them in each of the nine minute nerve centres before depositing them in the cells for the larva to feed upon. He regards it as impossible that such an instinct could have arisen by natural selection unaided by originally intelligent action. In regard to this it may be said that, if the complicated maternal instinct of the *Sphex* wasp is an "inherited habit," its ancestors must not only have possessed great industry, but also a very remarkable knowledge of anatomy. Moreover, it has been shown very recently (1898) by Mr. and Mrs. Peckam ("Instincts and Habits of the Solitary Wasps") that the instinct of *Sphex* is not so exact as was formerly supposed. Not only is there a great deal of individual variation in the instinct of this species, but there is a gradation from this through other genera to those having much simpler instincts. They have shown that instinct may be acted upon by natural selection, just as may any other function or structure.

In conclusion it may be said, therefore, that in the writer's opinion, while acquired characters are of great importance to the individual, and their periodic recurrence in successive generations may be necessary in the formation of co-adaptations as an aid to natural selection, the *inheritance* of acquired characters is not only not the prime factor in evolution, but that it is not a factor in any degree.

Differential fertility appears to be an important factor, being, according to the circumstances, either an aid or a hindrance to evolution; preferential mating is the best explanation of the origin of certain secondary sexual characters; and some form of isolation must be present, and without or else divergent evolution is impossible, and without isolation it would be impossible to explain the differentiation of species by characters of less than selective value; but the chief cause of organic evolution is natural selection, or the survival of the fittest in the struggle for existence. *Robert Payne Bigelow.*

BIBLIOGRAPHICAL REFERENCES.

Bailey, T. H.: Survival of the Unlike, New York, 1896.
Conn, H. W.: The Method of Evolution, New York, 1900.
Cope, E. D.: Origin of the Fittest, New York, 1887.
Darwin, C.: Life and Letters, London and New York. Works, London and New York.
Davenport, C. B.: Statistical Methods with Special Reference to Biological Variations. New York, 1899.
Elmer, T.: Organic Evolution. London, 1890.
Gray, A.: Darwiniana. New York, 1889.
Haeckel, E.: Evolution of Man, New York, 1896. History of Creation, New York.
Huxley, T. H.: Collected Essays, New York. Life and Letters, London and New York, 1901.
Jordan, D. S.: Foot-notes to Evolution.
Morgan, C. L.: Animal Behavior, London, 1900. Animal Life and Intelligence, London and Boston, 1891.
Pearson, K.: Chances of Death and other Studies in Evolution, London, 1897. The Grammar of Science, second edition, London, 1900.
Poulton, E. B.: Charles Darwin and the Theory of Natural Selection, New York, 1896.
Romanes, J. G.: Darwin and After Darwin, Chicago, 1892-97.
Wallace, A. R.: Darwinism, London, 1889. Natural Selection and Tropical Nature, London, 1891.

EVOLUTION OF MAN.—The science of anthropology has advanced with surprising rapidity since the discovery of the two principles, evolution and psychic unity, the latter contributing evidence in support of the theory of evolution similar to that furnished by the homologies of biology. From each of the recognized divisions of anthropology evidence has been accumulated to establish the unity of the human species and to warrant the assumption that it has developed from the original mammal through the lemuroid and anthropoid stages. A few zoologists would derive man directly from the lemurs, but while it is recognized that man has many characters in common with the half-apes and even with lower forms, anthropologists are unanimous in deriving him from a generalized anthropoid precursor. The phylogeny of the mammalian group is given in the preceding article upon *Evolution*, so that we may devote our attention here to the problems involved in the determination of man's immediate ancestry. We shall seek such evidence as may be found within the human group, neglecting argument by analogy, which can never be wholly convincing.

I. SOMATOLOGY.—The modern science of physical anthropology interprets the data supplied by embryology, ethnic and comparative anatomy, and statistical anthropometry by the aid of the theory of evolution which alone renders them comprehensible.

1. *Embryology.*—In addition to the indications of relationship to lower animal forms there are many marks of phylogenetic proximity to the anthropoids in the human fœtus. By the dictum of "the first biogenetic law" we interpret the greater resemblance of the young of anthropoids and man to mean that both sprang from a common ancestral type. Not to deal too exclusively with general statements let us review a few of the more salient facts.

