

JAMES ARTHUR LECTURE ON
THE EVOLUTION OF THE HUMAN BRAIN
1957

EVIDENCE OF PRENATAL FUNCTION
OF THE
CENTRAL NERVOUS SYSTEM IN MAN

DAVENPORT HOOKER

THE AMERICAN MUSEUM OF NATURAL HISTORY
NEW YORK: 1958

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EVIDENCE OF PRENATAL FUNCTION OF THE CENTRAL NERVOUS SYSTEM IN MAN¹

The first of the definitive organs of the vertebrate to separate from the germinal disc are the neural folds, which, following closure, develop into the central nervous system. In as much as the general course of embryonic development in vertebrates occurs in a head-to-tail direction (Kingsbury, 1924), the cervical portion of the neural tube begins differentiation into nervous tissue before its caudal end has been completed. As the neural tube extends caudally, the somites, from which some trunk musculature (and certain other elements) will develop, appear as subdivisions of the dorsal mesoderm, hitherto unsegmented. Other trunk musculature arises from the ventral unsegmented mesoderm.

The cardiovascular system, which begins differentiation at almost the same time as the neural tube, precedes all other organ systems in attaining initial functional capacity except, apparently, in certain sharks (Wintrebert, 1920).

¹ The physiological and morphological studies on human prenatal development, of which the present paper is Publication No. 27, have been aided by grants from the Penrose Fund of the American Philosophical Society, from the Carnegie Corporation of New York, from the University of Pittsburgh, from the Sarah Mellon Scaife Foundation of Pittsburgh, and from the National Institute of Neurological Diseases and Blindness of the United States Department of Health, Education, and Welfare. The work on which this paper is based, for some years a joint project of Davenport Hooker and Tryphena Humphrey, was done at the University of Pittsburgh School of Medicine. The author is grateful to the staff of the Osborn Zoological Laboratory of Yale University for their courtesy in providing him generously with space and facilities while the paper was being written.

The neural tube, however, which begins its formation before any muscles have appeared, requires a relatively long period of differentiation before reaching its first capacity for function. Hence the more cervically located trunk muscles become capable of contraction on electrical or direct mechanical stimulation before motor nerves establish effective connections with them. As the motor system develops in advance of the sensory, reflex activity does not appear until still later.

Mention has been made of the general head-to-tail direction of embryonic differentiation. Recognition of this trend was criticized by Kingsbury (1924), who recognized that this "law of cephalo-caudal differentiation" was general only. Actually, from the beginning of closure of the neural folds in the neck region, the central nervous system has two directions of differentiation, one involving the spinal cord, the other the brain itself. The upper cervical region is the starting point for both directions of differentiation, the first passing caudally, the second rostrally. Hence, for the nervous system and its associated structures, it is more accurate to refer to the two as the "cervico-caudal" and the "cervico-rostral" directions of differentiation, respectively (see Hooker, 1954). The cervico-caudal direction of differentiation is the more significant in early central nervous system function during embryonic life because its development, like its function, precedes that of the cervico-rostral.

Microscopic examination of the developing nervous system is, of course, important. However, it cannot be the final arbiter of certain of the finer points in fixing the exact time at which functional levels of morphological maturation are attained. For example, excellent as are modern techniques and microscopes, they cannot establish the time when synapses between neurons become functional. For that, it is necessary to supplement microscopic examination with

functional studies. Hence a combination of morphological and physiological techniques is advantageous in any investigation of the development of the nervous system and of its functional capacity at any specific age.

It is obvious that there can be no capacity for function not permitted by the level of structural differentiation. In broad terms, structure determines the capacity for function. This is true whether one is considering the entire organism or only its parts.

It should also be obvious that the functioning of a whole organism is its behavior, at whatever age it may begin to exhibit activity. The behavior of an adult human being is exceedingly complex, but it is still "structure in action." It is no part of the present discussion to attempt an analysis of adult human behavior. Fortunately, it is not necessary. A recent book, "The evolution of human nature" (1956), by the dean of comparative neurologists, C. Judson Herrick, presents the case as only that master can do it. All that is attempted here is a presentation of some of the findings of a study of certain aspects of human fetal behavior, set into enough of its phylogenetic background to permit interpretation of the clues offered as to the functional capacity of the embryonic and fetal nervous system.

The fact that developing organisms exhibit activity, and hence behavior, has long been known. However, the exact nature and sequence of these activities, their similarities and differences throughout the vertebrate scale, and their implications as indexes of the structural development of the nervous system have been submitted to truly scientific study only within the past half century or so. Much, but by no means the entire story, is now known about embryonic and fetal activity, the so-called "overt behavior" (Hooker, 1944) of developing vertebrate forms.

It must be borne in mind that overt activity, that activity

expressed through the skeletal musculature, is only a part of the behavior of any organism. Behavior is essentially the interaction of a living organism with its internal and external environments. Both these environments are closely interrelated, so closely as to be virtually inseparable. Each may affect responses of the organism as soon as their elements have attained functional capacity. Overt behavior, produced by the nervous and muscular mechanisms of the body and taking the form of bodily movement, is the more evident kind of behavior. There is, however, a covert behavior, largely hidden and unseen, going on within the organism and affecting the nature of overt behavior. Covert behavior is largely the response of the internal organs to changes in the external or internal environments. By means of many enzymes and hormones and by the muscular activity of the internal organs themselves, any organ may affect others, including the nervous system, and hence may have a profound effect upon overt behavior. Behavior is thus an expression of the activity of the entire organism, an interaction of all its parts with its varying environments, both external and internal.

When adult organisms are dealt with, it is difficult in any situation to assess the roles played by the elements of covert behavior. If this be true in man, where introspection is possible, how much more difficult is such assessment when one is dealing with animals that cannot communicate! In both man and other forms, a variety of methods must be employed to determine the contribution of the various internal organs to the sum total of behavior.

With the young embryo, the assessment of behavioral components may be somewhat easier. In the development of an individual embryo, the primordia or *anlagen* of the various organ systems tend to appear in a characteristic sequence. As is noted above, the cardiovascular system is the first to

reach a functional level in most vertebrates. This is a system essential to the life of the organism and in older animals one highly sensitive to changes in either the external or internal environments. However, in so far as is now known (and admittedly little is known about it) the early cardiovascular system appears to have little effect, other than sustaining the living organism, on the activity of other systems that appear at about the same time. In the light of our present imperfect knowledge, other organ systems affect activity to no greater extent in the embryonic period.

Embryonic respiration is carried on by gills for a long time, if not permanently, in certain animal forms. In the mammals, it is accomplished by means of placental interchange. The early alimentary canal is digesting yolk or, in the placental mammals, engaged in differentiation, while nutritional duties are cared for by the placenta. The urinary systems begin to function early (Guthmann and May, 1930), but there is no evidence to indicate that they have an effect on overt behavior in early fetal life. Hence the embryo offers an ideal opportunity for our observing the functioning of the muscular and nervous systems, relatively unhampered by other complicating factors.

