molecule, but that of its ions. In a dilute solution of sodium chloride, for example, the osmotic pressure is not measured by the number of molecules, for each ion exercises the same osmotic effect as a molecule of sugar, or as an undissociated molecule of salt.

Each cell in the body may be conceived as the inner vessel of a diffusion apparatus, separated from the surrounding fluids by a membrane, for though this membrane has no anatomical existence, the colloid nature of protoplasm has the same final effect as if the cell were surrounded by a membrane. All cells are permeable by water, but each kind of cell appears to differ in the facility with which it permits the permeation of salts and the other bodies dissolved in the body fluids. Some, for example, allow the passage of ammonium readily, while others refuse it entrance. Others take up sodium sulphate as readily as sodium chloride, while others accept the latter and reject the former. Now if the intercellular fluid contains any substance which is not capable of penetrating the cells, it must exert osmotic pressure on the cell; and unless this pressure is counterbalanced by other bodies in the interior of the cell which similarly cannot escape from it, the fluid of the cell will be drawn out and shrinkage will result. Every cell in the body then must be conceived as existing in a condition of equilibrium, the osmotic tension of the salts, etc., in its interior being pitted against that of the surrounding fluid, and the smallest change in either of these leading to an inflow or outflow of water from the cell. Now such changes are continually in progress, for as the proteids and carbohydrates of the cells are broken down into simpler bodies, soluble in water, each molecule so formed acquires osmotic properties, and either diffuses freely into the surrounding fluid, or causes an inflow of water into the cell. In either case the equilibrium is disturbed until the new product is removed by the excretory functions. The importance of diffusion and osmosis in the functions of the body cannot therefore be overestimated; in fact, it may be said that while the more obvious movements of the fluids of the body are determined by the circulatory mechanism, the finer but no less important exchange between the cells and the intercellular fluid is in large part directed by the laws of diffusion. And while a knowledge of the arterial supply of an organ is recognized to be necessary for an understanding of its physiology and pathology, it is probably no less desirable to ascertain the permeability of its cells for the constituents of the surrounding fluids. The osmotic pressure varying with the nature of the membrane or cell, and also with the salt in solution, the only way to determine the results of exposing the cell to a solution of the salt is the experimental, and a considerable amount of work has been done in this direction, so that the permeability of some cells is known for a large number of salts and other bodies. In this method of procedure the cells under examination, *e.g.*, the red blood cells, are exposed to solutions of different strengths, and the concentration which induces neither shrinking nor swelling of the cell is ascertained. This concentration is that balanced by the intracellular fluid, and the solution is said to be isotonic for that cell. The salt in solution must obviously fail to penetrate the cell, or do so only extremely slowly, for if it permeates freely the water in which it is dissolved will also pass into the cell and expand it. In such an isotonic solution the number of molecules percent is exactly equal to that in the interior of the cell, and a solution containing the same number of molecules and ions of any other non-permeating salt will also be isotonic and cause no change in the size of the cell. For example, if a 0.75-per-cent. solution of sodium chloride has been found isotonic for the blood cells, an equivalent solution of sodium sulphate or of ammonium chloride will also preserve the size of the cells unchanged, provided these salts are equally incapable of permeating the cell. If one of these, *e.g.*, that of ammonium chloride causes swelling of the cell and the escape of hæmoglobin, then this salt must permeate more freely than sodium chloride.

In the case of non-dissociating bodies, such as alcohol, sugar, or urea, equimolecular isotonic solutions can be made by calculating the atomic weights. In the case of the salts this method fails, for the dissociation varies for different salts and for different dilutions, and each ion exercises the osmotic pressure of a molecule. Other methods have therefore been adopted, and of these the estimation of the depression of the freezing point has come into general use in the last few years. This method, it must be emphasized, does not indicate the osmotic pressure for all membranes, nor the permeating qualities of the substance, but only the total number of molecules and ions in the solution. It depends upon the fact that solutions containing the same total number of ions and molecules per cent. freeze at the same temperature, which is lower than that at which distilled water freezes to ice. If two solutions lower the freezing point an equal extent below 0° C., therefore, they contain the same number of ions and molecules, and are isotonic toward a semi-permeable membrane. The estimations are made by means of thermometers reading to $\frac{1}{100}$° C., and allowing of approximations to $\frac{1}{1000}$° C., and with some care and practice in the method very exact determinations may be made. A very extensive use of this freezing method has been made in experimental work, and some results have also been obtained in clinical medicine, but the details of the method can only be given in works dealing specially with this subject. The depression of the freezing point of any solution below that of pure water is generally expressed by the symbol $\triangle$. If the salt is not capable of penetrating a cell, its osmotic pressure varies with the $\triangle$ of the solution, *i.e.*, with the concentration of molecules and ions, and if two solutions of non-permeating salts have the same $\triangle$, their influence on the movement of the fluid of the cell will be equal. On the other hand, if the salt permeates without difficulty, the $\triangle$ is of no significance in regard to the effects of the solution on the cells.

