2.58</td>
<td>2.95</td>
<td>3.37</td>
<td>0.42</td>
</tr>
<tr>
<td>Observed</td>
<td>17.0</td>
<td>2.0</td>
<td>2.0</td>
<td>5.0</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>Difference</td>
<td>-1.09</td>
<td>-.58</td>
<td>-.58</td>
<td>+2.05</td>
<td>- .37</td>
<td>+.58</td>
</tr>
</tbody>
</table>

and \( LAj \) are combined as are also \( laJ \) and \( laj \). These combinations must be made because of the impossibility of observing the "jumpy" condition in the "l" calves which are born dead. The goodness of fit between the observed and expected values (\( \chi^2 = 2.92; P = between 0.7 and 0.8) suggests the action of three recessive nonlinked genes.
Breaking the trihybrid ratio down into three monohybrid ratios, the expected and observed values are as shown in table 3, which also shows the expected and observed incidence of the "jumpy" animals among the nonlethals.

**Table 3.** Expected and observed values for lethal-normal, asymmetrical-normal, and "jumpy"-normal animals

<table>
<thead>
<tr>
<th>Contrasted types</th>
<th>Ratio—</th>
<th>( x^2 )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Expected</td>
<td>Observed</td>
<td></td>
</tr>
<tr>
<td>Lethal-normal</td>
<td>3.38 : 23.62</td>
<td>6 : 24</td>
<td>2.32</td>
</tr>
<tr>
<td>Asymmetrical-normal</td>
<td>3.38 : 23.62</td>
<td>3 : 24</td>
<td>0.05</td>
</tr>
<tr>
<td>&quot;Jumpy&quot;-normal</td>
<td>2.63 : 18.37</td>
<td>2 : 19</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Although the chi-square test has been used, the numbers are smaller than are desirable for such an analysis.

CONCLUSIONS

A new lethal in cattle, internal hydrocephalus, is described and shown to be probably a simple recessive in its mode of inheritance.

Two other conditions, asymmetry and "jumpy," are described and may be recessive and not linked with each other or with the lethal gene.

The data suggest that the sire used carried three rare recessive genes. Nevertheless, the probability that any one animal would carry three rare factors is very small. However, the facts are stated and a conclusion indicated, though the mode of inheritance of the characters "jumpy" and asymmetry should be studied further.

LITERATURE CITED

(10) Morril, C. V.
1932. Internal hydrocephalus in pure-bred and hybrid dogs.

(11) Schlotthauer, C. F.
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