Unfortunately, it would require greater space than is here available to review the work that has been done on the overt behavior of the various classes of vertebrates. To that end, reference can only be made to an earlier publication by the present author (1952). However, it is essential to review, though all too briefly, the embryonic development of overt behavior in that amphibian for which the most complete study has been made. This is the salamander, *Amblystoma*, which was the subject of intensive study by the late George Ellett Coghill from 1906 until shortly before his death in 1941.

Coghill presented his findings in a long series of papers

between 1909 and 1936. These are rather adequately summarized in his University of London lectures, "Anatomy and the problem of behaviour" (1929a). To test reflexes, Coghill used human hairs as the tactile stimulator. He has described a series of physiological response stages in *Amblystoma* and thoroughly worked out their underlying structural basis. These stages, with their characteristics, are as follows:

1. The premotile stage, in which no contraction of any muscle can be elicited by any method of stimulation. The muscle has not as yet differentiated to a structural state that permits function.

2. The non-motile stage, limited to those embryos in which certain muscles, located in the neck region, are sufficiently differentiated to respond to electrical or direct mechanical stimulation, but do not contract on tactile stimulation of the integument in any region of the body. At this time, no reflex arc has developed to the functional level.

There is strong presumption that, towards the end of this non-motile stage in *Amblystoma*, there is a brief period when electrical stimulation of appropriate areas of the spinal cord would excite the motor nerves to cause muscle contraction. It is certain that the motor nerves precede the sensory in their differentiation and that they are well developed and connected with the muscles in the cervical region at the latter part of this stage. Such muscular activity as a result of stimulation of motor nerves is well known in fishes, birds, and mammals, but apparently Coghill did not test for it in *Amblystoma*, as his primary interest was centered on the development of reflex activity.

3. The early flexure stage, characterized by the first reflex activity, follows abruptly on the last. Gentle tactile stimulation of the integument in the neck region causes a sharp bending of the head, almost perpendicular to the body

axis. The response is "typically away from the side stimulated" (Coghill, 1929a). Those embryos that at first exhibit ipsilateral flexion of the head, or even irregular laterality, eventually react contralaterally.

4. The coil stage, in which the caudally expanding muscle differentiation and motor-nerve connections with the muscles transform the localized neck flexion into a coil of the body, almost always to the contralateral side. Despite the caudally increasing spread of the neuromuscular connections, the sensory elements in the integument remain localized for some time before also expanding the reflex arc system towards the tail.

5. The S-reaction stage, "characterized by reversal of a flexure before it is completed as a coil" (Coghill, 1929a). As one flexure passes caudally along one side of the trunk, another appears in the neck region on the opposite side of the body and also passes caudally, to be succeeded by a third on the first side of the trunk, and so on, for a limited period. These waves of contraction, passing down the opposite sides of the body to slip off the tail, throw the trunk into alternating S- and reversed S-formations. A sinuous motion of the trunk is thus produced, which quickly becomes stage 6.

6. The swimming stage, as the tempo of passage of the alternate flexions increases and as they are longer continued. Then the young larva swims in sinuous fashion.

Several facts should be noted relative to the last four stages, those in which reflexes were elicited. In none do nervous elements above the medulla play any role in the responses. This was demonstrated by Coghill (1929a) by his severing the central nervous system at the level of the otic vesicles. In all cases observed, the commissural mechanism decussates, carrying the nervous impulse to motor cells on the opposite side of the spinal cord.

The earliest reflex response is localized in the neck region because, as Coghill pointed out, it is only here that motor-nerve connections to functional muscles have developed. As new motor connections are established seriatim in a caudal direction, the response spreads caudad. Hence it is obvious that all the functional reflex mechanism of the embryo responds to each effective stimulus. Because of this fact, Coghill termed these responses "total patterns."

As Coghill determined, the total pattern plays a significant role beyond the early stages. When the gills and then the extremities appear (first the forelimbs, later the hind limbs), these are moved only with the trunk during the sinuous movements of the body. They continue to do this for some time before they become capable of moving independently of the trunk, that is, before local reflexes of the limbs appear. Local reflexes are made possible by the development of additional nervous elements, chiefly motor, within the central nervous system. Coghill spoke of them as "partial patterns" which were "individuated" from the total pattern. However, Coghill was convinced that in *Amblystoma* the total pattern was always "dominant" over the partial patterns, though inhibited during the activity of local reflexes.

This concept of the development of behavior in *Amblystoma* is now generally accepted. Some of the original objection to it was based on the fact that the concept seemed to parallel the point of view of *Gestalt* psychology, which has not enjoyed universal acceptance. However, the great amount of detailed evidence furnished by Coghill was close to irrefutable.

Coghill believed that the concept of total pattern and partial pattern derived from his studies on *Amblystoma* established a principle basic to the development of behavior in all vertebrate forms. As he stated (1929a), "There is nothing

in our knowledge of the development of behavior to indicate that the principle does not prevail universally in vertebrates, including man." To test this belief, he set two of his students at Kansas, Swenson and Angulo, to the problem of the development of behavior in the fetal albino rat. The preliminary results confirmed Coghill's belief that his principle of total pattern and partial pattern held good for that form. Other persons who worked with him directly and still others who began studies quite independently on other vertebrates secured results which aligned them with the Coghillian concept.

However, not all students of embryonic behavior agreed with the Coghillian concept of behavioral development. Swenson had become impressed by the explosive activities of rat fetuses when the umbilical cord was ligated (1928b), a phenomenon often seen in many mammals but not in man. In the rat (1928a), he thought he recognized "simple movements." After he had left the Wistar Institute, he stated (1929) that local, "simple movements" could be elicited from rat fetuses and conceived of these as forming the building stones of behavior, which grew by the addition of one "simple movement" to another into the characteristic behavior of the organism. Windle and his co-workers, after tentatively agreeing with a Coghillian sequence in their first study on cat embryos (Windle and Griffin, 1931), became interested in local movements which could be elicited by certain specialized types of stimulation and swung over to Swenson's thesis.

Many investigators have studied the development of behavior in the embryos of a wide variety of vertebrate forms. Divergent conclusions have been drawn from the results secured. However, most fall into one or the other of two concepts, either into the concept of total pattern and partial pattern outlined by Coghill, or into the unit-plus-unit idea

originally put forward by Swenson and espoused by Windle.

No one, least of all Coghill, imagined that all animals in all vertebrate classes would develop their behavior exactly as does *Amblystoma*, any more than one would expect that all animals in these classes would develop structurally as does *Amblystoma*. There are great structural differences between animals within a class and greater between those in different classes. The question, however, was and is, Do all vertebrates, whatever their class and however greatly their adult structure and their adult behavior may differ, go through their early development, both structurally and behaviorally, in a sequence that has a definite, essential, basic similarity in principle or does each have a development that is unrelated to any developmental principle?