The relations of the salts to the tissues has been worked out in most detail in the case of the red blood cells. It is found that in a 0.75-per-cent. solution of sodium chloride, the cells maintain their form and size unchanged, *i.e.*, the salt fails to penetrate the cells and exercises the same osmotic pressure as the diffusible contents of the cells, or is isotonic with the fluid in the interior of the cell. If the cells be exposed to pure water, they swell up and discharge their hæmoglobin, and the same occurs in weak (hypotonic) solutions of sodium chloride. The salt here being in lower concentration than the contents of the corpuscles, a current of water sets inward toward the stronger solution. In solutions of greater concentration than 0.75 per cent. (hypertonic solutions) the cells shrink from the loss of water, which flows outward toward the stronger solution. Similar phenomena are seen when other salts of the fixed alkalies are employed, so that these salts appear to be unable to penetrate the corpuscles except to a very slight extent.

In solutions of ammonium chloride, on the other hand, the cells swell up and lose their hæmoglobin, whether the solution be isotonic with 0.75-per-cent. NaCl, or much stronger. The conclusion is that the ammonium chloride can penetrate the cells and thus exercises no osmotic resistance to the entrance of water, so that the effect of ammonium chloride solution is practically identical with that of pure water. Many other ammonium salts resemble the chloride in penetrating the red blood corpuscles; but others, such as the sulphate and phosphate, fail to enter the cell entirely, or penetrate with great difficulty. The sulphate and phosphate ions, therefore, like the sodium and potassium ions, are non-permeating, and exercise osmotic pressure on the cell wall. Unless both ions of a salt can enter the cell, neither does so. Many non-electrolytes, such as urea and compound ammonias, appear to enter the blood cells freely.

The absorption of salt solutions in the intestine also presents an interesting example of the importance of diffusion in vital processes. A solution of sodium chloride isotonic with the blood is absorbed readily, whence it is inferred that sodium chloride can penetrate the mucous membrane. A hypotonic solution is similarly taken up

easily, and still more readily pure water. A hypertonic solution, on the other hand, disappears from the bowel more slowly, and very often the fluid first increases in the lumen until it has become almost isotonic with the blood, and only then disappears into the tissues. The sodium chloride does not, therefore, permeate the bowel wall without resistance, otherwise a hypertonic solution would be taken up as quickly as distilled water. On the contrary, a hypertonic solution first exercises osmotic pressure on the cells and causes them to lose water. At the same time some of the chloride has disappeared into the cells, and the solution remaining is diluted with the water exuding, until it is so weak that the osmotic resistance is overcome by the absorbing forces and the whole is absorbed into the blood.

When the sulphate of sodium passes into the bowel in solution, this feature is still more marked. An isotonic solution has little tendency to be absorbed, and on the other hand is not increased in volume, the solution in the bowel counterbalancing the osmotic pressure of the cell contents. A hypotonic solution decreases slowly because its osmotic pressure is less than that of the cell contents, and water therefore tends to pass from the weaker fluid in the lumen to the stronger in the blood; but the fluid escapes from the bowel much more slowly than in the case of an hypotonic solution of sodium chloride. If hypertonic solutions be used, the bulk is at first much increased owing to fluid from the blood escaping into the stronger solution. Finally the sulphate solution becomes isotonic with the blood and is very slowly absorbed if the weight of the fluid in the bowel does not set up reflex peristalsis and cause evacuation. This slow absorption from the bowel is still more marked in the case of magnesium sulphate, in which both ions appear to be taken up with reluctance by the mucous membrane. As these salts fail to leave the bowel and retain the water in which they are dissolved, they render the contents more fluid than usual, and the unusual weight and distention cause peristaltic movements and evacuation. The purgative action of the saline cathartics arises from the difficulty with which they enter the epithelial cells. It is to be remarked that here, as in the case of the red blood cells, the sulphates diffuse with greater difficulty than the chlorides; on the other hand, the chlorides of the fixed alkalies are taken up freely by the bowel wall, while they fail to permeate into the corpuscles, and the oxalate of ammonium, which penetrates the blood cells, is rejected by the epithelium.

The presence of the salt solution in the stomach and intestine inducing such movements of fluid into the bowel and back into the blood, naturally causes considerable disturbance in the distribution of the fluids of the body. When a strong sulphate solution is diluted by fluid poured into the intestine, for example, this fluid comes from the blood and indirectly from the fluids of the tissues. A similar exchange without doubt follows the absorption of salt solutions into the blood, but this is difficult to follow experimentally. When salt solutions are injected into the blood-vessels, however, it is found that there is a marked disturbance of the equilibrium of the tissues. If the solution is hypertonic, there is a flow from the lymph spaces toward the blood which continues until the plasma recovers its normal density The current then is found flowing in the opposite direction from the blood-vessels into the tissues. The lymph measured in the thoracic duct is found to be lessened at first owing to the inflow into the vessels, but later more lymph passes along the duct than usual, owing to the current of fluid passing toward the tissues from the blood.

