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MORPHOGENETIC STUDIES OF THE RABBIT

VII. AORTIC ARCH VARIATIONS IN RELATION TO REGIONALLY SPECIFIC GROWTH DIFFERENCES [1]

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TWO FIGURES

INTRODUCTION

In previous communications (Sawin, '46 and Sawin and Nace, '48), evidence was found that skeletal variations at the thoraco-lumbar border and both skeletal and vascular variation at the lumbo-sacral borders of the axial skeleton serve in a general way to define the limits of growth centers of different magnitudes in each of several closely bred races of rabbits. In further attempts to delimit the area of influence of these centers, it has been of particular interest to consider the variation in pattern of the aortic arch. Such variation is both intra-specific and inter-specific. The varieties found in man have been discussed voluminously, dating back to the 15th century (Poynter, '16). The types commonly found in mammals were described by Cuvier (1810), and the most comprehensive study is that of Parsons ('02), who first suggested that such variations might depend upon body build rather than systematic relationships. Both phylogenetically and ontogenetically, the mammalian arch is recognized as a persistent 4th member on the left side in a series of 6 symmetrical pairs of arches. In

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birds it is the right arch which persists and the lower vertebrates (particularly in the lower categories) characteristically retain a more complete set. Variations resembling that of the bird, as well as combinations of both right and left arches in one individual have been reported occasionally in mammals. One of the first anomalies to be described in the rabbit was one of the former type (Legallois, 1824). Of more frequent occurrence are anomalies involving the carotid and subclavian arteries which correspond to remnants of two of the adjacent arches of the early, and in general, transient embryonic pattern. Such anomalies can be readily explained as irregular persistence or atrophy of parts of the embryonic pattern. Fusion of adjacent parts may also influence the pattern (Arey, '30), see also Baldwin ('20). Such an interpretation does not contribute to knowledge of the fundamental physiological processes on which the changes are dependent, although the general consensus seems to be that the adult arrangement of vessels is a result of mechanical factors modifying the usual habit of development, an opinion which goes back to Baader (1866), cited by C. W. M. Poynter ('16). Parsons ('02), in a comparative study of the arches, concluded that the type of arch was in some measure correlated with the breadth of the thorax and its proximity to the superior thoracic aperture. Lockhart ('30) suggests that a shift of influence determines the selection of parts of an anastomosing arterial network, some vessels of which enlarge while others degenerate through disuse. Such a process, operating by chance alone, affords unlimited possible variations. As Blincoe et al. ('36) remark: "the marvel is that the so-called normal arrangement is produced with such uncanny similarity so regularly and that such delicately adjusted processes so seldom go wrong." This stability suggests that the processes involved are hereditary, and that abnormal types either are the direct result of unusual environmental circumstances, or are in some way due indirectly to minor fluctuations in one of two or more genetic processes whose interaction does not quite achieve the proper threshold for complete fulfillment. Disastrous effects of re-

tardation at critical stages or of inadequate supplies of vitamin A, etc., upon the vascular system have been described by Wilson ('48). Since maximum growth can only be achieved by an optimum supply of both food and oxygen, the interrelation between vascular development and growth is obvious. The present study, therefore, is not only a study of the inheritance of variations in the pattern of the vessels arising from the aorta, but because of previous knowledge of differences in regional growth in the inbred races of rabbits used, it affords an opportunity to determine whether or not such regional growth differences are associated with any given pattern to a greater or lesser degree than with another.

MATERIALS AND METHODS

The specimens used in this study were for the most part the same animals used in earlier studies (Sawin, '45, '46 and Sawin and Nace, '48) and prepared either by gross dissection of adults or newborn or by injection through the ventricles with colored vinylite with subsequent clearing with KOH and glycerine. The same three races, III, V, and X, were used and, as previously, animals were raised under as nearly a uniform environment as possible, and matings were based upon the presence or absence of an extra or 13th pair of ribs. In the earlier portion of this study, all specimens were read by H.W.E., but later the specimens were read by P.B.S. Thus, a slight error in results may have arisen as a result of this personal factor, but it is believed that it is very small.

OBSERVATIONS

Twenty types of variation have been observed in the aortic arch of the rabbit. Fifteen of these were described by Edmonds and Sawin ('36) and are shown in figure 1.