The lanugo of the fœtus recalls the hairiness of primitive man and his immediate ancestor, a condition seen even now in an occasional unfortunate adult. The free projecting tail of the embryo certainly pertains to an earlier form than the anthropoid but not necessarily earlier than the lower primates. Again it is to be noted that this character sometimes persists in human beings until maturity, either with or without free vertebræ. Until the very end of the nineteenth century rumors of the discovery of tribes of tailed men were circulated from time to time. It has been suggested that such tables may have arisen from the practice of wearing a sort of caudal appendage, as among the Sioux Indians and the Nagas of Manipur. The theory of an ontogenetic shifting of the pelvic girdle is generally accepted, reducing the number of presacral vertebræ from the number existing in most of the anthropoid families and from the ancestral condition. The presence of cervical and lumbar ribs in the embryo recalls the type prevailing among the anthropoids where the orang alone has as few as twelve pairs. The shape of the entire thorax in the embryo is of the primary type seen in the lower apes. One of the most noticeable simian characters to be seen in the embryo is the proportionately long fore-arm which in the embryo of two and a half months equals 88.88 per cent. of the length of the humerus as compared to 72 to 73 per cent. in the adult European, 78 or 79 in the adult negro, and 90 to 94 in the chimpanzee. The os centrale of the human embryo is found in but one group of anthropoids among adults, though it occurs in most monkeys. The short lower limbs of the fœtus suggest the adult anthropoid condition. The fibular malleolus, much less important than the tibial in apes, is less developed in the fœtus and among Australians and other low races. The opposable condition of the great toe in fœtal, and even infantile life is an often cited example of the retention of an ape-like character.

Among the muscles we may refer to the condition of the pyramidalis which in the child resembles that of the apes and lower mammals; also to the interossei pedis muscles which in the human embryo are distributed as in some of the lower apes and in lesser degree the chimpanzee and orang. The vermiform appendix is proportionally larger in the fœtus.

In the brain, the most distinctively human of all the organs of the body, the ontogenetic changes in the character of the surface and the disposition of the vesicles repeat phylogenetic development in a marked degree. Resemblance between the young of the two groups is nowhere more striking than in this organ. Hints of the anthropoid condition are not numerous in the sense organs of the embryo, but in the external ear such conditions are fairly prominent; the tip shifts downward and not until the eighth month does the human ear fold begin to roll inward. The palatal ridges of the embryo (six or seven) suggest the anthropoid condition, though they are rather more numerous in the apes. The milk teeth of man and anthropoids are closely similar and the dental formulæ are identical in the two groups.

These are a few of the more important characters that point to an anthropoid ancestry. They are but a fraction of the number of characters that occur in the human em-

bryo which are indicative of lower stages of development, but taken altogether they lend strong support to the evolutionary hypothesis.

2. *Ethnic and Comparative Anatomy.*—Together with physiology and anthropometry it comprises the greater part of the science of somatology as now taught in our universities, and the evidence of the relationship of man to the anthropoids is rapidly accumulating, both from the work done in our laboratories and from that accomplished among what we are pleased to term the lower races, though it must be understood that in many respects these races as well as some of the lower animals exhibit characters of decided superiority. We may summarize the facts as follows: Man resembles the anthropoids more closely than do the latter the American monkeys. In other words, the gap between the human and the nearest non-human group is far less striking than that between many mammalian groups. Among skeletal characters we find that the spinous processes of the cervical vertebræ are simple and undivided among low races. The clavicle and the scapula are proportionately longer and hence more simian in the negro than in the Caucasian. The arm of the negro exhibits two opposing characters: it is higher in its shorter humerus and lower in the longer radius than the white; the proportion of the radius is more exaggerated in the Veddahs of Ceylon. With a slightly shorter femur and a tibia of equal length the negro possesses lower limbs of a more simian type than the white. In the torsion of the humerus the black races stand midway between the anthropoids (130°) and Europeans (164°). The condition known as perforate humerus or the occurrence of the supratrochlear foramen, which is most frequent in Veddahs and Bushmen, is common in the gorilla and the orang. Among non-European races it is not the blacks alone that retain the ape-like prehensile foot beyond the period of infancy; many Eastern peoples possess this character, notably the Japanese. However, it is a pincer foot, not a hand foot.