The injection of salts into the blood-vessels or their absorption from the bowel leads to considerable diuresis. The explanation of this diuresis is still a matter of discussion, but there can be no question that the diffusion and osmotic properties of the salts play an important rôle in this result. The accumulation of fluid in the blood at the expense of the tissues naturally leads to an unusual bulk of the contents of the blood-vessels, and this in turn to an increased pressure in the capillaries. This engorgement of the vessels cannot be relieved by an outflow into the tissues, for this is prevented by the current of lymph pouring into the vessels. Only one way of escape remains, that through the kidneys, and the inflow of lymph is therefore accompanied and followed by diuresis, which is thus in large part explained by the physical forces, although there is doubtless much still obscure in the process. Different salts vary in their diuretic properties, and this might at first seem to indicate that the diffusion was of secondary importance. As a matter of fact, however, many of these differences can be explained by varying rates of diffusion. For example, the sulphates are as a general rule inferior diuretics when given per os, because they fail to reach the blood for the most part from their cathartic action. On the other hand, sulphate of sodium, injected intravenously, causes much greater diuresis than an equimolecular solution of sodium chloride, even if it causes the same inflow into the vessels and the same degree of hydræmia. This has been explained, however, by the renal tubules failing to absorb the sulphate, while taking up the chloride readily. If this is the case, as appears very probable, the sulphate failing to penetrate the renal tubules and thus return to the blood, must hold a certain amount of water in the tubules which would otherwise return to the blood. The chloride, on the other hand, returns readily through the epithelium lining the tubules, and thus retains less water in the tubules and causes less diuresis In this view the epithelium of the tubules resembles that of the intestine in repelling sulphates and phosphates and admitting chlorides readily, but differs from it in showing little avidity for urea and sugar.

The urine is generally a much more concentrated fluid than the blood; that is, it contains a larger number of molecules and ions. The kidney must thus do a considerable amount of work in concentrating such a fluid from the more dilute blood plasma, and by estimating the $\triangle$ of the blood, which is remarkably constant (about − 0.56° C.), and comparing it with that of the urine, the actual work done may be estimated exactly. Dreser calculated the work done by the kidney in forming 200 c.c. of average urine at the large sum of 37 metre kilograms, or over 270 foot-pounds, but this may be greatly exceeded in cases of very concentrated urine. Attempts have been made to use this method of estimating the work of the kidney in clinical medicine, and the subject has been treated of at great length in recent years under the title of cryoscopy. As yet no results of importance bearing on diagnosis or prognosis in renal affections have been arrived at.

When very concentrated solutions of salts or other diffusible bodies are brought in contact with living cells, some fluid escapes from these into the solutions, and this often deranges the activity of the cell. This may be observed in the stomach when strong solutions of such harmless bodies as common salt or sugar are swallowed, the disturbance of the equilibrium manifesting itself in irritation, nausea, and vomiting. In the same way a strong solution applied to wounds or mucous membranes causes irritation and pain from the withdrawal of fluid and precipitation of proteids. The same desiccation of the tissues may arise to a less degree from the presence of excess of salt or sugar in the blood. The organs which suffer chiefly are the brain and spinal cord, as is manifested in tremors and convulsions, and later by paralysis and asphyxia, when strong solutions of salts, sugar, urea, or other diffusible substances are injected intravenously in animals. *Arthur R. Cushny.*

DWARFISM.—Nanosomia or microsomia is a condition, found in both animals and plants, in which the stature and weight fail to reach the normal minimum for individuals of the same species. The word *nanosomia* is derived from two Greek words, νᾶνος, a dwarf, and σῶμα, a body, the former being the equivalent of the Latin *nanus* or *pumilio*, the Anglo-Saxon *dweorg* or *dwerg* and the German *Zwerg*.

From stray references to the subject in the pages of writers of antiquity, we may infer that a belief in the existence of dwarfs has been general from the most remote times. Homer, Herodotus, and Aristotle, among others, speak of a pigmy race that was to be found near the sources of the Nile. In India, too, there was a current belief in dwarfs descended from Hoonuman, the monkey-god. Many of the statements in regard to dwarfs are, however, so wildly improbable that they were, no doubt, based on mere "sailors' yarns," and are entitled to about the same amount of credence as the famous "Travels" of Sir John Mandeville. That they contain a modicum of truth, nevertheless, is proved by the discovery of diminutive peoples by modern explorers, such as Paul Du Chaillu, Schweinfurth, Battel, and Kolle. Dr. Schweinfurth, for instance, has found in the country to the south of the Nyam-Nyam a race called the Akkas, varying in height from four feet to nearly five, who are probably the same as those referred to by Herodotus. Any exhaustive discussion of the subject of dwarfism from an ethnological point of view would be out of place in a work of this nature, which is more properly concerned with the biological and pathological problems involved, but yet, apart from the interest that always invests the curious, it may not be entirely stale, flat, and unprofitable to possess ourselves of the main facts.