If one shifts the emphasis from the manifest differences between adults and later fetuses of vertebrate forms to their possible basic similarities in embryonic life, too much confirmatory evidence exists to deny that there is a definite basic principle continuously present throughout the morphological development of embryos in all vertebrate classes. This is, perhaps, best illustrated in the development of the nervous system itself. No "higher" form repeats the adult stage of any "lower" form, as the long-since discredited "recapitulation theory" once maintained, and equally there is no basic similarity in the method of development of vertebrate and invertebrate animals (see Meyer, 1935). If, however, there is a common basic principle governing the structural development of all vertebrate embryos, the question whether there also exists a common basic principle in vertebrate functional development very naturally arises. Indeed, it is forced upon us, if structure determines function.

Unfortunately, the work to date in this field offers no unequivocal proof one way or the other. Many investigators,

perhaps a majority, have offered evidence consonant with the view that there is a basic principle of structural development at work in the early embryos of the vertebrate series and that early functional development consequently also proceeds along similar lines, allowing for class, generic, and specific differences. Among those whose results and interpretations seem to favor such a point of view are: Pankratz (1931) on the rabbit; Tuge (1931) on the terrapin; Angulo (1932-1951) on the rat; Coghill (see Herrick, 1949, p. 96 *et seq.*) on the toadfish; Tuge (1934, 1937) on the pigeon; Youngstrom (1938) on *Rana*, *Bufo*, and other anurans; Barcroft and Barron (1939a, 1939b) on the sheep; Wang and Lu (1941) on *Rana*; and Smith and Daniel (1946) on the loggerhead turtle. The evidence furnished by these investigators has been highly favorable to the assumption of Coghill that the concept of total and partial pattern determined for *Amblystoma* applies to the embryonic functional development of other vertebrates.

However, others have opposed this concept. Some, such as Swenson and Windle (the latter in his papers after 1931), have embraced the concept of the cumulative union of "simple movements" to form behavioral patterns, though admitting the probable truth of the Coghillian sequence for *Amblystoma*, but for that genus only. Still others believe that each form is different from all others in the formation of its own pattern of behavior. Kuo (1932, 1938), working on chick embryos, rejected both the Coghillian and Windelian concepts. The results secured by Coronios (1933) on cat embryos afforded some support to the existence of a Coghillian sequence in that form. However, neither Coronios nor Carmichael, under whose direction the cat fetal studies were made, has any particular sympathy with the total-pattern ideas of Coghill. Carmichael himself (1934) made probably the most thorough study of reflexogenous

areas as yet undertaken on any fetal form. He used the fetal guinea pig, and his results are both interesting and instructive. As interpreted by him (and, indeed, in actuality), they do not support the total-pattern concept. Bridgman and Carmichael (1935) continued the work on guinea pigs. Again, their results do not support the total-pattern concept, but indicate that independent (though in no sense "simple") movements may occur at almost any time in fetal life in that form.

Brief reference has already been made to the views of Windle and his associates, but their evidence cannot lightly be brushed aside. More than 20 communications between 1930 and 1950 have adequately set forth the views of their senior or sole author on the basis of studies on fetuses of cat, rat, guinea pig, and man. Windle has not only championed the concept that behavior is primarily built up by the progressive addition of "simple" reflexes secondarily integrated into a functional whole, but he has also claimed that the total-pattern type of response can be secured only from mammalian fetuses suffering from oxygen want (Fitzgerald and Windle, 1942). The effects of anoxia are considered below, but it should be stated clearly here that most neuro-embryologists consider the integrative processes in the nervous system to occur in normal development as a primary procedure, antedating the beginning of functional capacity in any part of the nervous system.

A factor that often may prove puzzling in the interpretation of results is the exact nature of the stimulus applied. Coghill used human hairs to apply tactile stimulation to his *Amblystoma* embryos. In the Pittsburgh human fetal studies, discussed below, both human and horse hairs were used as stimulators. These were very carefully calibrated on a delicate balance to insure that the maximum pressure exerted did not exceed 10, 25, 50, or 100 milligrams or 2, 5,

or 10 grams in each category. Other investigators have used steel and fiber needles, scalpels, forceps, camel's hair brushes, glass rods, metal probes, and even cactus thorns. Light stimulation can be applied with such instruments, if sufficient care be taken, but there is no way of proving that the stimulation was light in any given case. Windle implies (1944) that strong stimulation is required to elicit movements of the early type obtained in the Pittsburgh studies, but we have elicited them routinely with hairs having "pressure values" of from 10 to 50 milligrams. It is not the pressure of a single "spot" type of stimulation that evokes responses, but the brushing of the stimulator over the reflexogenous area that elicits reflexes. This affords spatial summation over a series of sensory endings.

The mammalian embryonic integument is thin, and the underlying muscles may readily be excited to contraction by pressure exerted upon them. Direct mechanical stimulation of even small groups of muscle fibers may sometimes be seen through the semitransparent skin. In the Pittsburgh studies, hairs with "pressure values" of 50 or 100 milligrams were often used, but every embryonic response has been tested at some time, often repeatedly, with 10- or 25-milligram hairs to prove the exteroceptive nature of the resulting reflex and to establish the identity of its character under both conditions.

The problem of oxygen want or anoxia in mammalian fetal studies has already been mentioned. Without question, the best way in which to observe mammalian fetal reflexes is with the fetus in the opened uterus with intact placental connections, but without deep maternal narcosis. These conditions impose the serious problem of immobilizing the mother animal. Swenson (1925), Angulo (1932), Windle and Minear (1933), and others have accomplished this by producing maternal brain anemia by ligating blood

vessels to the head in the rat and other small mammals. Barcroft and Barron (1939a, 1939b) used spinal anesthesia on their sheep.

Few investigators of human embryos and fetuses have been able to observe them with intact placental connections. Where the specimens for observation are secured by operation, the welfare of the mother is paramount, especially as such operations are performed only for the most compelling medical reasons. In spontaneous premature deliveries, the fetal portion of the placenta ordinarily separates before examination of the fetus can be completed. Separation of the placental connections and consequent removal of the fetus immediately impose a number of additional complications, chief among which is anoxia.

The effects of anoxia are definite, and, to date, little has been accomplished in the way of combating them. If the time between beginning placental separation and the initiation of observations is short (not longer than one and a half to two minutes), even the very young human embryo may exhibit activity which we have come to recognize as characteristic for its age. Then there ensues a gradual slowing of responses, though they are still characteristic. Eventually, within a matter of seven to 10 minutes for young embryos, and longer, up to 20 minutes, for somewhat older fetuses, all activity ceases. When respiration may be established, observations may be greatly prolonged beyond these time limits. It is usually possible to establish respiration on at least a temporary basis when the fetus is about 23 weeks old.

The belief of the Pittsburgh investigators that the reflexes elicited by tactile stimulation are normal is based on two considerations. In the first place, these reflexes form a continuous series consonant with the morphologic development of the fetal nervous system as shown by Hogg (1941),

Humphrey (1952, 1954, 1955), and Brown (1956a, 1956b). Second, a careful study of the literature on reflexes that undergo progressive anoxial states indicates that, so long as reflexes can be elicited, they are an entirely normal expression of the functional capacity of the reflex arcs involved (Humphrey, 1953). It should be stated, however, that progressing anoxia does suppress the most recently developed reflexes so that all exteroceptive responses disappear in the reverse order of their development (Angulo, 1935; Humphrey, 1953; Hooker, 1954). Consequently, reflexes observed as anoxia increases do not necessarily indicate the most recent functional development. Only those reactions observed immediately upon delivery most nearly indicate the functional capacity of the age level considered.