The skull continues to be the most significant portion of the skeleton for classificatory purposes notwithstanding some contradictions presented by single characters. The projecting brows of the gorilla are seen in certain prehistoric crania to be described later and in the Melanesians as well as in rare instances among Caucasians. Many human groups possess the flat nose of the anthropoids. The fusion of the nasal bones that is normal in apes occurs more frequently in lower races than in higher. Australians, Hawaiians, and others have no sharp line of demarcation between the nasal opening and the maxilla beneath it. The temporal crest assumes a simian appearance among the Oceanic blacks. The meeting of the temporal with the frontal in the form known as pterion in K is most frequent in the Veddahs, Australians, and negroes; in anthropoids it is seen in the gorilla. Considerable variation in the foramina of the skull occur: the parietal are more frequently wanting in the higher races, the middle lacerated is larger in Europeans than in lower races and is wanting in anthropoids. The palatine suture of certain low races by its curved and irregular course resembles that of the apes. The form of the palate among low races often resembles the U-shaped alveolar arch of the anthropoids and occurs occasionally among Caucasians as an individual variation. The teeth of the Australians increase in size backward as in the apes. The New Caledonians not rarely develop a third pre-molar, the normal condition in New World monkeys. The shortened inferior maxillary of the European is causing a reduction in the number of teeth so that the upper outer incisors are sometimes wanting and the wisdom teeth as well. This change is also taking place among Amerinds. We have observed cases of suppressed third molars among the Esquimaux and all stages between rudimentary third molars and those larger than the first and second molars among other Amerinds. The hyoid of negroes resembles that of apes more closely than does that of Caucasians. The prognathism of the ape is conspicuous in the extinct Kalangs of Java, the Akkas and other Africans.

The only well-marked gap existing between the crania of man and anthropoids is in capacity. The highest recorded capacity for the latter is about 590 c.c. while the lowest for the former is that of a normal Veddah skull of 950 c.c. While the methods of determining cranial capacity are unsatisfactory, and the results of different observers are scarcely comparable one with another, yet approximately correct averages have been recorded for most human groups which show that the lowest capacity exists among the dwarf races of Africa, the Veddahs of Ceylon and their neighbors, the Andamanese. The question of capacity is the most interesting one concerning fossil human crania.

3. *Variation.*—Notwithstanding the potent influence of mixture of races, the constant mingling of blood owing to conquest, slavery, or friendly alliance, all tending toward uniformity of type, the human body is in the highest degree variable. The tendency toward uniformity has produced a well-defined species with varietal differences within the group; but each organ of the body and the proportions of the whole vary to such a degree that the examination of a large series of anthropometric data cannot but cause the investigator to marvel at the continuance of the human type. We now know that the black, white, yellow, and red varieties of the race perfectly intergrade; hence we need not expect by such comparisons as have been made in the preceding paragraphs to discover differences in the various human groups that shall equal those existing between this species and the anthropoids belonging to four separate families.

Even in the size of brain case, the range of normal variation in man is from 900 to 1,800. c.c. while the range from microcephalic idiots to pathologic megacephalic skulls is from 350 to 3,500 c.c. The range of variations in cranial capacity in a small series of 42 Auvergnat skulls was 676 c.c. The range from the earliest times to the present is inconsiderable and inconclusive. The proportions of the brain case are fairly constant within the tribe but not in the larger divisions of the species: we have long-and-short-headed Caucasians, Mongolians, negroes, and Amerinds, with all possible intermediate forms. In the torsion of the humerus, often cited as a good zoological character separating man from the other animals, the variation is from 164° in Europeans to 134° in Australians, the minimum being at least seven degrees below the average for the gorilla, less than the gap separating the lowest anthropoid from the lower apes and monkeys which, in their turn, are lower than the marsupials and others. Independently of the normal variation in the length of the humerus, the difference between the right and left sides sometimes amounts to 2 cm. The other long bones exhibit a corresponding variability; indeed, the tibia has been termed the most variable long bone in the limbs of man. The thickness of its shaft varies from forty to one hundred per cent. of the antero-posterior diameter and the outline varies from almost a circle through oval, triangular, and quadrangular forms. Physiological causes are supposed to bring about the platycnemic or flattened condition and the retroversion of the head as well as various degrees of curvature of the shaft. Examples of similar variations might be multiplied indefinitely from an examination of other parts of the skeleton and of the other tissues, particularly the muscles, where variation becomes excessive, and we yet continue in our laboratories to record cases of "new muscles."

II. ETHNOLOGY.—The study of the culture of living races furnishes little evidence in favor of our thesis; although it is true that in the Amerindian division the Fuegians, the Seri of the Gulf of California, and perhaps the Botocudo stand out little above the apes. Subsisting mainly upon raw food and manufacturing implements and weapons of the simplest sort they are not industrially much superior to the anthropoid that has learned to preserve the conveniently shaped stone for breaking cocoanut shells. Among the blacks, the Andamanese, the Veddahs, some Australians,

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and perhaps a few other groups are equally savage in culture.