The most common type (normal) in rabbits is the A type in which the brachiocephalic and innominate arteries are of approximately equal length and prominence. Type C lacks a brachiocephalic artery. Types B′, B″, and E all possess a nor-

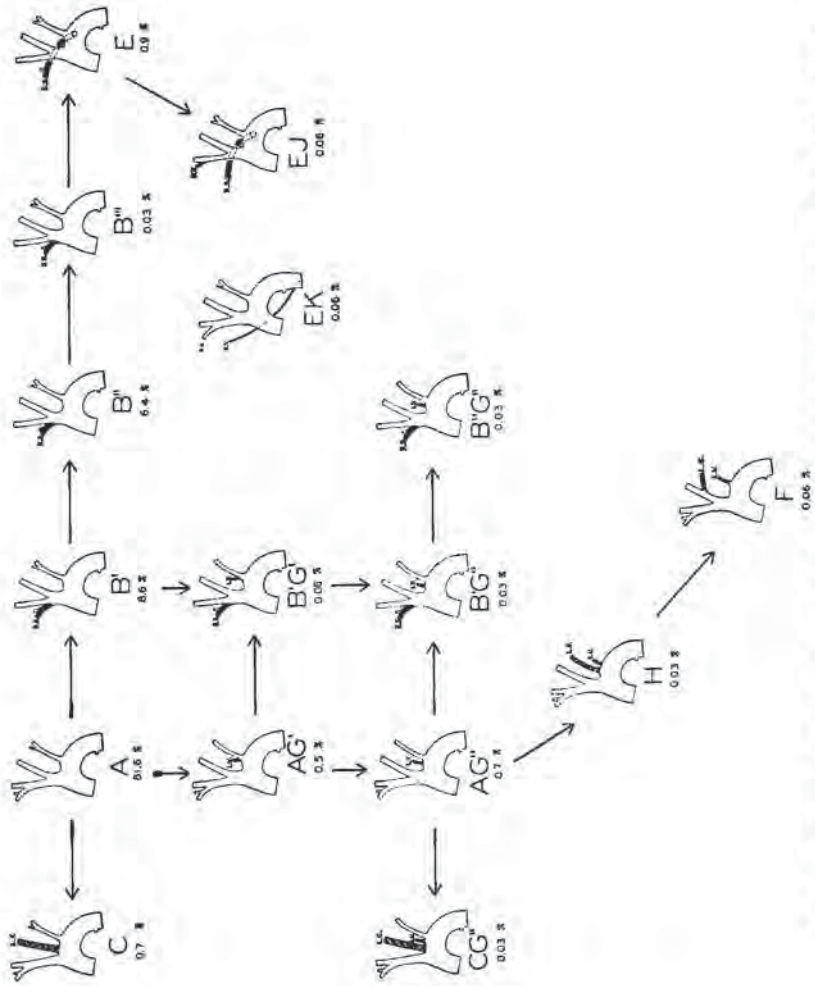

Fig. 1 Incidence of types of aortic arch found in postmortem examination of 3000 rabbits.

mal brachiocephalic artery, but due to the posterior migration of the origin of the right subclavian artery to or below the level of the bifurcation of the brachiocephalic artery, the innominate artery is reduced or absent. Such reduction in the rabbit was reported as early as 1868 by Krause. In type E, which is well known in man and commonly designated as a retroesophageal right subclavian artery (R.R.S.A.) the right subclavian takes its origin from the aortic arch as its last branch, and passes dorsal to trachea and esophagus to reach its point of termination. It is commonly supposed that the R.R.S.A. represents a persistent portion of the right dorsal aorta of the embryo. Specimens of this type were reported in the rabbit by Kussmaul and Tanner (1857), Smith (1891), White (1893), and Eales ('27). Types EK and EJ are variations of the E type in which the origin of the right vertebral artery is also varied and the G′ and G″ and H variations in which the origin of the left vertebral artery is varied.

The incidence of each of these types among the first 3000 rabbits as typed by H. W. E., are shown in figure 1. For the purposes of this study the subtypes involving the vertebral arteries were not differentiated. Since 1936 it was found convenient to record 4 additional types, Asb (intermediate between C and A), A- (intermediate between A and B′), and combination types A-sb and B′sb.