From the golden days of imperial Rome it was the fashionable thing to keep dwarfs. The most famous of these were Conopas and Andromeda, belonging to Julia, the niece of Augustus, each of whom measured only two feet four inches. Many of these dwarfs were, no doubt, the natural article, but the number of these was insufficient to supply the demands of cruel display and luxury; consequently they had to be produced by artificial means. One favorite method was the simple one of depriving children of suitable food. They became rickety, and while many died, those who survived were highly prized. Another plan, in some vogue, was to rub the back with the fat of bats, moles, or dormice. Somewhat similar was the practice of washing the backs and feet of pups, the drying and hardening of the parts resulting from this being supposed to stunt the growth. Even at the present time, it may be remarked, attempts are made to limit the growth of boys intended for jockeys by sweating. The practice of keeping dwarfs persisted through the Middle Ages into the eighteenth century. Lady Mary Wortley Montagu, when in Germany, found the dwarf a necessary appanage of every noble family. She describes the imperial dwarfs at Vienna "as ugly as devils," and, "bedaubed with diamonds." In these days dwarfs were not infrequently noted for their wit and wisdom, and, like the court jesters, whom in fact they superseded, were allowed unlimited freedom. It is said that one of the Danish kings actually made his dwarf prime minister in order to get at truths that other men were afraid to utter. Peter the Great, among other vagaries, was interested in dwarfs, and in 1710 gave a feast to celebrate the marriage of his favorite Valakoff with the dwarf of the Princess Prescovie Feodorovna, at which seventy-two dwarfs of both sexes were present. The practice of keeping dwarfs was widespread, and has been immortalized in the canvases of some of the most celebrated painters, notably Velasquez, Raphael, Paul Veronese, Domenichino, and Mantegna. Their delineations are in some cases of much value in enabling us to determine the nature of the dwarfism known to former times. In fiction, too, the dwarf has played a prominent part, as readers of "Peveril of the Peak" and "The Black Dwarf" will remember.

Some personages, famous in history, have been of small or even diminutive size. Philetas, of Cos, tutor of Ptolemy Philadelphus, was, according to Ælian, so light as well as small that he was obliged to carry leaden weights in his pockets to prevent his being blown away. Others that might be mentioned are Attila the Scourge, Æsop the fabulist, Procopius, Gregory of Tours, Pepin le Bref, Prince Eugene, Admiral Gravina, Fleury and Garry the actors, Arendt the Danish antiquarian. In England the history of dwarfs is traceable to mythological times. The origin of the almost generic title of "Tom Thumb" is to be found in an ancient ballad, which informs us that "In Arthur's court Tom Thumb did live." The most famous English dwarf was Sir Jeffery Hudson, who was born at Oakham in 1619. He made his first appeal to fame when he was presented by the Duchess of Buckingham to Queen Henrietta Maria as he stepped out of a pie. From the age of eight till thirty he was only eighteen inches high, but afterward suddenly shot up to three feet nine. He became a well-known courtier and was entrusted with several matters of delicacy. He did not lack courage for he fought two duels, one with a turkey-cock, celebrated in the verses of Davenant, and another with Mr. Crofts, who came to the meeting with a squirt. A more serious encounter, however, followed, for little Jeffery, who was mounted on horseback to compensate for his inferior height, shot his opponent dead. He was twice made prisoner, once by the Dunkirkers as he was returning from France, and once by the Barbary pirates. On each occasion he was soon ransomed. He eventually, however, fell on evil days, for he was accused of participating in the popish plot and was sent to the Gate House, where he died in 1682.

About the same period, or somewhat earlier, Charles I. had a page at his court called Richard Gibson, who was remarkable for his small size, and was, appropriately enough, a miniature painter. He married Anne Shepherd, the dwarf of Henrietta Maria, the ceremony being performed by Edmund Waller. Together they only measured two inches over seven feet. Evelyn designated Gibson as a "compendium of a man," and the pair were painted hand in hand by Sir Peter Lely. Mistress Gibson had nine children, five of whom survived and were of normal size. She died at the age of eighty, and her husband at seventy-five.

One of the most celebrated dwarfs was a Polish gentleman, Joseph Borwilaski, who became noted throughout Europe as a handsome man, a wit, and something of a scholar. His parents were tall, but three of his brothers were small. He was born in 1739, and died at the advanced age of ninety-eight in the city of Durham, where, by the irony of fate, he is buried by the side of the Falstaffian Stephen Kemble. His height was thirty-nine inches. Diderot wrote a history of the family.

Another remarkable dwarf was Richebourg, a servant and pensioner of the Orléans family, who died in Paris at the age of ninety. He was only twenty-three inches high, and his diminutive size was taken advantage of during the stirring times of the Revolution when, masquerading as an infant in his nurse's arms, he carried despatches in and out of Paris.

Coming to more recent times we may mention Charles Stratton, or "Gen. Tom Thumb," one of the greatest of Barnum's successes. At birth he was above the normal weight of the new-born, but ceased to grow when five months old His height at that time was less than twenty-one inches. He created a sensation in Europe and amassed a large fortune.

Perhaps the next most striking sensation has been the "Lilliputians," a troupe of singers and comedians possessing much talent as burlesquers. They were probably the same individuals who were examined by Joachimsthal in Germany.

Many of the recorded dwarfs have been very diminutive. Buffon mentions dwarfs only twenty-four, twenty-one, and eighteen inches high, and describes one who, when thirty-seven years old, measured sixteen inches, whom he considers to have been the smallest person on record. The "Princess Topaze," a French dwarf, is twenty-three and a half inches tall (or rather short ?), who weighs only fourteen pounds. Her parents were of normal size.