From the discoveries of recent years it is now known that the earliest migrations peopled the earth before or shortly after the transition to the human stage of development, so that the several native cultures have been moulded by environment and acculturation rather than by common descent. Naturally, similar environments, similar conditions, result in like products which are termed ethnic parallels, and the phenomenon is known as psychic unity. The extreme position which maintains that "thinking merely goes on within us" governed by unalterable laws that direct every race through the same phases in its upward struggles has been abandoned by most anthropologists, but the controversy has stimulated research and indicated the true factors governing primitive cultural development. By the study of present-day savages we learn of those of prehistoric times. But again we are not forced to rely solely upon analogy. Let us see what positive evidence is available.

III. PREHISTORIC ARCHÆOLOGY.—From the Glacial gravels of Europe, Asia, and Africa have been taken flaked stone implements of a rude and simple sort that mark the beginning of the industrial art in stone. Apparently without domestic animals, possessing a knowledge of the use of fire, our Pleistocene ancestors appeared in Europe at least as early as the Interglacial epoch and possibly before. Cultural remains are fairly abundant from which we may reconstruct the history of this far-off people, but of skeletal remains but few have been discovered. Many mistakes have been made in the identification of more modern skeletons as of Pleistocene provenance; however, at least two skulls and two other inferior maxillaries are referred to the Chellian or earliest paleolithic period; about a dozen in all may be assigned to the Quaternary epoch and possibly earlier in a fragmentary condition. Obviously the attempt to reconstruct the physical type of the earliest known inhabitants of Europe from such scanty material is extremely hazardous. Naturally enough the most minute and exhaustive study is made of these specimens, the observer usually bent upon discovering pithecoid or anthropoid characters.

The human remains that may be accepted without controversy are the skulls from Olmo, near Chiana in Tuscany, and from Egisheim in Alsace. The maxillaries are those from the cave of La Naulette, near Furfooz in Belgium, and the fragment from the Schipka cave in Moravia. The skulls are dolichocephalic but not at all ape-like. The jaws present certain low characters that are not uncommon among whites at the present day. One of the most widely known skulls is that of Neanderthal, Rhenish Prussia, which cannot be proven to be a genuine Quaternary relic, and even if it be such no great weight can be attached to its somewhat simian brows and low frontal because we find its modern counterpart in men of no inferior intelligence, as, for example, Robert Bruce. Possibly such individuals are to be accepted as examples of reversion, though here again we must remember that normal variation about a mean will produce a low frontal in the millionth skull. It is noteworthy that the oldest skulls of Europe present fairly uniform proportions of breadth to length, and are dolichocephalic. In America both long and round skulls are found in Quaternary strata, showing that at that distant day differentiation had proceeded far enough to establish two distinct types. At Santos, on the south coast of Brazil, was found a skull that resembles the Pithecanthropus erectus of Java. It is somewhat less dolichocephalic but has the same marked constriction behind the orbital region, a characteristic of the gibbon skull. Other South American skulls show this same trait, and from their study the conclusion has been reached that man is more closely related to the gibbon than to any other anthropoid. This conclusion is independently reached from the study of the skull or brain cap together with two molars and a femur from Trinil in northeastern Java. These remains indicate that the animal to which they belonged was dolichocephalic, had a cranial capacity of about 1,000 c.c.

(average for Europeans 1,565 c.c.), was tall, and walked erect. This creature was named Pithecanthropus erectus by its discoverer, who believes that it represents a true transition form from the anthropoids to man and that continuity in the upward scale of development has been established at last. The skull differs from the ape's cranium in having a higher vault, in being devoid of strong crests and ridges, and in having an occiput arched like that of man though somewhat suggestive of that of Hylobates. Pithecanthropus is regarded as having descended from Anthropopithecus sivalensis of the Indian Miocene which with Hylobates stands nearest to man of all the anthropoids. Pithecanthropus comes from the Upper Pliocene or Lower Pleistocene, hence in sequence of time stands between anthropopithecus and man. The discussion concerning the significance of this fossil is not yet closed notwithstanding the fact that various authorities announce from time to time that it is; however, the preponderance of opinion is in favor of the acceptance of the original theory that pithecanthropus is a true transition form.