Mating of specific types

As was the case in early studies of rib variation, the preliminary study of arch variations reported by Edmonds and Sawin ('36), seemed to indicate some approximation to typical mendelian proportions between normals and certain of the abnormal types, but like the rib variation, continued study has demonstrated a more complex background. In table 1 are shown the data obtained from matings of known specific type. It is seen that although matings of the C type (lacking a brachiocephalic artery) (mating 1, table 1) produce their own type in a majority of instances, they also produce Asb, A, and

even A-. Although Asb type reproduces itself in 29% of cases, it produces a few C's (8.3%), and 62% of A type. A types (mating 6) produce the entire range of variation, of which 69% are like themselves. The progeny obtained from B types is too small to be of great significance, but it is important to note that they also produce the normal type. Mixed matings (especially matings 2, 4, 5 and 9) in general appear to produce a greater range than those of like types, but a notable tendency

TABLE 1

Per cent incidence of aortic arch types in progeny of parents of specific arch types. Type A is regarded as the normal type. Types deficient with respect to the brachiocephalic artery are shown to the left. Those deficient in the innominate are shown to the right, and type E involving the R.R.S.A. to the extreme right.

MATING		DEFICIENT BRACHIOCEPHALIC			NORMAL	DEFICIENT INNOMINATE			R.R.S.A.	TOTAL
		No. of matings	C	Asb	A	A-	B′	B″	E	
1.	C × C	3	58.3	16.6	16.6	8.3				12
2.	C × Asb	21	22.6	14.3	51.8	4.8	6.0	.6		168
3.	Asb × Asb	7	8.3	29.1	62.5					48
4.	C × A	14	7.9	27.6	53.9	4.0	5.3	1.3		76
5.	Asb × A	33	3.4	14.3	69.5	.5	9.4	3.0		203
6.	A × A	42	4.9	10.9	69.4	.4	8.5	3.9	2.1	284
7.	Asb × A-	4		3.4	82.7		13.6			29
8.	A. × A-	4		9.0	66.6		24.2			33
9.	A × B	14		3.0	66.6	.3	15.0	14.3	.6	300
10.	B × B	1			40.0		20.0	40.0		5
11.	B × E	1			33.3		66.6			3

is found for the distribution to be centered to the left in the tabulation in matings of deficient brachiocephalic arteries; to the right in matings of deficient innominates; and to cover a greater range in matings of the two extremes or of normals with either extreme. Dominance of one type over another, and segregation according to the usual mendelian ratios are not apparent. Furthermore, the continuity of types, although neither perfect nor strictly symmetrical in the tabulation, is more like that which is considered typical of quantitative inheritance in which several factors are involved. Thus, it ap-

pears as if the two major abnormal types (reduced or absent brachiocephalic or reduced or absent innominates) may be manifestations of similar fundamental influence as found in ribs, ventral spinous processes, etc.

Patterns in inbred races

The first evidence of the relation of the aortic arch variations to the regional growth differences previously described is found in the inbred races themselves.

In table 2 and group A, figure 2, are shown the distributions of the aortic arch types in populations of races III (mating 1), V (mating 3) and X (mating 2), each of which population is known from previous studies to possess a specific vertebral

TABLE 2

Per cent distribution of aortic arch patterns in 5 races of rabbits

MATING	E	A	A-	B'	B''	B'''	A-sb	B'sb	Asb	C	TOTAL
III	..	17.3	4.0	8.0	..	..	1.3	7.3	33.3	28.7	150
X	..	58.0	6.7	10.8	3.0	..	..	.4	16.4	4.8	269
V	.1	65.0	7.0	18.1	3.8	..	.2	.1	5.5	.1	853
V466	1.1	26.5	12.1	39.7	12.6	3.4	.6	..	4.0	..	173
IIc	4.1	74.1	..	6.1	6.8	.7	..	..	6.8	1.4	147

pattern. In this table and figure, as well as those which will follow, the data are arranged in a slightly different order, from left to right, normal (both innominate and brachiocephalic present), innominate deficient, and finally brachiocephalic deficient, which as will be shown later, is according to the anteroposterior level at which the variations occur. When thus arranged, each population tends to fall in a continuous but asymmetrical distribution which is different in each case. Although this continuity must be kept in mind, it will be convenient in describing races to refer merely to the proportion of normals, of innominate deficient or of brachiocephalic deficient as shown by the individual figures. Race III (mating 1) characteristically has a short or no brachiocephalic artery

(60% of cases). Twelve per cent of its individuals manifest a short innominate, and only 17% are of the recognized normal type.

In contrast, race V (mating 3, table 2 or figure 2 A) has 65% of the individuals with the normal A type. Six per cent are deficient in the brachiocephalic artery but 28% are deficient in some measure in the innominate.

