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Asymmetric Hindquarter Syndrome (AHQS) in Pigs

Even the most perfectly proportioned human being or animal is, at the anatomical level, asymmetrical. Even where there is an apparent bilateral symmetry of paired structures at birth a disproportion between the two sides often develops later. When a visible disparity in size of the hind limbs is present in children at birth it is referred to as congenital hemiatrophy or hemihypertrophy or, preferably, congenital asymmetry (Smithells 1965). Asymmetry in adult human leg muscle weights has been demonstrated by Chhibber & Singh (1970).

This paper is an account of a naturally occurring condition in the pig characterized by a variable asymmetry of the hindquarters in general and particularly of individual muscles of the posterior, outer and inner aspects of the thigh. Provisionally named the asymmetric hindquarter syndrome (AHQS), the condition does not interfere with locomotion under ordinary farm conditions but it can adversely affect carcase conformation and may seriously detract from the usefulness of carcase dissection studies as a basis for genetic selection.

Incidence

The condition was first identified in 3 herds in West Germany in 1966 and described as a 'protrahierte Atrophie der candelen Oberschenkelmuskulatur beim Schwein' (Bickhardt *et al.* 1967); and an additional case has been reported in Belgium (Hoorens & Oyaert 1970). In Britain cases occurred at least as early as 1965 but the condition was not recognized as such until one of us (J T D) had an opportunity to see some of the affected German pigs. Since then large outbreaks have been seen in two separate herds in southeast England and smaller numbers of cases have occurred sporadically in England, Wales and Scotland.

AHQS does not seem to be evenly distributed throughout the pig population; the great majority of cases have occurred within a small number of herds, and apparently within particular families within these herds. The condition has been seen in a number of cross-bred pigs, but the only pure breeds in which we have seen it are the Large White, Hampshire and Lacombe; the latter two breeds are numerically very small in Britain. Both females and intact and castrated males are affected; no unequivocal cases have been seen in adult boars, but they represent only a minute fraction of the pig population. In severe cases the condition can be recognized clinically by the time the pig reaches 40 kg live weight (about 12 weeks) and it is usually obvious by 80 kg (about 20 weeks). We have not seen muscular asymmetry in piglets at birth, but the relative size of the experimental error in dissection studies at this age would tend to obscure all but very large differences.

Characteristics of the Disease

Clinically one hind limb is seen to be smaller than the other, though the legs are apparently the same length and there is usually no abnormality of gait. The asymmetry presents mainly as an apparent reduction in size of the musculature of the posterior thigh in one leg, particularly the semitendinosus, semimembranosus and biceps femoris, and an asymmetric distribution of subcutaneous fat (Fig 1). An interesting feature of the disease is that within a particular herd a clear majority of the affected pigs show a similar asymmetry, i.e. most of the pigs with AHQS have the smaller leg on the same side; thus there tend to be left-sided or right-sided herds.

Dissection of the leg also demonstrates the asymmetry of muscle size and, to a lesser extent, of fat distribution and bone size also (Fig 2). For convenience we have used the expression $\frac{\text{weight of lighter muscle}}{\text{weight of heavier muscle}}\%$ as an index of muscle asymmetry and have arbitrarily regarded values of 90% or less in one or more muscles as diagnostic of AHQS. The number of muscles obviously affected and the extent of the disparity in