Both in the New World and in the Old the discussion yet continues concerning the length of the last Glacial and the Post-Glacial period. The estimates vary, according to the method or the prejudice of the investigator, from a few centuries to hundreds of thousands of years. Could we definitely establish the existence of Tertiary man the period of human occupation would be immensely increased. We may postulate a Tertiary "precursor," a "proanthropos," but exhibit one of his bones in the broad light of day we cannot. Human bones have been occasionally found buried in Tertiary strata, but they have been shown to be much later than the strata in which they had been interred. Artifacts purporting to be of the Tertiary epoch are announced from time to time, but there is always some flaw in the evidence: they are natural flint flakes that are erroneously supposed to be artificial, worked animal bones that are found to have been gnawed by wild beasts, whale bones that have been grooved by the teeth of sharks, cracked bones that are shown to have been naturally broken, and, finally, there is often doubt as to the exact age of the strata themselves. Again, fraud is suspected, as in the case of the Calaveras skull, and the evidence must be rejected. However, no valid objection to the existence of Pliocene or even Miocene man can be maintained. The hypothesis that man could not have retained his specific characters throughout such a long period of time without doing violence to the natural laws of zoologic development seems untenable when we see how slight has been the change in other animal species, for example the lion, that was the contemporary of the European cave-dwellers of early Quaternary times, as compared with the modern species.

Whether man lived in Europe before the Interglacial period is, then, an unsolved problem, but if true that he first appeared on that continent after the first Glacier, we know next to nothing of the length of time that he had lived in more tropical regions. The now sterile Sahara was once a well-watered region, as is shown by the terraced valleys worn by flowing streams and by the crocodiles that yet survive from the aquatic period in the Ahaggar Mountains. There, too, we find pictographs portraying animals that no longer live in the region. It is nearer the centre that archæologists now regard as the place of origin of the entire race. That there was but one place of origin is no longer disputed by any competent anthropologist, and this centre is located in either the northern or northeastern part of Africa or in the so-called Lemuria, the region now occupied by the Indian Ocean. The geologic evidence of the existence of this continental area is indisputable; that it was occupied by primitive man seems probable from the fact that the climatic conditions were most favorable for the welfare of a naked frugiverous animal; it is within the limits of this area that the most primitive fossil form has been found; it is on the borders of this area that the most ape-like human beings now live; and on the eastern and western limits of this zone that anthropoids yet

flourish; it is on the northen borders of this area that the earliest civilizations have arisen. The dispersion from this centre must have taken place not later than the Old Stone Age, and the primary divisions of mankind were already specialized in their several geographic areas before the development of any distinctive culture. Paleolithic implements are regarded as very much the same in character in the Eastern and Western hemispheres, but all Neolithic and subsequent artifacts differ according to the locality whence they come.

Since the first peopling of the earth there seems to have been little migration in the New World, Australia, or to any significant extent in Central Africa. These countries have produced strongly marked varieties. The evidence is rapidly accumulating to show that the Caucasic division arose in Africa in the region of the Sahara and northward, and not in Asia. Two or three land bridges then spanned the Mediterranean, and there was land connection to the British Isles, so that no obstacle prevented the invasion of Europe or the migration to and fro of the tropic and temperate fauna of the two continents. The movements of the European and Asiatic races have been chiefly within, in limits of similar environmental conditions, so that the extensive migrations, as contrasted with the limited ones of the black and red races, have not apparently interfered with the specialization of racial types. Indeed, we are discovering that the principal types of Caucasians were already specialized in Africa before the migrations to Europe began.

We may summarize the facts so far as known concerning the time and place of man's origin and the characteristics of his early culture as follows: Before the period of proto-historic Egyptian, Mediterranean, and Eastern civilizations there was an epoch during which implements and weapons were made of stone and were smoothed and polished. At a yet earlier period chipped or flaked flints and other stones were used. The rudest types of these come from strata that are referred to the Interglacial period of Europe. In those strata human artifacts cease; there also occur the earliest traces of human skeletal remains. These remains are few and fragmentary, but they indicate that the race of that remote epoch differed but little in physical characters from that of to-day. The order of succession of these geologic and culture periods is known, their duration is not. The place of origin is provisionally located in the tropical region north of the Soudan in Africa or in the sunken Lemuria. Paleontology furnishes but one bit of evidence of any value, the remains from Java. No other skeletal remains have been found anywhere that can be regarded as belonging to any generalized precursor of the human race. In fact only a few fragments of fossil ape bones have been discovered. Embryology and ethnic and comparative anatomy combine to prove the theory of development from a generalized primate the remains of which may be found to-morrow or which may never be found. The Pliocene fossil-bearing beds of the lands bordering upon the Indian Ocean offer the most promising fields for research to-day. The problem is now one for paleontology and geology to settle, biology can do little more.   *Frank Russell.*