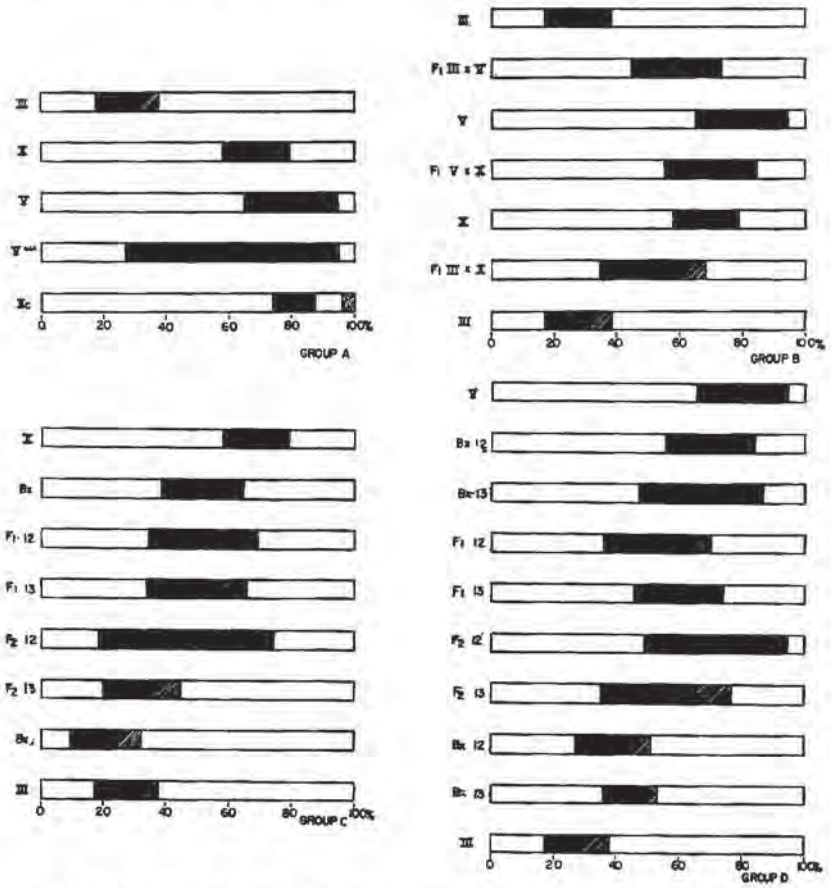

Fig. 2 Per cent distribution of the 4 major types of aortic arch pattern. Normal type (A) at left; deficient innominate (A-, B′ and B″) in black; deficient brachiocephalic (Asb and C) to right; combination types (cross-hatched), and type E, the retroesophageal right subclavian artery (stippled).

Race X (mating 2, table 2 or fig. 2 A) likewise has a high per cent (58) of normal A type individuals and the abnormal types are about equally divided, 22% deficient in brachiocephalic and 20% in the innominate.

Thus, race III characteristically manifests the more posterior deficiency, race V the more anterior deficiency, and race X neither one more than the other.

One subline of race V is of interest because continued selection for 5 generations resulted in a population with a much higher proportion of deficient innominates. Progeny were selected to be parents for each generation from parents which had previously produced higher proportions of the B type of arch, and the data shown were taken from the last two generations. They show approximately 70% of innominate deficient individuals as compared with the general population of race V (see mating 4, table 2). One more race (IIc) is shown in table 2 (mating 5). This race had the same common origin as race V, but when examined for the arch pattern, after approximately 5 generations, its members characteristically produced a very high proportion of A type arches as compared with the other races, and also the largest proportion of the E type arch (which represents a persistent portion of the right dorsal aorta of the embryo). Sufficient data on patterns of the aortic arches in crosses of these two races unfortunately are not available. These distinct racial differences clearly indicate the genetic background of the variation.

Pattern of distribution of F_1 hybrid generations

The distribution of patterns in the hybrid generations derived from crossing these races is shown in table 3 (matings 2, 4 and 6), and in figure 2, group B. In each case the position of the central tendency of the distribution of the F_1 tends to be shifted to the right or left in such a manner as to fall approximately intermediate between its comparable positions in the parental races. In the III $\times$ V cross (mating 2), the proportions of short brachiocephalic, normal and short innominates

are approximately intermediate between those of each type of the parental races. The same is true in the V × X F_1's. Race X is quite different from race III, and while in the F_1's of the III × X cross the proportions of deficient brachiocephalics and of normals likewise tend to be intermediate, the distribution is such that the number of deficient innominate arteries of the several kinds exceeds either of the parent races by more than 10 or 20%. This tendency for the F_1 in most cases to be intermediate but in some cases to exceed either parent is the same sort of phenomenon noted by Sawin ('46) and Sawin and