Another factor which must be given careful consideration in the observation of human embryos and fetuses removed from the uterus or seen *in utero* is the effect of maternal anesthesia on the specimen being observed. Anesthetics used in the operations pass readily through the placenta in most cases and may have widely varying effects on the fetus. These range from the abolition of all fetal responses, as is the case with heavy doses of the barbiturates, to no discernible modification of movement or response, as in the case of local or spinal novocaine. Maternal anesthesia under local or spinal novocaine, with only Demerol and atropine sulphate as preliminary medication, is undoubtedly the optimum for the observation of operatively removed fetuses. As the selection of drugs for premedication and anesthesia is exclusively the prerogative of the surgeon, many fetuses have been tested under less than optimal conditions. However, anesthetics, like anoxia, do not appear to alter the essential character of the reflexes elicited, but rather to suppress more recently developed reactions (see Humphrey, 1953).

At least as important for fetal observations as anoxia or anesthesia is the care used in handling mammalian fetuses of the younger ages. These are delicate organisms, easily injured by even slight added pressures exerted on them. Such injury materially shortens the period of reactivity, although it does not alter the character of those responses that are elicited.

It is also essential that avian and mammalian embryos and fetuses be maintained at temperatures close to those of their incubation or intra-uterine environment. Chilling will cause activity to cease within a very short time. For this reason, early mammalian fetuses must be immersed in a constant temperature bath of physiological saline or other isotonic solution at all times. However, we have observed that slight variations from normal temperatures appear to facilitate the activity of human fetuses.

Isolated accounts of observations made on single human fetuses have appeared in the literature for over a century. Usually these fetuses were observed under quite unfavorable conditions. Hence the recorded results are open to question.

The first series of scientific observations of human fetuses was that of Minkowski, summarized in his publication of 1928, though begun in 1920 or earlier. He studied some 75 human cases, and his observations are the classic foundation of human fetal studies. The work of Bolaffio and Artom (1924) was unfortunately not always done under favorable conditions.

In the autumn of 1932, it became possible to begin a study of human fetal reflex behavior in the Department of Anatomy at the School of Medicine of the University of Pittsburgh. Those who entered on these studies are greatly indebted to many of their clinical colleagues in several of

the hospitals of that city and its environs for the opportunity to observe fetuses that became available, some prematurely delivered spontaneously, some derived from operations to conserve the life of pregnant women. During this period of over 24 years, 149 cases have come to observation, ranging from six weeks of menstrual age to a postmature of 45 weeks. In the following account, menstrual age estimated from the Streeter (1920) tables is used. This age is two weeks, plus or minus two or three days, longer than actual age, which of course cannot be determined.

As is mentioned above, morphologic methods of study do not permit the determination of the time when functional synaptic relations are established. The appearance of the various reflexes themselves, therefore, offers the most satisfactory evidence of function in the central nervous system of the human fetus. Consequently, in the following description of these reflexes the reflex arcs that probably function are mentioned in many instances.

In human embryos, the area of integument first sensitive to tactile (exteroceptive) stimulation and capable of eliciting reflexes is restricted to that portion of the face about the mouth and the lateral aspects (alae) of the nose. The receptor nerves from this region belong to the maxillary (V_2) and mandibular (V_3) divisions of the trigeminal (V) nerve. This restricted area of sensitivity gradually expands until, at about 14 weeks, it more nearly corresponds to that of the adult supplied by these two divisions.

The first reflex elicitable by stimulation with 10- or 25-milligram hairs in the restricted perioral region of the face occurs from the middle of the seventh week to the beginning of the eighth week. It consists of a contralateral flexion of the neck. At this time the embryo is 20 to 23 mm. in crown-rump (CR) length. Only a few such reflexes have been observed, and not all fetuses tested in this age range

exhibited responses. Fitzgerald and Windle (1942) report having observed this type of response in two cases. No case of an ipsilateral response has been seen before eight weeks, but such does occur occasionally at the latter age. It is, of course, possible that it may occur earlier, but it has not been seen in the few reflexes so far elicited. It should be borne in mind that this and other accounts of human fetal activity

TABLE 1

FIFTH CRANIAL NERVE REFLEXES IN THE HUMAN EMBRYO AND EARLY FETUS:
SOMATIC REFLEXES, 1

| Menstrual Age in Weeks | Region of Stimulation | Divisions of V Involved | Nature of Response |
|------------------------------|--------------------------|--|--|
| 7½ | Perioral | V ₂ and V ₃ (limited) | Contralateral flexion of neck (avoiding) |
| 7½-8 | Perioral | V ₂ and V ₃ (limited) | Contralateral flexion of neck and uppermost trunk, with at most slight quivering of upper ex- tremities |
| 7½-8½ | Perioral | V ₂ and V ₃ (expanding) | Chiefly contralateral flexion of neck and upper trunk, with extension of both brachia at shoulder and slight rotation of pelvis towards contralateral side, all movements becoming more pronounced and trunk flexion extending farther caudad as 9½-week age is approached |
| 10½ | Perioral | V ₂ and V ₃ | Contralateral trunk flexion, with occasional trunk extension |
| 11-12 | Perioral | V ₂ and V ₃ | Relatively constant trunk ex- tension, with medial rotation of both brachia and head rotation away from stimulus; returning to contralateral flexion when anoxia increases |

can record only observed movements. As the Pittsburgh studies have progressed, it has been necessary to revise both the repertoire of reflexes observed and the earliest age at which they have been seen.

As the eight-week period is attained (table 1), the extent of the trunk response to stimulation of the restricted maxillomandibular region spreads caudally to include the uppermost part of the trunk. This caudal expansion of the neuromuscular mechanism capable of responding to stimulation in the perioral skin area continues until, by $8\frac{1}{2}$ to $9\frac{1}{2}$ weeks, the entire trunk is involved in the usually contralateral response. During this period also, the area of integument sensitive to stimulation increases in extent, although it does not attain the typical distribution of the maxillary and mandibular divisions of the trigeminal until 11 to $11\frac{1}{2}$ weeks.

During the expansion of the neuromuscular mechanism between 8 and $9\frac{1}{2}$ weeks, the trunk flexion becomes more complete and, though discernible at $8\frac{1}{2}$ weeks, pelvic rotation is increasingly evident from that age to $9\frac{1}{2}$ weeks. Although the trunk flexions are predominantly contralateral during this period, ipsilateral flexions occasionally occur.