On consideration of the facts recorded in the above remarks we are led to certain important conclusions. Most dwarfs have been well proportioned, without deformity, and of average or more than average intelligence. Some of them have been persons of great vigor and force of character. In fact they may be said to dif-

fer but little from ordinary individuals save in the one point of size.

Dwarfs fall naturally into two classes: Those that are diminutive at birth and subsequently develop slowly, so that they always remain more or less stunted; and those that are of normal or even more than normal size at birth and later cease to grow. Authentic information as to the size of dwarfs at birth is hard to obtain. We may, however, correctly infer that they are often below the average size, for dwarfed mothers have frequently borne children in a natural way, and physical considerations would preclude us from coming to any other conclusion. Conversely, normally developed mothers have not infrequently given birth to dwarf children. Instances are on record of new-born infants weighing a pound and three-quarters, or even less, at full term. The subsequent history, however, of these children is unfortunately often unknown. Home (Philosophical Transactions of the Royal Society of London, 1825) speaks of a child borne by a woman following the Duke of Wellington's baggage train, which weighed at birth only one pound, and measured between seven and eight inches long. At the age of nine it was only twenty-two inches high. This is said to be the same child, called Caroline Crachami, whose skeleton is in the museum of the Royal College of Surgeons near that of O'Byrne, the "Irish Giant."

Inasmuch as in the cases of dwarfism that we have so far been considering the parts are perfect in form and the limbs are in the normal proportion to the trunk, although the body as a whole is defective in size and weight, it has been suggested that here we really have to do with a condition of infantilism which may be defined as a state of imperfect and delayed development, whereby the individual preserves the characteristics of childhood long after these should have disappeared. This view is supported by the fact that in many cases of dwarfism the head is proportionately large, as it is in the infant, the genitalia are undeveloped, and the signs of puberty are absent or delayed. Joachimsthal (*Deutsche med. Woch.*, 1899, xxv., SS. 269–271, 288–290), studying with the Roentgen rays a troupe of exhibiting lilliputians, found that bone formation was imperfect, the various centres of ossification being strictly comparable to those of a child, although the individuals in question were about thirty years of age. Undoubtedly, in some at least of the deficiencies complete development and function may eventually be attained. For instance, many of these dwarfs have proved themselves capable of propagating their kind. One cannot fail to be struck also with the fact that dwarfs frequently reach an advanced age, the reverse of what is found in the case of that other contrasting anomaly of development, gigantism. This suggests certainly not a defect in the vitality of the body as a whole, but rather an anomaly in the nature and direction of the growth. The normal balance between structure and function is upset and the individual may possess the mind and faculties of the adult in the body of the child.

With regard to the etiological factors at work in the production of dwarfism we are compelled to admit that our knowledge is far from complete. Our views therefore must partake largely of the nature of hypotheses. Up to the present time but few cases of dwarfism have been studied, and it is chiefly upon the facts gleaned from these and the results of experimentation that our inferences must be drawn.

The condition of dwarfism is clearly but one aspect of the larger question of dystrophy or dysgenesy. Consequently it can be apprehended only by a reference to the elementary principles governing the formation and growth of tissues.

The developmental forces concerned in the elaboration of a new individual may be inadequate to bring the process to completion. If they are totally inadequate, death of the embryo results. Short of this extreme result, however, the nutritional processes may be so modified that we get a deficiency or excess in growth of the organism, either in part or as a whole, or they may be so perverted that we have actual malformation and deformity. There is, therefore, a close relationship between dwarfism, gigantism, malformations, and monstrous births. The peculiarities of development that result in such anomalies may be inherent in the sperm cell or ovum or both, and in this sense are inherited, or they may be due to causes operating on the ovum subsequently to fertilization, either before (intra-uterine acquired causes) or after birth (post-natal acquired causes). We have, therefore, to take into account primitive peculiarities of cell substance on the one hand, and external causes, nutritional or mechanical, acting on the fruit, on the other.

In this particular certain general considerations are worth noting. Thoma ("Untersuchungen über die Grösse und das Gewicht der anatomischen Bestandtheile des menschlichen Körpers im gesunden und im kranken Zustande," Leipzig, 1882) has called attention to what might be called a general "law of deviation." In adults the normal length of the body is on an average 169 cm. in the male and 163 cm. in the female, while the average weight is 60 kgm. and 56 kgm. respectively. Considerable variations on either side of this norm may occur. Taking a large number of individuals, in one-half the amount of deviation will be anywhere between 0.0 and 3.8 cm. In accordance with the law he has formulated, the fifth multiple of this figure when added to or subtracted from the normal average height will give the outside limit of giant or dwarf growth, and will be reached only once in every thousand cases. According to this an adult would be regarded as a dwarf if the height fell below 163 minus 19 cm., or 144 cm. Similarly 5 kgm. is the approximate aberration in weight from the normal in the adult. The fifth multiple of this, 25 kgm., subtracted from 56, gives 31 as the upper limit in weight for dwarf growth. With regard to weight, we have, of course, to be careful to exclude such conditions as marasmus and loss of height from spinal disease. In the case of the new-born the normal average in length is 50 cm. and the weight 3.2 kgm. The amount of deviation is approximately 1.4 for length and 0.28 for weight. The upper limit for dwarf growth in mature infants at birth would therefore be 43 cm. and 1.8 kgm. respectively. Some allowance for individual peculiarities must be made, for many children that are diminutive at birth make up for the deficiency by rapid growth afterward, while, again, some children that are normal in size and weight at birth subsequently become retarded in their growth and development. This "law," while it gives us convenient data for classification, is, needless to say, very far from being an explanation of the anomaly.