EXALGINE.—Exalgine is the trade name of methyl-acetanilid. Its chemical formula is $C_2H_5NCH_3C_2H_3O$; it is formed by the addition of the methyl group, CH_3, to acetanilid, $C_6H_5NHC_2H_3O$, replacing one atom of hydrogen.

It occurs as beautiful needle-shaped crystals, colorless, and with a faintly aromatic odor and slightly pungent taste. It is almost insoluble in cold water, slightly soluble in hot, and very soluble in dilute alcohol. From sixteen to twenty grains may be dissolved in half a drachm of rectified spirit, and this solution may be diluted with two or three ounces of water without producing any precipitation. Its melting point is 100° C., and it may be heated to its boiling point, 240° or 250° C., without causing decomposition. By the addition of soda it is decomposed and partially converted into methylaniline. Hydrochloric

acid causes the same decomposition. Exalgine may be distinguished from acetanilid, phenacetin, and methacetin by treating two grains of the suspected salt with twenty minims of hydrochloric acid. Phenacetin remains undissolved; acetanilid dissolves but separates again in crystals; methacetin also dissolves and gradually colors the solution reddish-brown on the addition of one drop of nitric acid. Another test for the presence of phenacetin or acetanilid is to treat a chloroform solution with ten volumes of petroleum ether; if either of these substances is present a turbid mixture is formed. The presence of methylaniline and other compounds of the same base may be detected by the irritating fumes produced when the impure salt is heated with alcoholic solution of potash and chloroform. Its purity may be further tested by dissolving in nitric acid, which forms a colorless solution; when heated this becomes of a bright yellow color, and evolves irritating fumes.

Methylacetanilid was discovered in 1874 by A. W. von Hofman. Its therapeutic properties were studied to a certain extent by Kahn and Hepp during their researches upon acetanilid and other antipyretics, but it was not until March, 1889, that Dujardin-Beaumetz and Bardet made known its value as an analgesic, in a communication to the French Academy. A very careful series of experiments, both physiological and clinical, enabled them to indicate its therapeutic qualities with a marked degree of accuracy. In common with the other members of the aromatic series it was found to possess antiseptic, antipyretic, and analgesic properties, and they also pointed out that its action on the nervous system should make it of value in the treatment of many functional diseases. It was as an analgesic that they particularly advocated its use; the addition of the methyl atom to acetanilid had intensified this action without affecting its antipyretic properties, but it was found that a dose large enough to produce antipyresis was accompanied by such alarming toxic symptoms that its use could not be considered. They advocated its employment in headache, migraine, neuralgia, neuroses of the viscera, the pains of locomotor ataxia, and in all non-febrile affections accompanied by pain. The dose they advised was from gr. iv. to gr. vi. (0.25 to 0.40 gm.) in a single dose, or from gr. vi. to gr. xiss. (0.40 to 0.75 gm.) in the twenty-four hours.

In Great Britain the notice of the profession was particularly directed to the value of this remedy by Professor Fraser, of Edinburgh,[1] who gave the results of his experience with it in the Royal Infirmary. The remarkable point in Professor Fraser's paper was the smallness of the dose and the success that followed its use in such quantities. The usual dose was half a grain in spirituous solution, repeated three or four times a day, according to the return of the pain. In some cases it was increased to one or even to two grains, and in a few instances four grains were given; the largest quantity given was fourteen grains during the twenty-four hours. In the cases of neuralgia and angina half-grain doses relieved the pain in ten or fifteen minutes, and in one hour there was perfect ease, which lasted for from three to nine or ten hours, and in many instances a complete cure was obtained. In sciatica and locomotor ataxia one and two grains secured the same freedom from suffering. In cancerous disease and in the pain accompanying an aneurism the success was less marked, and it was in these cases that the larger doses were given. Dr. Fraser considers that the smaller dose is the proper method of administering the drug, and that all its virtues may thus be as readily secured as with the larger doses.