TABLE 3

Per cent distribution of aortic arch patterns in races III, V and X and in their F_1 hybrid progeny

MATING	R.R.S.A. E	NORMAL A	INNOMINATE A-	INNOMINATE B'	INNOMINATE B"	COMBINATION A-sb	COMBINATION B'sb	BRACHIO-CEPHALIC Asb	BRACHIO-CEPHALIC C	TOTAL
1. III	.	17.3	4.0	8.0	..	1.3	7.3	33.3	28.7	150
2. F_1	..	42.5	8.9	17.1	2.1	2.1	0.7	21.2	5.5	146
3. V	.1	65.1	7.0	18.1	3.8	0.2	0.1	5.5	0.1	853
4. F_1	..	56.5	5.8	20.3	1.4	..	..	10.1	5.8	69
5. X	..	58.0	6.7	10.8	3.0	..	0.4	16.4	4.8	269
6. F_1	..	34.3	11.6	14.9	2.2	1.9	3.4	22.8	9.0	268
7. III	..	17.3	4.0	8.0	..	1.3	7.3	33.3	28.7	150

Nace ('48) in connection with studies of ventral spinous processes and iliolumbar arteries, and it is of further interest to determine what happens to this accumulated deficiency in the innominate artery in subsequent generations. Before turning to these, however, it should be noted that when the F_1's of the III × X cross are separated into two populations (mating 3 and 4, table 4) on the basis of possession of 12 or 13 ribs, it is seen that 12-ribbed F_1's tend to have the greater number lacking in the innominate arteries, whereas 13-ribbed have the greater number lacking in the brachiocephalic. The same is true of the F_1 of the III × V cross (matings 4 and 5, table 5), except that in this cross it is the normal type which is largest in 13-ribbed F_1's rather than the brachiocephalic deficient

types. In general, there appears to be a tendency for more innominate deficient types to be produced throughout. This fact is of considerable significance, as will be seen later.

Pattern distribution of F_2 and backcross generations. In table 4 (and in fig. 2, group C) are shown the distributions of the F_2 (matings 5 and 6) and backcross populations (matings 2 and 7) of the cross of races X and III in relation to the parent populations (matings 1 and 8) and the F_1 (matings 3 and 4). Here in the total F_2 are found a much higher proportion of deficient brachiocephalics, particularly of the Asb type, than in the F_1 or in the backcross to race X, and a corresponding decrease in normals and the deficient innominate types A-, B′ and B″. It is again interesting to note that, particularly as compared with the F_1, 13-ribbed individuals (mating 6) have the greater proportion of deficient brachiocephalic arteries and less of the deficient innominate types. It is also important to note the greater incidence of the combination types A-sb and B′sb in the two F_2 populations.

TABLE 4

Per cent distribution of aortic arch patterns in the cross of races III and X

MATINGS	NORMAL	INNOMINATE			COMBINATION		BRACHIO-CEPHALIC		TOTAL
	A	A-	B′	B″	A-sb	B′sb	Asb	C	
1. X	58.0	6.7	10.8	3.0		0.4	16.4	4.8	269
2. $Bx^X(12)$	38.4	10.6	12.6	1.3	0.7	1.3	26.5	8.6	151
3. $F_1(12)$	34.5	13.6	15.3	1.7	1.1	3.4	23.2	7.3	177
4. $F_1(13)$	34.1	7.7	14.3	3.3	3.3	3.3	22.0	12.1	91
5. $F_2(12)$	18.6	12.8	9.3	..	10.5	3.5	33.7	11.6	86
6. F_2	20.0	10.8	5.0	0.8	4.2	4.2	45.8	9.2	120
7. Bx^{III}	9.5	6.0	6.5	0.7	3.0	7.7	50.0	16.6	168
8. III	17.3	4.0	8.0		1.3	7.3	33.3	28.7	150

Both backcrosses (matings 2 and 7) show a tendency for their distributions to return to that of the particular parent race concerned. The Bx^{III} particularly resembles race III in possessing the exceedingly high proportion (66%) of brachiocephalic deficient individuals, and there is also an increase in the number of combination types as in the F_2.