Again, certain adventitious circumstances, acting apparently on the germinal cells, may play a part. It has long been known to stock-raisers that continued in-breeding will result in the production of diminutive offspring. And it is said that after Napoleon's campaigns there was a diminution of from one to two inches in the stature of the French people. This has been attributed to the fact that the strongest and best developed males were drawn for military service, but, no doubt, poverty, famine, and disease, affecting the people as a whole, were important factors. These observations suggest that defective physical development on the part of one or both progenitors may lead to insufficient vitality, or what might be termed "relative vegetative inertia" on the part of the germinal cells. This leads us to the consideration of the importance of heredity in this connection.

The inheritance of a developmental anomaly is well illustrated in the case of polydactylism. This peculiarity has been known to persist for three, four, or even five generations, although it may in time be eradicated by marriage with normal persons. The Foldi family, belonging to the Arabian tribe of Hyabites, all have twenty-four digits. They never marry outside the family, and the anomaly is so constant that any child having the normal number of digits is put to death as the offspring of adultery. Reference will be made later to the influence of pressure of the amniotic sac upon the growing embryo in the production of this and other deformities, but it would be absurd to suppose that such a cause could be present throughout several generations and in a whole race. We are driven to conclude that there must have been some anomaly in the formation and development of the "Anlage" arising in the earlier stages of embryonic life. This being so, it would not be surprising to find the influence of heredity somewhat marked in the condition of dwarfism. As a matter of fact, dwarfism is not invariably an expression of a hereditary peculiarity, although sporadic cases may occur in several generations derived from the same stock. Certain parents nevertheless seem to have a tendency to produce dwarfs. To cite only one example, the celebrated Borwilaski had a brother and sister who were dwarfed. The fact, however, that while certain members of a family may be dwarfs, others may be normally developed indicates that the cause, whatever it be, is not a constantly acting one, or else that there are a number of factors which must be correlated before the given result will take place. That the issues involved may be very complex is well illustrated by an extraordinary instance related by Ekman ("Dissertatio medica descriptionem et casus aliquot osteomalaciæ sistens," Upsaliæ, 1788) where dwarfism and osteopsathyrosis were associated through three generations. The ancestor could not walk because of deformity. He had four children, of whom one son was a dwarf and one daughter was small and deformed. This son begat by a healthy wife a son who had curved extremities, and was liable to fractures on the slightest provocation. This son in turn married a healthy woman who gave birth to a son who had so many fractures that when he reached adult life he could not move, and a daughter who was dwarfed and also suffered from multiple fractures in childhood. Apparently, then, heredity may manifest itself, not only in the rate and amount of growth, but also in the structure and composition of the tissues. Moreover, these two factors, simple growth and organic formation, are not always correlated, and may even be antagonistic. Numerous exceptions to hereditary transmission, however, occur, for when both parents have been dwarfs, the offspring have frequently proved to be normal in size and proportion. What, however, is an occasional anomaly in the case of civilized peoples is a constant racial characteristic in certain of the African tribes, such as the Akkas and Bushmen. This can hardly be explained on any other assumption than that an acquired peculiarity, due to unfavorable environment, has become transmitted and in time impressed upon a great number of individuals, unless we are prepared to accept the other alternative that all races of mankind were originally much smaller than they are at present, and, owing to natural selection and the growth of civilization, gradually developed into a superior organization, a view that, at all events, is not supported by history or tradition. Heredity probably has the same bearing in dwarfism as it has in the case of other anomalies; no more and no less.

The influence of extraneous circumstances on the vegetative power of the germinal cells is well illustrated by some comparatively recent and most suggestive experiments.