As the trunk response extends below the shoulders, both brachia extend (move backward) at the shoulder joint. The arm extension is quick, and the brachia return to the resting position before the trunk. At this time, there is no movement at the elbows, wrists, or in the hands. In one case observed at 8 weeks (22.6 mm. CR), the brachia appeared to "quiver," as though their neuromuscular mechanism were almost, but not quite, at the point of participation in the contralateral flexion of the trunk. The brachia move only with the trunk, having no capacity for independent movement before $10\frac{1}{2}$ weeks, and then only seldom.

It is during this two-week period between $7\frac{1}{2}$ and $9\frac{1}{2}$ weeks of age that the method of stimulation must be most carefully controlled. Even what appears to be rather light stimulation of the integument over the trunk muscles may exert enough pressure to result in their direct mechanical stimulation. It is therefore imperative to test with truly light tactile stimulation, although the movements that result from direct stimulation can readily be distinguished from reflexes. Muscle contractions evoked by direct mechanical stimulation of the musculature are localized, ipsilateral, and without the accompaniment of other elements of the typical reflex, such as brachial extension or pelvic rotation.

Little change in the nature of the trunk reflexes elicited by stimulation of the perioral region of the face occurs between $9\frac{1}{2}$ and $10\frac{1}{2}$ weeks of age. As the latter age is approached, however, there is a tendency for the trunk flexion to give way to trunk extension. At first, trunk extension appears only occasionally in a series largely consisting of contralateral trunk flexions. By 11 or 12 weeks, trunk extension has become the predominant type of body-wall (somatic) muscle reflex elicited by stimulation in the area of sensory supply through the maxillary and mandibular divisions of the trigeminal nerve.

At this age also the brachial movement accompanying the trunk response changes to a medial rotation, rather than an extension, of both brachia, but there is still no movement at elbow or wrist as a part of the arm response elicited by trigeminal nerve stimulation. The head has also altered the nature of its response. It now rotates so that the face is removed from the stimulus by this means, rather than by merely flexing laterally. This type of response continues, with little alteration, as typical of the human fetus until 13 or $13\frac{1}{2}$ weeks of age.

That certain fibers of the trigeminal nerve constitute the earliest receptor pathway to develop in the mammals has been demonstrated morphologically by Windle (1932, 1933) for the cat, by Angulo (1951) for the rat, and by Windle and Fitzgerald (1937) and by Humphrey (1951, 1952, 1954) for man. It has been confirmed physiologically by Barcroft and Barron (1939a, 1939b) for the sheep and by the Pittsburgh investigators (Hooker, 1939, 1942, 1944, 1952; Hooker and Humphrey, 1954) for man.

Humphrey, by a microscopic study of serial sections of a number of human fetuses, was able to determine the fetal age at which fibers of the spinal tract of the trigeminal nerve reach the spinal cord (1954) and add new evidence regarding the ultimate point of termination of its three divisions at spinal cord levels (1951, 1952, 1954). By 8½ weeks, maxillary and mandibular fibers were found, in one case, to reach the cephalic part of the fourth cervical segment of the cord and, by 9½ weeks, ophthalmic fibers appear to extend as far caudalward as do those of the other two divisions (1954). Of more interest from the standpoint of fetal activity is Humphrey's observation that, by 6½ weeks, all three divisions of V have reached the first cervical segment and, by 7½ weeks, the age at which the earliest reflex in response to perioral stimulation has been observed, these fibers have grown throughout the first and into the second cervical segment of the spinal cord (1954). Later, the maxillary and mandibular fibers, those first responding to stimulation, outdistance the ophthalmic fibers in their growth caudalward, but by 9½ weeks the ophthalmic fibers have reached approximately the same caudal levels as the others.

Even before the spinal tract of the trigeminal reaches the spinal cord, Windle and Fitzgerald (1937) noted that commissural fibers were well developed in the upper cerv-

ical levels of the spinal cord. At 7½ weeks, when the first reflex has been observed, these commissural fibers, connecting the area of termination of the spinal tract of V with the contralateral ventral horn motor neurons, are well developed, as Humphrey (1952) has shown. Consequently Humphrey (1952) suggested that this pathway constitutes the reflex arc whereby contralateral flexion in the neck region occurs in response to perioral stimulation. Similar commissural connections with the contralateral spinal accessory (XI) nucleus enable the sternomastoid and trapezius muscles to participate in producing this reflex. Later, when the face is rotated away from the site of stimulation, either collaterals from these commissural fibers or internuncials between V and the ipsilateral nucleus of XI will aid in producing the rotation.

We know from the results detailed above that there is a reflex arc system which becomes functional at about 7½ weeks in the human fetus. The maxillary and mandibular divisions of the trigeminal nerve serve as the receptors of this arc which finds effector neurons in the contralateral cervical spinal nerves as well as in the contralateral spinal accessory nerve. These maxillary-mandibular reflexes, so far described, affect only the trunk musculature and hence have been denominated as somatic in character. They form an expanding type of trunk response with upper and lower extremity participation only in conjunction with the trunk movements. They are, then, the counterparts of Coghill's total-pattern responses (see p. 8). However, beginning at about 9½ weeks, certain local facial reflexes (table 2) make their appearance. At this age, of course, not all the trunk responses to be elicited by trigeminal stimulation have fully developed.

The first local facial response to appear is active but incomplete opening of the mouth by lowering of the mandi-

TABLE 2

FIFTH CRANIAL NERVE REFLEXES IN THE HUMAN FETUS: LOCAL REFLEXES OF THE FACE

| Menstrual Age in Weeks | Region of Stimulation | Divisions of V Involved | Nature of Response |
|------------------------|---------------------------------|-----------------------------------|--|
| 9½ | Edge of lower lip | V ₃ | Active mouth opening by lowering of mandible |
| 10-10½ | Upper eyelid | V ₁ | Occasional contraction of orbicularis oculi muscle |
| 10½ | Rima oris | V ₂ and V ₃ | Deglutition |
| 11 | Upper eyelid | V ₁ | Occasional contraction of corrugator supercilii muscle |
| 12½ | Tongue and/or rima oris | V ₂ and V ₃ | Momentary lip closure and, if repeated, deglutition |
| 12½-13 | Upper lip or, rarely, lower lip | V ₂ and V ₃ | Contraction of orbicularis oculi muscle |
| 13 | Rima oris | V ₂ and V ₃ | Maintained lip closure |
| 13-14 | Upper lip and nose ala | V ₂ | Contraction of quadratus labii superioris muscle and rotation of head away from stimulus |
| 17 | Upper lip at rima oris | V ₂ | Protrusion of upper lip |
| 20 | Lower lip at rima oris | V ₃ | Protrusion of lower lip |
| 22 | Rima oris | V ₂ and V ₃ | Simultaneous protrusion and pursing of both lips |
| 29 or before | Rima oris | V ₂ and V ₃ | Audible sucking |

ble. This reflex is elicitable at about 9½ weeks, following stimulation of the edge of the lower lip. It has been elicited only by stimulation of the mandibular division of the trigeminal nerve. The sensory fibers of this division (V_3) pass through the spinal tract of the trigeminal to the spinal nucleus of V, thence by intermediate neurons to the ventral horn motor neurons of the first three cervical nerves which innervate certain suprahyoid and infrahyoid muscles participating in mouth opening (Humphrey, 1954). In as much as there is no indication of activity of the facial nerve (VII) until 10 to 10½ weeks, when there is "squinting" of the eyelid (see below), and no indication of action over the motor fibers of the mandibular division of the trigeminal before 12½ weeks, when mouth closure occurs, the incomplete mouth opening at 9½ weeks is probably unrelated to the action of muscles innervated by either of these nerves (VII or V_3).