Similarly in table 5 (and in fig. 2, group D) are shown the distributions for races III (mating 10) and V (mating 1) and their hybrid generations. The same intermediate types of distribution are to be noted for each generation. Again, as in the F_2 (III $\times$ X) there is to be noted a general increase in type A or normal and particularly the innominate deficient types A- and B′, and a decrease in the deficient brachiocephalic types. Of special significance is the fact that this tendency is more pronounced in the 12-ribbed progeny, and that in the 13-ribbed progeny there are larger numbers of brachiocephalic deficient types and fewer normal and innominate deficient

TABLE 5

Per cent distribution of aortic arch patterns in the cross of races III and V

MATING	R.E.S.A. E	NORMAL A	INNOMINATE A-	INNOMINATE B′	INNOMINATE B″	COMBINATION Asb	COMBINATION B′sb	BRACHIOCEPHALIC Asb	BRACHIOCEPHALIC C	TOTAL
1.V	0.1	65.1	7.0	18.1	3.8	0.2	0.1	5.5	0.1	853
2. Bx(12)	0.5	57.8	9.9	14.3	1.8	..	0.6	13.7	1.9	161
3. Bx(13)	..	47.8	7.6	24.5	5.4	0.5	0.5	9.8	3.8	184
4. F_1(12)	..	36.0	2.0	28.0	2.0	2.0	2.0	24.0	4.0	50
5. F_1(13)	..	45.5	13.1	11.1	2.0	1.0	1.0	20.2	6.1	99
6. F_2(12)	..	49.0	21.6	13.7	2.0	7.8	..	5.9	..	51
7. F_2(13)	..	34.3	16.0	13.1	1.9	6.5	4.7	22.1	1.4	213
8. Bx(12)	..	27.0	8.1	8.1	..	..	8.1	32.4	16.2	37
9. Bx(13)	..	36.0	3.6	8.3	0.6	1.2	4.1	33.7	12.4	169
10. III	..	173	4.0	8.0		1.3	7.3	33.3	28.7	150

types. This is in contrast to the F_1 ancestral populations (matings 4 and 5, table 5) in which there is the higher proportion of normal type among the 13-ribbed progeny.

Of particular significance is the fact that the F_2 and backcross populations of this cross as well as the F_1 all show a greater incidence of the more normal and innominate deficient types than in the comparable matings of the III $\times$ X cross.

In the backcross to race V of the III $\times$ V cross, (matings 2 and 3, table 5), the normal types are relatively in excess in the 12-ribbed group, but in the 13-ribbed population, the innominate deficient types are in larger proportions. In the Bx^{III}

the relationships between 12 and 13 ribbed individuals compares with that of the F_1. In both backcross populations there is the same tendency to be intermediate between that of the F_1 and the particular parent race concerned.

In summary, it may be said that the difference in distribution of types between races V and X are reflected in all of the hybrid populations with the major differences being associated with differences in the number of ribs, 12-ribbed populations tending in general to show a higher proportion of normal or innominate deficient types and 13-ribbed tending to manifest higher proportions of brachiocephalic deficient types. The exceptions to this being the F_1 of the III $\times$ V cross.

DISCUSSION

The concept of growth as a determining factor in morphological patterns is not new, and particularly is this true in connection with studies of vascular patterns. Parsons ('02) in a comprehensive systematic study, regarded the type here described as Asb as the most common mammalian type, and recognized the other variations as ranging in two directions, either towards concentration, as in our type A (forming a true brachiocepahlic trunk), or towards separation, as in our type C (three of 4 separate branches of the arch). Parsons considered the immediate cause of concentration to be compression from side to side and the cause of separation to be increased breadth of the thorax. Congdon ('22) has discussed the influence which growth, relative position and blood current have in transforming the arches of man. Hammond ('37) is convinced that variations in these factors at some stage or stages in development cause a corresponding divergence in the ultimate expression of form. He believes that the aortic arches reach their final form and position as a result of growth of the organism as a whole, and that intrinsic factors play no part in this process. As he describes the arch formation in the calf, for example, "The position of the *left* subclavian changes during the 17–22 mm stages from a point well below the pulmonary arch; upward along the dorsal aorta over the arch and

thence to its final location on the arteria brachiocephalica. The short bicarotid stem does not put in an appearance until about 25 mm. With the sinking of the heart and the incorporation of the aortic trunk into the anterior heart wall as the arch level sinks, there is consequently a drawing together of the upper portions of the arches. This results in a fusion of the carotid stems, or a 'concentration of aortic arch branches' according to Parsons, thus producing a common stem of origin," (the brachiocephalic). This being true it appears that brachiocephalic deficient and innominate deficient types described in this paper are probably due to a difference in the amount of "posterior migration" of the heart relative to adjacent structures. This raises a question with respect to this very interesting phylogenetic and ontogenetic phenomenon. It is a well known fact that historically the position of the heart is relatively anterior in the lower vertebrates, as in embryos of higher vertebrates. Progressively the heart takes a more posterior position, until in mammals it finds its final location in the thoracic cavity. Whether this is an actual migration of the heart, or whether it is a relative change due to elongation of the vertebrae and associated structures pushing the head farther from the original point of attachment of the heart, is a question which needs further consideration (see Arey, '40).