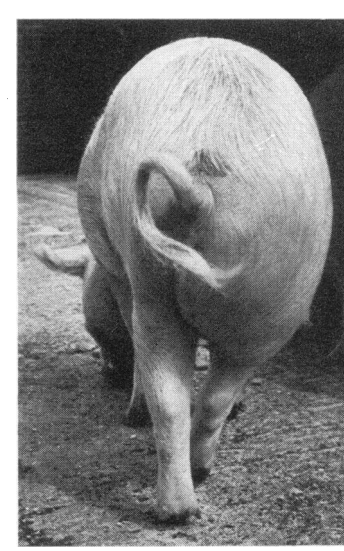

Fig 1 *Pig with AHQS showing marked hypoplasia of left thigh*

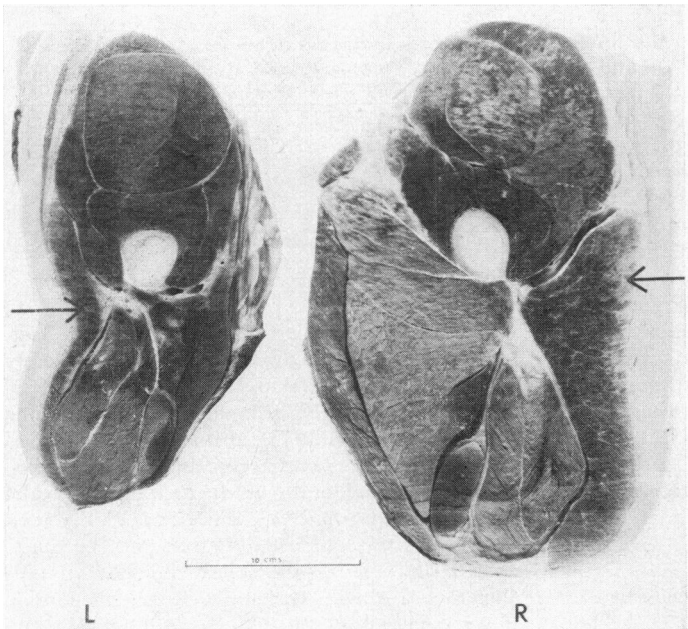

Fig 2 *Sections through the thighs of the same pig as Fig 1 at mid-femur level. The cross-sectional areas of the left biceps femoris is approximately one-quarter of the corresponding muscle on the right (arrows)*

size varies between pigs and tends to increase with age. As Fig 3 shows, the muscles most frequently and most severely affected are the semitendinosus, semimembranosus and biceps femoris, and values as low as 14% have been obtained for the semitendinosus muscle (43/300 g in a pig of 81.2 k live weight). Within a herd pigs may be found with the smaller muscles on either the left or the right side, but within individual pigs the asymmetry is never mixed, e.g. a small left semitendinosus and a small right semimembranosus. Comparison with normal bilaterally symmetrical pigs of the same age indicates that it is the smaller muscles of unequal pairs which are abnormal and suggests that the condition might be better regarded as a hemiatrophy than a hemihypertrophy.

The classical histological description of the condition by Bickhardt *et al.* (1967) records necrobiotic changes in the muscles on the smaller side with interstitial and perineural fibrosis, groups of small muscle fibres suggestive of denervation atrophy and accumulations of fat cells. These authors also demonstrated transiently elevated plasma creatine phosphokinase (CPK) and aldolase activity in two of their pigs, a finding not entirely consistent with the concept of a protracted muscle atrophy. In the 'undersized' muscles of our AHQS cases we have found histological changes essentially similar to those described by Bickhardt *et al.* (1967). Qualitatively similar changes can, however, be seen in the corresponding muscles of the opposite limb and in normal muscles of the same limb; and the more severe atrophic lesions are not seen at all in some undersized muscles. Furthermore, analysis of normal and undersized muscles in terms of total lipids, fat-free dry matter, protein nitrogen, DNA and hydroxyproline per unit fresh weight has shown no significant difference between sides (Patterson & Allen 1972); asymmetic muscles are biochemically similar. It is reasonable to argue

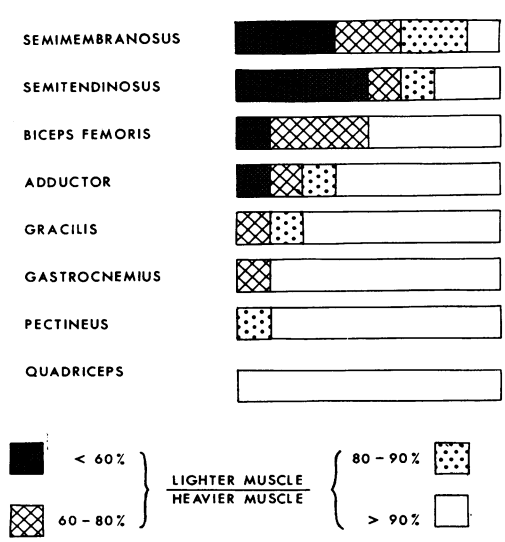

Fig 3 *Diagrammatic representation of the relative involvement of individual muscles in 8 pigs: one clinical and one subclinical case of AHQS from each of four litters*