Within a few days thereafter, at 10 to 10½ weeks, the area of integument over the upper eyelids becomes sensitive to tactile stimulation. This region, along with the forehead, is supplied with sensation by the ophthalmic division (V_1) of the trigeminal nerve. Restricted at first to the upper eyelid, very light tactile stimulation of this area causes a "squinting" of the eyelid, a contraction of most of the fibers of the orbicularis oculi muscle. When it is first seen, the eyelid "squinting" is only occasionally elicitable, but becomes constant by 11 to 12 weeks. At 12½ to 13 weeks, an eyelid "squint" has been observed to follow stimulation of the upper lip or, rarely, of the lower lip. In this case, the reflex arc consists of sensory fibers of the maxillary division of V, or more rarely of those in the mandibular division, the impulse passing through internuncial neurons to the facial nerve (VII).

At 10½ weeks, also, repeated stimulation of both lips

sometimes, though rarely, causes swallowing. Though deglutition may at times be elicited under certain conditions from this age on, it is not frequent until near the middle of gestation. If better tests are found, it is quite possible, however, that swallowing might be more frequently observed than it has been heretofore.

By 11 weeks, that is, shortly after the eyelid "squint" has first been seen, the sensitive area supplied by the ophthalmic division of the trigeminal spreads onto the forehead. Stimulation over the upper eyelid or near the eyebrows may then cause occasional scowling. Both "squint" and scowling become quite constantly elicitable as reflexes when the upper eyelid is stimulated by 12 weeks. These reflexes would presume the functioning of intermediate neurons between the spinal nucleus of V and the facial nucleus (Humphrey, 1954).

Opportunities to test the tongue do not often present themselves, as the mouth is rarely open sufficiently for the tongue to be touched without at the same time stimulating the lips. The earliest that tongue stimulation has definitely been accomplished is at 14 weeks, but it is possible that it may yet be carried out at an earlier age. Tactile stimulation of the tongue at 14 weeks resulted in its withdrawal. Sensory fibers from the anterior two-thirds of the tongue, the only region so far stimulated, pass along the lingual nerve (V_3). All the tongue muscles concerned with its retraction are innervated by the hypoglossal nerve (XII). Hence by 14 weeks, if not before, evidence exists for a functional reflex arc consisting of V_3 -internuncial neurons-XII.

By 12½ weeks, also, stimulation of the maxillomandibular complex at the rima oris causes momentary lip closure and, if repeated, has elicited swallowing. This is evidence of the ultimate passage of trigeminal nerve impulses to the facial nerve (VII) for the lip closure and to the glossopharyngeal

(IX) and vagus (X) nerves for the swallowing. By 13 weeks, stimulation of the rima oris may cause maintained lip closure. At this age as well, the first active mouth closure by mandibular movement has been observed on stimulation of the lower lip alone. This activity is additional evidence of trigeminal sensory (V_3) connections with the motor root of V, via internuncial neurons. The motor root of V accompanies the fibers of the mandibular division to the muscles of mastication.

Between 13 and 14 weeks, depending on the level of maturation of the neuromuscular mechanism in the particular fetus observed, general trunk responses to stimulation of the maxillary and mandibular divisions tend to cease in large part, as mentioned above. From this time on, stimulation of any of the skin areas supplied by the trigeminal nerve causes chiefly local reflexes. At this age also, stimulation of the side of the upper lip and the wing (ala) of the nose elicits contraction of the quadratus labii superioris muscle which elevates the upper lip and the ala of the nose, producing what has earlier been referred to as a "sneer" (Hooker, 1952, etc.). The effector element in this reflex is again the facial nerve (VII). It may be noted that the various branches of VII become functional not all at the same time but in a somewhat seriatim manner. Ordinarily, the response consisting of elevation of the upper lip and nasal ala is accompanied by rotation of the head, which carries the face away from the stimulus.

Rotation of the head, turning the face away from the stimulus, is an avoiding reaction, as was the earliest head movement, contralateral flexion, seen at $7\frac{1}{2}$ weeks and older ages (see Coghill, 1916; Angulo, 1932; Hooker, 1952; Humphrey, 1952, 1954; Hooker and Humphrey, 1954). Each of these responses, and each equally effectively, separates the sensitive area of facial skin from the stimulus. At

13 to 14 weeks, the same avoiding reaction by the turning of the face away from the stimulus is seen as a local reflex, without other trunk participation, and not as a part of a general trunk response. As a component of the quadratus labii superioris reflex, head rotation is none the less produced by a reflex arc originating in V_2 or V_3 and passing through intermediate neurons to contralateral cervical nerves, as it was at 11 to 12 weeks, when it was part of the trunk response.

It might be pointed out here that reflexes elicited by stimulation of the mucous membranes of the lips and tongue (opening of the mouth, tongue movements, deglutition, lip closure, and mouth closure) are successive phases in the development of the feeding responses (Hooker and Humphrey, 1954). The remainder of the phases in the development of feeding responses may be covered briefly. At 17 weeks, stimulation of the mucous membrane of the upper lip causes that lip to protrude. No protrusion of the lower lip, upon its stimulation at its edge, has been observed before 20 weeks. Between $12\frac{1}{2}$ and 20 weeks, the lower lip merely closes. However, at 20 weeks, both lips protrude on stimulation of the rima oris and, at 22 weeks, are pursed as well. The earliest that sucking movements have been observed in this study is at 29 weeks. There is some clinical evidence that sucking movements may occur earlier, although by no means all premature infants are capable of nursing if much younger than 28 or 29 weeks of menstrual age at birth.

In the foregoing review of human fetal reflexes, whether of the trunk or entirely local, for which one or another of the divisions of the trigeminal nerve has served as the receptor part of the arc, it is evident that the fifth cranial nerve makes connections, via various internuncial neurons, with six of the cranial nerves (V, VII, IX, X, XI, XII) and with a series of cervical spinal nerves.

The fibers of V, given off by the cells in the Gasserian

ganglion, enter the central nervous system to synapse with intermediate neurons which lie wholly within the medulla and spinal cord. The effector nerves of all these reflex arcs originate within the central nervous system, though their fibers leave it to be distributed to the muscles concerned. Thus, evidence has been afforded to demonstrate that the central nervous system in human fetuses is capable of functioning, not only prenatally, but very early in gestation.