If the variations in aortic arch pattern described in these races of rabbits are considered from this point of view, certain very interesting relationships are noted. Race X, with a high proportion of normal (A type) arches, and small, equal proportions of the two deficient types of arch, is the race which Baumgartner and Sawin ('43) found (in comparison to race III) to have an early accelerated and anterior onset of ossification of the ribs. Since race X seldom has extra ribs (Sawin and Hull, '46) and its ventral spinous processes are relatively poorly developed and anterior (Sawin, '46) it was concluded that race X has an enlarged or accelerated growth area localized somewhere in the anterior thoracic region. This unusual growth would explain the high proportion of normal aortic

arches with well developed innominate and brachiocephalic arteries.

Since race X also has a considerable portion of individuals with deficient brachiocephalic arteries, it would have to be assumed (following this line of reasoning) that these are individuals in which the accelerated area did not carry quite far enough posterior to insure the complete development of this artery.

Race III, which is so definitely lacking in a brachiocephalic artery in such a high proportion of cases (as compared with races V and X) is the race which Baumgartner and Sawin found to have a delayed onset of ossification of the ribs, particularly anteriorly, and presumably this retarded growth is general in the anterior thoracic region of this race. Once ossification (and presumably growth generally) does begin more posteriorly, there is good evidence (Sawin et al., see Sawin and Nace, '48) to show that as compared with either races V or X, there is a much more extensive region of general enlargement including both the thoraco-lumbar and lumbo-sacral borders. It seems probable that if Hammond's interpretation of the patterns found in the calf also applies to the rabbit, the relative position of the heart, and the right subclavian artery in race III is anterior to this accelerated growth area in a region which, as compared with the other races, is more or less retarded.

Little is known about the early rib ossification of race V but because of its high proportion of 13-ribbed individuals and magnitude and location of its ventral spinous processes it was previously concluded that an enlarged thoraco-lumbar growth area extended some distance anterior to the thoraco-lumbar border. Upon finding now that this race also has a large proportion of A type arches and is particularly characterized by a relatively high proportion of innominate deficient types it seems probable that if these vascular variations are associated with the previously recognized growth area of this race that area must cover in part the same region as that in race X. In other words, elongation of the axial skeleton and

associated structures at the time the limb bud was being established has proceeded so rapidly that the limb and the subclavian artery is attached more posteriorly resulting in innominate deficiency.

Since the C and Asb appear most numerous in both races III and X, which are known to be retarded in the posterior thoracic region, and because evidence was previously found to show that the accelerated growth area of V, in which the C and Asb types are almost nil, extends farther anteriorly than in III it seems reasonable to suggest that the high proportion of innominate deficient types (A-, B′ and B″) in race V is due to a relatively accelerated growth of the axial skeleton, in relation to the heart and the developing limb buds in the mid-thoracic region, at the time when the limb bud and its circulation are being established. Further evidence that this is a sound interpretation is found in the hybrid generations.

Attention has already been called to the fact that in the F_1's of all crosses the distribution of the populations into the 10 classes described tends to be intermediate between those of the two parent races, with the exception that in one cross (III $\times$ X) there is a greater proportion of deficient innominates than in either parent race. This happens to be the cross in which previous studies indicate that the enlarged growth areas of the two races are so located that they probably overlap very little if at all. When combined in an F_1 cross the extreme anterior and extreme posterior types might be expected to be large because of the parental contributions, but combination might well result also in sufficient overlapping of growth stimuli that a large proportion of the innominate deficient types would result. In this case it is well to point out that this is more pronounced in the F_2 12-ribbed progeny than in the 13-ribbed which tend to resemble more closely race III. In the F_1 V $\times$ X in which there is overlapping of the growth areas, the proportion of innominate deficient types is intermediate between the proportions found in the two parent races. Further, as will be shown later, the incidence of brachiocephalic deficient types as compared with the III $\times$ X cross, which is

the lowest found in any F_1 population, is further evidence that the anterior limit of the accelerated area of race V is more anterior than that in race III.