In experimenting with the fertilized eggs of some of the humbler forms of life, Roux showed that if, in the two-cell stage, one of the blastomeres be destroyed, the other will regenerate the missing half and eventually give rise to a complete embryo. Endres, Walter, and Morgan have come to similar conclusions in the case of the frog, with the additional observation that the peculiarity is characteristic of the earliest stages only and may be entirely suppressed. In 1891 Driesch separated, by shaking, the blastomeres of the sea urchin's egg when in the two- and the four-cell stage. Blastomeres thus separated produced in time a complete blastula, and the resulting gastrula was a perfectly formed dwarf of one-half or one-quarter the natural size, as the case might be. Zoja, too, in some remarkable experiments on the medusa was able to produce dwarfs one-sixteenth of the normal size. Morgan has further discovered the important fact that either a half embryo or a complete half sized dwarf will result according to the position of the blastomere. If, after one blastomere is destroyed, the other be allowed to retain its normal position a half embryo is always produced, as Roux had already shown. If, however, the blastomere be inverted, it gives rise either to a half embryo or a whole dwarf. In this connection we might recall certain early experiments of Saint Hilaire, who produced dwarf chickens by shaking the egg in the direction of its long axis. Thus it would appear that a rearrangement of the cell material may restore that equilibrium of the entire ovum necessary for the production of a whole embryo. This extraordinary power is, however, less marked in the higher forms and is ultimately lost. In view of the fact, however, that parthenogenesis, which is a constant occurrence in some of the lower forms of life, is sometimes to be observed even in such a highly organized creature as the hen, and in fact has been advanced by some authorities to explain the development of certain tumors of the human ovary, it is not impossible that anomalies in the segmentation of the ovum in human beings, may, although rarely, give rise to one type of dwarf at least, namely, that dwarfed from birth. Two factors would appear to be necessary: some cause to blight one-half of the ovum in the very earliest stage of its development, and another producing a disturbance of the cell equilibrium. As to what these factors may be, whether developmental, traumatic, or inflammatory, we have absolutely no information. One or two facts may possibly point us in the right direction. Malposition of the fertilized ovum as a whole may be brought about by intratubal and intra-uterine inflammation, instances of this being tubal gestation and placenta prævia. It is not inconceivable, therefore, that endometritis and deciduitis might lead to blighting of a portion of the embryo and disturbance of protoplasmic equilibrium. That a modification of external conditions does have a profound effect on the developing ovum, in some animals at least, we have ample proof. Dareste, by incubating hen's eggs at a temperature more elevated than that usually employed, got early development and dwarf formation. Gerlach and Koch ("Ueber die Produktion von Zwergbildungen im Hühnerei auf experim. Wege," *Biol. Centralbl.*, xxii., 1884) also obtained a retardation of development and dwarf growth by varnishing eggs so as to exclude all but a small amount of air.

The effect of primitive peculiarities inherent in the germinal cells in producing developmental anomalies of the Anlage has already been noted in regard to polydactylism, and it is now pertinent to inquire in how far deficiencies in the formation of those structures more especially concerned in the general maintenance of nutrition, namely, the cardiovascular and nervous systems, and the thyroid gland, are of importance in the production of dwarfism.

If the circulatory apparatus be deficient either in the size and extent of the vessels or in the formation of the chambers and valves of the heart, it is obvious that the circulation of the blood must be inadequate for the needs of the organism, which consequently may be inhibited in its growth. Long ago Virchow pointed out the association of cardiovascular hypoplasia with other developmental defects, such as scanty production of the pubic hair and small size of the genitalia, conditions that may be regarded as manifestations of partial infantilism, if we take the view of Hertoghe, that there is such a thing as partial infantilism ("Die Rolle der Schilddrüse bei Stillstand und Hemmung des Wachstums und der Entwicklung," Spiegelberg, München, 1900). Gilbert and Rathery (*Presse méd.*, May 7th, 1900) have, it may be mentioned, found a moderate grade of dwarfism in some cases of mitral stenosis.

With regard to the influence of the nervous system in the production of dwarf growth the available evidence is not conclusive. The close relationship of the central nervous system to the nutrition of the tissues is of course admitted by everybody, and we are aware how often injuries to certain ganglion cells or nerve trunks are fol-

lowed by atrophy or other degenerative disturbance. It would not be surprising, then, to find that a defective development of the central nervous system might lead to aplasia or hypoplasia in the embryo. Of course the more extensive defects of the central nervous system, as anencephaly and amyelinia, are incompatible with life, and consequently cannot be adduced as conclusive evidence on the subject of dwarfism. As a matter of fact, however, whatever information we possess seems to negative the position that dwarfism is a neurotrophic disorder. For instance, as Cruveilhier has shown, the most extensive hydranencephaly may exist without a trace of defective development in the rest of the body, and Vogt, Klebs, and Aeby have pointed out that in microcephaly the individual as a whole may in other respects be well developed. The most we can say is that certain forms of local hypoplasia may with some probability be referred to central nervous disturbances. The probability is increased when in a child with such a defect the process extends subsequently, as in a case recorded by Emminghaus (*Deutsches Archiv f. klin. Med.*, Bd. ii., S. 96, u. Bd. xii., S. 49), where there was congenital microplasia of one arm followed in the tenth year by a trophoneurosis of the eye and corresponding side of the face.