that the atrophic changes, since they are neither constantly present in, nor limited to the 'undersized' muscles, are not typical of AHQS and that the essential primary characteristic is a muscular hypoplasia. The small size of affected muscles may in theory be attributable to a deficiency of muscle fibres, a reduction in fibre size or a combination of both. We are unable to count total muscle fibre numbers in large muscles but, as Table 1 shows, the mean fibre diameter in a typically affected muscle is slightly but significantly greater than in the normal muscle; hence the number of muscle fibres in the affected (left) biceps femoris must be less than in the corresponding muscle on the other side. Although it is possible that some muscle fibres on the left side have disappeared completely, the fact that in this case there were no signs of progressive myopathy or residual fibrosis strongly suggests a basic deficiency of fibre numbers.

Possible Mechanisms of Muscle Hypopolasia

Breidenstein *et al.* (1964) and Wilson & Williams (1968) have shown that for practical purposes pig muscles are bilaterally symmetrical with a weight variation of less than 3% between sides. It is necessary, therefore, to consider how differences of the magnitude seen in AHQS may be brought about.

There are four main possibilities for explaining an asymmetric deficiency of muscle fibres in the adolescent pig:

(1) A basic (genetic) difference in muscle fibre complement: however, Staun (1972) concluded that the number of muscle fibres in pig muscles is fixed at the embryonic stage and that after birth the number of cells remains constant.
(2) A disproportionate loss of myotubes during fetal life (cf. Webb, 1972, who reported the normal loss of preformed myotubes in the human fetus in the first half of gestation, and suggested that an aberration in the mechanism of muscle cell death in the fetus could account for some of the genetically determined disorders of muscle).
(3) A disproportionate loss of muscle fibres during postnatal life (cf. Muir, 1970, who observed that there was a continual spontaneous degeneration and regeneration of muscle fibres in healthy Pietrain pigs).
(4) Differential rates of muscle cell proliferation and/or loss.

A difference of fibre numbers at birth cannot be ruled out, though it might be expected that disproportions in size as great as 7:1 in individual muscle pairs would be clinically apparent if they existed at that stage.

Table 1

AHQS: Muscle size and muscle fibre size in biceps femoris

Estimates of cross sectional areas and muscle fibre diameters in biceps femoris of the pig shown in Figs 1 and 2

	Left side	*Right side*	*Ratio L:R*
Cross sectional area (mm^2) measured at mid-femur level	158	569	0.277
Mean fibre diameter (μm) measured from 25 fibres in 5 fields at 6 levels for each muscle	92 ± 0.785	82 ± 1.105	1.124

The skeletal muscle fibre of the modern, fast-growing pig is a highly vulnerable cell greatly addicted to spontaneous degeneration and regeneration (Muir 1970) and liable to metabolic stress (Allen *et al.* 1970). It is moreover exposed systemically to potential protoplasmic poisons, e.g. iron compounds given to prevent piglet anæmia (Patterson *et al.* 1969) and locally to a variety of injections usually given into the thigh. It is, therefore, not difficult to imagine circumstances in which substantial losses of muscle fibres could occur postnatally without the need to postulate an increased genetic liability to muscle damage.

Possible Etiology

Genetic: To say that all the field observations on the disease are consistent with the hypothesis that AHQS is attributable to a single autosomal dominant gene with incomplete penetrance and variable expressivity may mean little more than that the incidence is not random. In the two large outbreaks studied, all the affected pigs were sired by a small number of boars, in one case by two of three litter mates (*see* Table 2) and no more cases occurred after they were removed. On the other hand AHQS females had affected progeny by both a carrier boar and by a completely unrelated boar with several hundred normal progeny to his credit.