Additional evidence in this connection is the fact that whereas the F_2 of both the III $\times$ V and III $\times$ X crosses show a pronounced increase of the combination types Asb and B′sb, they are most numerous among 13-ribbed progeny in the III $\times$ V F_2 and among the 12-ribbed progeny of the III $\times$ X F_2 (see tables or histograms group C and D, fig. 2). Similar threshold differences of this kind are found in several of the backcross generations, for example in the III $\times$ X cross, where in mating 7 (table 4) the Bx^{III} has a greater proportion of deficient brachiocephalic arteries than either parent race or F_1. Similar cases of this type were found in the studies of both the vertebral processes (Sawin, '46) and the ilio-lumbar arteries (Sawin and Nace, '48). In the case of the vertebral processes, particular attention was called to the fact that the relative anterior-posterior position of these processes seemed to have much to do with the relative degree of their development. Whether it is strictly a matter of the antero-posterior level or whether it is more specifically a matter of the proximity of the variation to one or more areas of accelerated growth or even proximity to a point where the influences of two such areas overlap, is a question which cannot be answered at this time.

Having found evidence of relationship between these variations and the regional growth areas, it is of further interest to consider whether the variations also may help to define the limits of the growth areas. It would seem that the nature of their frequency distribution should indicate in some degree the limits of the growth areas. As was found to be the case in the study of the ilio-lumbar arteries, the pattern of blood vessels (aortic arch patterns) is not as satisfactory as skeletal units for determining the limits of these growth areas because of the non-metameric nature of vascular variation. Nevertheless the present observations combined with information from previous studies do help to restrict the limits of these recog-

nized growth areas. For example, the C and Asb types are found most numerous in races III and X in which races there is considerable reason to believe that relatively retarded growth areas occur in the posterior thoracic region. In race III the retarded area is anterior to a much accelerated one in the lumbar region, in race X it is behind an accelerated area in the anterior thoracic region. Race V, however, has a high proportion of normal individuals (with both innominate and brachiocephalics present) as does also race X, but it differs in having a high proportion of innominate rather than brachiocephalic deficient individuals thus indicating acceleration more anteriorly than in race III and more posteriorly than in race X. From this it seems reasonable to conclude that all three of these accelerated growth areas have their limits somewhere in close proximity to the heart. That in race X must have its greatest influence anterior to the level of attachment of the heart. That in race III can have influence very little anterior to the heart and that of race V would appear to extend anteriorly well into the territory of that of race X.

Since the highest peaks of incidence of each variation are not necessarily confined to any one particular mating (generation) such as the F_1, but may occur in the F_2 or in backcrosses as well, prediction of what will result from any given cross seems to depend entirely upon a knowledge of the relative distribution within the previous parental generation and thus upon the centers of accelerated growth which they define. It seems most probable that the type of aortic arch pattern is not determined so much by the limits of growth areas as by the relative position (adjacent to, at the margin of, or near center of greatest effect) with respect to the important regional growth areas.

Of interest is the fact that the E type of arch, in which the right subclavian artery arises as persistent right dorsal aorta, did not appear anywhere in these crosses, although a very small per cent was observed in race V, and in the selected line of race V this variation did increase slightly. It is also notable that in race IIc as many as 4% of such animals were observed.

This racial difference suggests a hereditary background for such a variation, possibly effective through a rare combination of accelerated regional growth influences. While in this study particular consideration has been given to the relationships of these arch patterns to regional differences in body length, we do not wish to minimize the possible relationships of width, particularly of the thoracic aperture as suggested by Parsons. We believe his idea is of sufficient merit to warrant further study, and genetic material is now available which will make possible a critical examination.

SUMMARY AND CONCLUSIONS

Domestic rabbits can be classified into 20 different types according to the origin and distribution of the major vessels arising from the aortic arch. Matings within and between these types show little indication of dominance and segregation characteristic of mendelian inheritance, although there is a notable tendency for individuals deficient in either the brachiocephalic or innominate arteries to breed true, and for the normal types possessing both of these vessels in well developed form to produce the entire range of variation. Each of three inbred races is characterized by different proportions of these types, and in crosses there is the same tendency for subsequent generations to show a distribution of types intermediate between those of the parent populations concerned. This fact, together with the notable exceptions in which the frequency of certain types exceeds that found in either parent race, and also the fact that in the F_2 and certain backcrosses there is a characteristic increase in the proportion of combination types deficient in both the innominate and brachiocephalic arteries, is considered evidence that these deficiencies are hereditarily determined by their relative position in relation to certain previously demonstrated areas of accelerated growth in this region. The manner in which these variations further serve to define the anterior limits of the different growth centers previously recognized in these races is described.

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