Following Dr. Fraser's paper came a number of reports of successful results with half- and one-grain doses, by Drs. Herschell,[2] Farrar,[2] Holden,[3] Maloney,[4] and many others. Further experience has proved exalgine to be an analgesic and antispasmodic of much value, which, although not in very general use, is constantly employed. It is of service in all pains of a purely neurotic origin, and by many it is thought to be particularly valuable during the course of a febrile attack. It has proved of less value in painful conditions due to organic disease or

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mechanical causes. In England the small dose advocated by Fraser appears to predominate, but in other European countries and in America the larger dose of four grains is generally given.

Exalgine has been used with favorable results in infantile troubles. Dr. Moncorvo[3] publishes his experience of its use in twenty-one cases of children ranging from one to twelve years of age, in which it was given for the relief of pain. He considers it a very useful agent. It was well borne in every case, no unfavorable symptoms being ever noticed. The dose commenced with was three-fourths of a grain, increased in some cases to five grains. In one case choreic symptoms were present and were improved.

Its use in chorea has been reported upon by Dr. Hugo Löwenthal.[6] Thirty-five cases were treated with doses of three grains, given usually three times a day and never exceeding fifteen grains in the twenty-four hours. The effects were very satisfactory. The mild cases were cured quickly, but the more severe ones were less influenced and required more time. The beneficial effects of the treatment were most marked in the cases in which it was given early in the course of the disease, in two cases a cure being effected in eight days. A favorable influence over the mental state was also noticed; the fear and nervousness were lessened and the intelligence brightened. In some of the cases in which it was administered for a prolonged period, nausea, vertigo, headache, and other distressing symptoms were noticed.

Unfortunately the occurrence of toxic symptoms is not infrequent. No fatal termination has yet been reported, but the condition of the patient sometimes becomes very alarming both to the friends and to the physician. The toxic disturbances, however, occur long before the fatal dose is reached. Experiments on animals have shown that the lethal quantity is seven and a half grains for each two pounds of the weight of the animal, and three grains, it has been found, will give rise to severe symptoms. The poisoning arises from the action of the drug on the nervous centres as well as from the alteration that occurs in the condition of the blood. The changes in the blood are the same as those which are produced by all aniline compounds; that is, the hæmoglobin is altered into methæmoglobin and the function of oxidation is interfered with. The patient is made aware of the approach of the toxic action by a sense of fulness in the head, a constriction and oppression of the chest, dyspnœa, vertigo, dizziness, numbness, and disturbances of vision. This is followed by a rapid pulse, shallow respiration, and all the sensations of death with symptoms of asphyxia and collapse. Unconsciousness is common in the severe cases of poisoning; convulsions do not so frequently occur.

Generally, very large quantities are given before any ill effects are noticed. It is very rarely that any disturbance of the skin takes place, but cases have been reported in which an erythematous rash has appeared on the skin, and in some instances the buccal mucous membrane is also affected.[5] In one instance[4] the drug was continued for seventeen days, in gradually increasing doses, and during the last seven days eighteen grains were administered daily. In another case[9] thirty-six grains were given within nine hours, and in still another[10] twenty-four grains within two hours. The ill effects of the drug generally follow its prolonged use or the administration of large doses, but in some instances quite small doses have produced very alarming effects. An instance[11] is reported in which two doses of three grains each caused all the serious symptoms of poisoning, and another instance is known in which two doses of five grains each were given with the same effect. A remarkable case[12] is reported in which, in an adult, two doses of one and two grains, respectively, produced most profound prostration. The symptoms came on about an hour after the administration of the last dose, while the patient was sitting at a table engaged in a game of cards. He first complained of a fulness in the head and suddenly fell prostrate, unable to speak or move, and gasping for breath. A second at-

tack took place in about an hour, and the oppression and dyspnœa continued for several hours. In another instance a dose of eight grains produced alarming symptoms.[13]

Very different from these cases are those in which very large quantities have been given without evil consequences. Dr. Churton[14] reports two such cases. In the refilling of a bottle of medicine a mistake was made by which a solution was prepared of one grain to a drachm, instead of one grain to the ounce. The medicine was given as usual, four grains instead of half a grain being contained in each dose. This was continued for several days, and during the last twenty-four hours before the mistake was detected the patient was given forty grains. The pulse and respiration were rapid, and the patient complained of a burning sensation in the stomach, but no other effects were noticed. The second patient was given twenty-four grains from the same preparation, but it failed to produce any other effect than slight vertigo and a sense of being "dazed," which caused her to walk unsteadily. The quality of the drug is vouched for, as it was given to a number of patients with satisfactory results, and small doses were again given to the first patient, and its analgesic action was secured.