Trophic factors: The restriction of affected muscles to one limb coupled with dystrophic and atrophic histological changes suggests the in-

Table 2

Number of pigs clinically affected with AHQS in one heard.

There were no contemporary cases among aproximately 2000 pigs sired by other boars

Boars (full sibs)	*Sows*	*Progeny affected*	*Progeny at risk*
(A) Hampshire × Pietrain	1 Landrace	5	9
	1 Large white	11	15
(B) Hampshire × Pietrain	4 Landrace	2	44
	2 Large whites	1	22
(C) Hampshire × Pietrain	3 Landrace	0	31
	4 Large whites	0	39

fluence of a common vascular or nerve supply. However, the muscles affected have a number of different anatomic functions and do not share any common nerve or blood supply. The dystrophic and atrophic lesions are inconsistent and might well result from the fibrosis, itself an inconstant feature.

Trauma: The injection of 100–150 mg of an iron-polysaccharide complex into the thigh muscles during the first week of life is a hazard to which most pigs in Britain are subject and is clearly a possible precipitating cause of AHQS. In one herd 23 full sibs of AHQS pigs were inoculated intramuscularly with iron dextran into either the left or right thigh in the first week of life and dissected out at 40 or 80 kg live weight; 7 developed AHQS in the ipsilateral leg, 4 in the contralateral leg and 12 in neither leg. On the other hand no clinical cases of AHQS developed in approximately 2000 similarly treated piglets born in the same herd to parents of whose previous progeny none had been affected with AHOS.

Infection: Neurotropic enteroviruses are widespread in the pig population, and herpesvirus suis exists also in Britain. Though it is unlikely that a virus infection would result so consistently in a unilateral denervation atrophy the possibility that a latent infection might be triggered by local trauma cannot be ignored.

Conclusion

The best conclusion regarding causation that we can draw from the available data is that some pigs have a genetic liability to AHQS, that the hypoplasia of affected muscles probably occurs postnatally but that the environmental factors operating have not yet been identified.

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Incidence, Nature and Etiology of Malformations of the Heart in Man

Congenital abnormalities of the heart and great vessels are an important group of malformations, both in numerical terms and in terms of the need for accurate and early diagnosis if effective treatment is to be carried out. Various large population studies have given figures which vary from 0.3–0.65% of live births for the incidence of this group of conditions; recent studies with some years of follow up and resultant improvement in ascertainment suggest a figure of 6–7 per 1000 live births to be fairly accurate (for large surveys *see* McKeown & Record 1960, Leck *et al.* 1967).

Etiological factors in congenital heart disease (CHD) may be divided into three main groups. A number of defects (1%) are part of clinical syndromes determined by a single mutant gene (Marfan's syndrome, Ellis-van Creveld syndrome, Ehlers-Danlos syndrome, &c.); rarely a defect (often atrial septal defect) may be found in several generations of a family with apparently autosomal inheritance. A larger group (4%) includes the gross chromosomal abnormalities, in particular autosomal trisomy. Trisomy 21 has a frequency of approximately 25% associated CHD; Trisomy 13–15 and 18 are further examples of syndromes in which CHD is an important component. Turner's syndrome is frequently associated with coarctation and other defects. However, these genetically determined cases, together with the small number caused by rubella and possibly Coxsackie virus type B (Brown & Evans 1967) account for a relatively small proportion of human congenital heart disease. Most defects are determined as a result of the interaction of many genes with the environment, the so-called 'multifactorial' pattern of inheritance (Carter 1969).

Defects showing this pattern of inheritance have the following characteristics: they are common, there are familial aggregates, the recurrence rate in siblings is of the order of 1–5% whilst the concurrence rate in identical twins is between 20% and 50%, non-identical twins have rates approximating to recurrence rates in siblings. Further evidence of modification of the effects of genetic factors by the environment is provided by variations in frequency with seasons of birth, birth rank socioeconomic class, geographical variability, and the effects of changes in parental age. Nora (1968) has shown that these