That the thyroid gland exerts an important and often controlling influence in the processes of nutrition cannot now be denied. In how far athyroidea has to do with dwarfism is still a moot point. The whole question as to the relationship of the thyroid gland to myxœdema, cretinism, and deficient development generally will be dealt with more at length shortly. Suffice it to say here that there is considerable evidence to support the view that there are many minor forms of cretinism in which the most striking and characteristic features are absent, and where the analogies to dwarfism are close. Küster extirpated the thyroid gland in a boy of fourteen, whose growth was thereby arrested so that he always retained the characteristics of a boy of that age. Eiselsberg (*Langenbeck's Archiv*, Bd. xlix., 1895) removed the thyroid in two lambs a week old. At the end of six months they weighed 10 and 14 kgm. respectively, while the controls weighed 35 kgm. The disturbance was general and involved the brain as well as the skeleton. Kappeler also found in a boy of twelve and a half years, who had been deprived of the gland, that he did not grow and developed some of the symptoms of myxœdema. It may well be, therefore, that infantilism, as Brissaud holds ("Leçons sur les maladies nerveuses," Paris, 1895), is simply an attenuated form of cretinism. Additional support is given to this view by the fact that some of the cases have been improved by thyroid feeding. Cases of this kind have been recorded by Wunderlich (*British Med. Journ.*, ii., p. 1420, 1897) and Dukes (*British Med. Journ.*, i., p. 618, 1898). In Wunderlich's case palpation proved the thyroid to be extremely small. In this connection also should be cited an interesting case of Sulzer's (*Deutsche Zeitschrift f. Chirurgie*, 1893) in which a goitrous thyroid was removed from a boy twelve and a half years of age. In five years he was a typical cretin. He then began to improve and in four years had regained the normal condition. It was found that a portion of the gland had been left behind at the operation, and that this portion began to grow some eight years afterward. In the same way the compensatory development of an accessory thyroid has an important bearing on the question of cretinism. These facts afford a probable explanation for such curious cases as that of Sir Jeffery Hudson, who, as we have seen, after remaining eighteen inches high for twenty-two years, suddenly shot up to three feet nine inches. Even if we are prepared to admit that infantilism is due to athyroidea, the identity of infantilism with dwarfism is not beyond cavil. At most can we say that the explanation may hold good for some of the cases. For, as Lorain was the first to point out, instances are met with in which there is no disturbance of the thyroid gland, and the defect in size is not true infantilism, but rather to be attributed to premature epiphyseal ossification.

So far we have been discussing the relationship of defective organization of the "Anlage" of the various systems to the question of general hypoplasia.

We pass on now to the question of intra-uterine malnutrition. In this connection ill health or improper diet affecting the mother or a local anomaly of placentation is the chief factor concerned. The former act by bringing a poor quality of blood to the support of the fœtus, and the latter presents a hindrance to the free interchange that should go on between the maternal and fœtal bloods. The existence of syphilis, tuberculosis, or chronic alcoholism in the mother might be expected to produce its effect upon the offspring, largely in the form of lowered vitality and increased susceptibility to disease. It is suggestive in this connection that the Japanese are in the habit of producing dwarf pups by feeding the mothers with alcohol. Charrin, furthermore, could produce a similar result by the injection of ptomaïns. Yet the children of mothers the subjects of long-standing disease or cachexias are by no means always diminutive or poorly nourished. The vitium shows itself, not so much in immediate anomalies of physical development, as in disordered function and defective reserve power. Much discussion has centred round the question as to whether there is such a thing as fœtal rickets. Rickets generally makes its appearance during the first or second year of life, after the sixth month, and is commonly attributed to insufficient and improper alimentation, although unhygienic surroundings may also play a part. It is not impossible that analogous causes, operating during intra-uterine life, might produce the same effects. Rickets is not hereditary, although congenital influences may play a part. In former times, and indeed to a large extent even in these days, the term "fœtal rickets" has been used in a very loose way to include several affections characterized by imperfect bone formation, such as syphilis, osteogenesis imperfecta, and chondrodystrophia fœtalis, which are now, thanks to recent studies, separated fairly well one from the other. It is now the general censensus of opinion that congenital rickets, in the sense of a rickets that has run its course previous to birth, does not exist. To this, however, we shall return.

In one or two cases the study of dwarf fœtuses has revealed the fact that there is an abnormal relationship between the fœtal placenta and the maternal structures. The chorionic villi were scanty and were composed of thin strands of connective tissue covered by an abnormally thick layer of epithelium, while at the same time the projections of the maternal decidua did not extend through the thickness of the fœtal placenta, as is usually the case. The explanation of this that has been offered is that there was a defective development of the decidua, but this is almost certainly incorrect. Chipman ("Observations on the Placenta of the Rabbit," "Studies from the Royal Victoria Hospital," Montreal, vol. iv., December, 1902) has shown that the more intimate connection between the fœtal and maternal parts is brought about by a process of absorption, the ectodermal cells of the chorionic villi proliferating and invading the openings of the uterine glands and extending along the sheaths of the blood-vessels. The maternal tissues are thus eroded as it were, and are quite passive in the matter. It may well be, then, that such an anomalous development of the placenta is due, not to malnutrition and imperfect cell growth on the part of the mother, but to a primary fault in the growing embryo that evidences itself in an imperfect development of the placenta. Apparently, however, before such an abnormality can result in dwarfing of the fruit it must be quite extensive, for the given result does not always follow. As Langhans has pointed out, a similar peculiarity of placentation occurs in cases of tubal gestation, where the fœtus is usually well developed.

Further, the proper interchange of blood and nutriment through the placenta may be gravely interfered with owing to inflammatory disturbances. Here syphilis plays a leading rôle. As is well known, in syphilis hereditaria tarda there is a delayed development of the bony and muscular systems, so that a young man of twenty