TABLE 3

SPINAL NERVE REFLEXES IN THE HUMAN FETUS: LOCAL REFLEXES OF THE UPPER EXTREMITY

| Menstrual Age in Weeks | Region of Stimulation | Nature of Response |
|------------------------------|--------------------------|--|
| 10½ | Shoulder | Rare independent extension of brachium |
| 10½ | Palm | Occasional partial finger closure, rarely with pollex flexion |
| 11 | Palm | Constant partial finger closure, usually with wrist flexion, sometimes with elbow flexion, medial rotation of brachium, or forearm pronation |
| 11½ | Shoulder | Occasional abduction of brachium |
| 13 | Palm | Occasional nearly complete finger closure, rarely with pollex opposition |
| 13½-14 | Palm | Occasional complete finger closure |
| 15-15½ | Palm | Maintained finger closure |
| 18½ | Palm | Weak, true grasp |
| 27 | Palm | Sufficient grasp almost to support body weight momentarily |

There is, however, additional evidence still to be adduced for functioning of the central nervous system in fetal life.

After both trunk and local reflexes have been elicited by trigeminal stimulation, but before either type has completed its repertoire, local reflexes can be evoked in both the upper and lower extremities (tables 3 and 4). Whereas both upper and lower limbs begin their movements as components of the trunk activities, at about 10½ weeks independent limb movements are exhibited. These local reflexes are mediated by reflex arcs through the spinal cord, consisting of spinal ganglion cells, internuncial neurons, and motor neurons. Consequently, these reflexes, as well as those involving cranial nerves, are indicative of functioning of the central nervous system.

At 10½ weeks, stimulation of the shoulder with hairs having sufficiently low "pressure values" to insure that the resulting movement is a reflex, not caused by direct mechanical stimulation of the muscles involved, has in a few cases elicited extension of the brachium. At about this age, possibly a little before, light stimulation in the palm may cause a quick, partial closure of the fingers, except the thumb. The pollex has been observed to flex as well, but this is rare at almost any fetal age. A few days later (11 weeks), nearly every fetus exhibits partial finger closure on palmar stimulation. Usually, at this age, the wrist also flexes. At times, elbow flexion, medial rotation of the brachium, forearm pronation, or all three movements may accompany the finger flexion.

By 11½ weeks, occasional abduction of the brachium may occur as part of the local reflex of the upper extremity. This is always followed by brachial adduction, as part of the return to its resting position. It so happens that abduction or adduction of the brachium at the shoulder has not been recorded as an independent movement before 27 weeks.

Halverson (1937) has concluded from his studies that prehension in children involves two elements, finger closure and grasp, appearing in that order. These two components of postnatal prehension have a reflex background in fetal life, and in the same sequence. The appearance of partial finger closure at about 10½ weeks and its development into a constant response at 11 weeks are described above. Finger closure remains only partial until 14 weeks, when a few fetuses exhibit almost complete flexion of the fingers. The number of fetuses showing complete finger closure increases by 14 weeks, but the reflex is still quick, with almost immediate opening of the hand. It is not until 15 to 15½ weeks that the immediate return of the fingers to the resting position ceases in a few fetuses. By 18½ weeks, the first evidence of true grasp occurs when a glass rod or a hair may be retained inside the closed fist. Grasp at this time is weak, and any object held by the fingers may easily be withdrawn. However, grasp becomes steadily stronger and by 27 weeks will nearly support the body weight momentarily. As yet, no case of simultaneous bimanual grasp has been observed. In each case tested, a true grasp with one hand is immediately released when a similar object is placed in the palm of the other, and it has proved impossible to secure grasp when both hands are simultaneously presented with any object.

Prechtl (1953) has mentioned the difficulty of securing the grasping reflex in premature infants of 1200 to 2500 grams except while the babies were suckling quietly. He further states that neonates at term, before suckling, exhibit only weak grasp which becomes stronger during feeding. However, a few weeks after the neonatal period, strong grasp may be elicited without simultaneous sucking activity. In our observations, there is no question of the effectiveness of the grasp exhibited by at least one 27-week fetus in which

this reflex was sought within 15 minutes after birth. It has proved difficult to elicit grasp from many fetuses in this general age range, and we have been unable to test the grasp reflex during feeding in any premature infant.

Up to this point in our discussion we have been concerned only with exteroceptive reflexes, those elicited by external stimulation. Another type of reflex is manifest early in fetal life. This is the proprioceptive reflex. Whenever the length of a muscle is altered as a result of mechanical stretching, proprioceptive sensory endings within the muscle are stimulated. The reflexes set up through these arcs have to do primarily with postural effects or with adjusting the action of the muscle concerned to its activity (see Herrick, 1947). In general these reflexes are mediated by two-neuron arcs, though intermediate neurons may be present in some cases. If a muscle is stretched by even an infinitesimal amount, a stretch or myotatic reflex is induced. In the Pittsburgh studies, the first clearly demonstrable stretch reflexes occur at 9½ weeks. Windle (1944) believes that they may occur much earlier. He has ascribed the upper extremity movements reported by him at 7½ to 8 weeks, and elicited by tapping on the amnion or by "flipping" the limb, to the group of stretch reflexes. As stretch reflexes are always highly localized and affect only the part stimulated, they might give the appearance of being "simple movements." It would thus appear that the "simple movements" of Swenson and Windle might be of this nature, although we have never observed them at so early an age. It may well be that such reflexes do occur earlier than we have seen them. If the "simple movements" of Swenson and Windle are of this nature, they play but a minor role in the development of fetal behavior, because stretch reflexes remain localized in nature even in the adult (see Humphrey, 1953). Their chief significance would probably lie in the realm of postural rela-

TABLE 4

SPINAL NERVE REFLEXES IN THE HUMAN FETUS: LOCAL REFLEXES OF THE LOWER EXTREMITY

| Menstrual Age in Weeks | Region of Stimulation | Nature of Response |
|------------------------|-----------------------|--|
| 10-10½ | Sole of foot | Plantar flexion of all toes |
| 11½ | Sole of foot | Either plantar flexion of all toes or dorsiflexion of hallux and fanning of other toes, sometimes with knee flexion, then extension (as a kick) and with hip flexion, rotation, or abduction |
| 12½ | Sole of foot | Principally dorsiflexion of hallux and toe fanning, dorsiflexion of foot at ankle, flexion at knee and hip |
| 13½ | Sole of foot | Occasional dorsiflexion of all toes |
| 32 or before | Inside thigh | Cremasteric reflex |

tions. At 9½ weeks, in the Pittsburgh studies, stretching of the biceps muscle or repeated stretching of the fingers has given some evidence of the presence of stretch reflexes.

Although the first reflex elicited by stimulation of the sole of the foot (table 4) has been seen in the same age group (10 to 10½ weeks) as the first appearance of partial finger closure on palmar stimulation, in any individual fetus exhibiting a plantar response the finger-closure reflex is already established. Observations by Angulo (1935) and others have demonstrated that the most recently established reflex is the first to be extinguished by progressive anoxia (see also Humphrey, 1953). Double simultaneous stimulation tests of palm and sole (see Hooker, 1954) have also shown that anoxia extinguishes the plantar reflex before the palmar reflex disappears. This earlier suppression of the plantar reflex, as

anoxia progresses, offers added evidence for its later appearance developmentally.

In the human fetuses tested in the Pittsburgh studies, the earliest response observed on stimulation of the sole of the foot was plantar flexion of all toes at 10 to 10½ weeks. This is in agreement with the extensive plantar reflex studies of Minkowski (1923). However, in a later communication, Minkowski (1928) revised his opinion on the basis of further observations, then stating that the earliest plantar reflex might be either plantar flexion of all toes or dorsiflexion of the big toe (hallux) and fanning of the other toes. It has proved difficult to set exact ages for the fetuses examined by Minkowski, but it is our belief that the age of the youngest fetus observed by him was also about 10 weeks. In the Pittsburgh studies the earliest mixed responses to plantar stimulation were not found until about 11½ weeks. At this time, the same fetus may exhibit both types of response interchangeably. Whichever type of response is exhibited, it is often accompanied by flexion at the knee, then quick extension of the leg in a kick. At the same time, the thigh may flex, rotate in either direction, or abduct, with subsequent return to resting position.

From about 12½ weeks until birth (and for a time thereafter, for that matter), the plantar reflex takes the form chiefly of a dorsiflexion of the hallux and fanning of the other toes. This is a Babinski-like response. Plantar flexion of all toes may occur at any age, but it is an isolated type of response after 12½ weeks. Furthermore, from 13½ weeks, or possibly earlier, dorsiflexion of all toes may at times be observed as a response to plantar stimulation. In general, this type of response is more rare than plantar flexion of all toes.

It is fully realized that the foregoing account of the se-

quential appearance of exteroceptive reflexes in the human fetus is not a complete statement of all that is known on the subject. Space does not permit a more detailed review of the Pittsburgh studies here. Much remains to be done along several lines, and these studies are not yet completed. Before a few additional comments are made, it seems desirable to place the activities given in their proper relationship to the problem of the development of embryonic behavior in vertebrates.

It may be recalled that the early reflex movements elicited by exteroceptive stimulation of the human fetus begin as a contralateral flexion of the neck at about $7\frac{1}{2}$ weeks. The amount of trunk musculature that participates in the response spreads caudally in accordance with the recognized principle of cervico-caudal differentiation of the neuromuscular mechanism. As the trunk musculature capable of contraction passes the upper extremities and finally reaches the pelvic region, the brachia and the lower extremities move with the trunk. This is clearly an expanding total pattern in the sense in which the term was used by Coghill.

As the nervous system continues its differentiation and new neuromuscular connections are established, specific local reflexes appear, first in the face, then in the upper and the lower extremities and in the trunk (table 5). Such reflexes are not exhibited earlier than $9\frac{1}{2}$ weeks. This appearance of local reflexes after the establishment of the total pattern corresponds to Coghill's description of the individuation of partial patterns from the total pattern.

In consequence, the development of human fetal reflex behavior appears definitely to substantiate Coghill's (1929b) dictum that "the same law prevails in the development of behavior of human beings as that which has been observed in *Amblystoma*." Note that it is the "law" or principle that behavior develops first as a total pattern, from which partial

TABLE 5

SPINAL NERVE REFLEXES IN THE HUMAN FETUS: LOCAL TRUNK REFLEXES

| Menstrual Age in Weeks | Region of Stimulation | Nature of Response |
|------------------------------|--------------------------|--|
| 13 | Chest | Isolated respiratory chest contractions |
| 15 | Abdomen | Abdominal muscle contractions |
| 22 | Chest | Temporary diaphragmatic contractions |
| 23½ | Chest | Temporary effective respiratory chest contractions and phonation |
| 27 | On delivery | Permanent respiration established |

patterns are later individuated, that constitutes the important consideration here. There is no implication that more than this basic principle holds good between man and *Amblystoma* in the development of the behavior of either.

In the human embryo and young fetus, both the reflexes evoked by stimulation of the integument supplied by the trigeminal nerve and the early reflexes of the extremities mediated through spinal nerves are stereotyped in character. Within very narrow limits, each response secured from a given reflexogenous area is, in amplitude, character, and duration, almost exactly like every other elicited by like stimulation of that site in any individual or, indeed, in any fetus of the same response age. The stereotyped character of these early reflexes does not disappear until the fetus reaches 13 or 14 weeks of age. Furthermore, all reflexes that appear later during fetal life are also stereotyped when they are first elicitable and remain so for a period thereafter before they lose this quality.

In the development of postnatal behavior there is fre-

quently, at least, a repetition of the sequence of events seen in the development of fetal reflexes. This is well illustrated, for example, in a comparison of the development of the fetal grasping reflex (Hooker, 1938) with the development of voluntary grasping postnatally (Halverson, 1937). The cortically controlled voluntary act, however, becomes smoothly coordinated and may have great variability.

It has already been indicated that much has been omitted from this review. In some instances, as is the case with the organs of special sense, omission is due to the fact that no significant tests have as yet been made in the course of these studies. The whole problem of spontaneous movements has been ignored. Emphasis has been placed upon early reflex activity to the exclusion of most of the later behavior of the fetus. These, and other, omissions are regretted, but space for their consideration is lacking.

It is hoped, however, that this account of human fetal reflex behavior has demonstrated that the fetal nervous system is able to function at a very early age. If such function occurs *in utero*, human behavior becomes a continuum from about 7½ weeks of menstrual age to death. Whether or not the earliest activities elicited by tactile stimulation ordinarily occur *in utero* during an uninterrupted gestation is beside the point. That the capacity for such movements exists has been demonstrated, and these earliest responses, even though they may not first appear at the same age *in utero*, are part of the continuum of human behavioral development.

The exteroceptive reflex arcs utilized by the fetus are not isolated units. They are components of a primarily integrated nervous system having innumerable connections with other areas of the central nervous system. As the developing organism grows, its nervous system grows with it, making new connections within the brain and spinal cord, as well as with structures outside the central nervous system.

During the earlier part of fetal life, the behavior that develops is purely reflex in nature. The intricate nervous mechanisms which make possible the continuing patterns of reflex behavior lay the foundation for future voluntary acts by the postnatal child. The receptors, the internuncial neurons, and the neuromuscular connections used in early fetal reflex behavior are the structural basis on which later action patterns are built. This is retained and utilized in the development of postnatal behavior.

Not even the reflex arcs are discarded as such. They continue to serve the organism throughout its life. As Sir Charles Sherrington (1950) has pointed out, "Reflex action has contributed much to the integration of the individual. It would seem to be reflex action and not mind which primarily integrated the motor individual." And again, "motor behavior in the individual has two components. One is reflex. . . . The other is superstructure and is not reflex." The superstructure here mentioned is the cerebral cortex. The cortex probably plays no role in early fetal activity, and it is uncertain when it begins to assume its functions. However, as it differentiates and gradually takes over in infancy and childhood, it transforms the patterned activity of late fetal life into the infinitely varied behavior of the child and the adult.

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