The quality of the drug undoubtedly affects its action, and in many instances explains the varying results that follow its use; but certain conditions of the system must exercise a decided influence, probably by promoting the decomposition of the drug and the formation of more toxic compounds. Mr. Bokenham[8] dwells upon this point in his remarks upon two cases of poisoning and suggests that some condition of the blood preceding menstruation may assist this reaction. The activity of the action is also influenced by the time of its ingestion. Professor Fraser and others, who find benefit in the small doses, always recommend that it should be given on an empty stomach, while those who use the larger doses advise it to be given after meals, and others still have remarked that the toxic symptoms arise when it has been given before meals. In the majority of cases the toxic symptoms pass away without requiring any assistance, but when the depression and dyspnœa are severe, stimulating remedies must be used. Alcohol has been resorted to, in most of the cases of poisoning, with apparent benefit, and hypodermic injections of ether have also been employed. In the cases reported by Dr. Jones[8] marked relief was secured by the use of strychnine in addition to the stimulants. Two minims of the liquor strychninæ were given hypodermically and ten minims of tincture of digitalis by the mouth. In these cases the inhalation of nitrite of amyl and the administration of nitroglycerin by the mouth, in doses of gr. $\frac{1}{100}$, increased the cyanosis, showing that the arterial as well as the venous blood was altered.

Upon the lower animals the hypodermic injection of exalgine produces violent epileptiform convulsions, salivation, fall of temperature, dyspnœa. The blood becomes dark in color and contains an abundance of methæmoglobin.

The following conclusions have been arrived at by Marandon de Montyel[15] from clinical observations on patients in whom the use of the drug had been pushed to its physiological limits: It has no influence on digestion. If the stomach is empty it causes an increased flow of saliva, a bitter taste, and a sense of tightness about the epigastrium. The pulse, respiration, and temperature are lessened in patients without convulsive tendencies. Vertigo, flashes of light, and ringing in the ears are frequent. A local or general cyanotic surface, sensations of cold, numbness, and formication, are prominent symptoms. The action of the drug is prompt and the effects are recovered from promptly, the brain being the first organ affected and the first to recover. When it is administered after meals its physiological action is less marked.

Beaumont Small.

[1] British Medical Journal, February 17th, 1890.
[2] Ibid., July 19th, 1890.
[3] Ibid., September 27th, 1890.

[4] Ibid., October 18th, 1890.
[5] Bull. Gén. de Thérap., May 30th, 1891.
[6] Berlin. klin. Wochen., March, 1892.
[7] Squibb: Ephemeris, 1890.
[8] British Medical Journal, February 8th, 1892.
[9] Medical Press and Circular, March 16th, 1892.
[10] The Therapeutic Gazette, February, 1892.
[11] British Medical Journal, July 12th, 1890.
[12] Ibid., May 3d, 1890.
[13] Ibid., June 11th, 1898.
[14] The London Lancet, May 28th, 1892.
[15] La Tribune médicale, June, 1892.

EXAMINER, MEDICAL.—The State of Massachusetts, in common with other States of the Union, employed the coroner's inquest as the official mode of inquiry in cases of deaths from sudden, violent, or suspicious causes, from the early history of the colony until 1877.

In consequence of corrupt practices which had become of frequent occurrence, and also in consequence of the inefficiency of the existing system, and of the inherent incongruity of an office requiring expert knowledge both of law and of medicine, a persistent movement was made by the Massachusetts Medical Society, ably assisted by T. H. Tyndale, Esq., and other members of the legal profession, having as its prime object a radical change in the coroner system. This movement was heartily endorsed by the Massachusetts Legislature of 1877, and resulted in the enactment, by that body, of the following statutes, which constitute in the main the law now in force in Massachusetts:

ACTS OF 1877.—[Chap. 200.] *An Act to abolish the office of Coroner and to provide for Medical Examinations and Inquests in cases of Death by Violence.* Be it enacted, etc., as follows:

"SECTION 1. The offices of coroner and special coroner are hereby abolished.

"SEC. 2. The governor shall nominate, and by and with the advice and consent of the council shall appoint, in the county of Suffolk not exceeding two, and in each other county not exceeding the number to be designated by the county commissioners as hereinafter provided, able and discreet men, learned in the science of medicine, to be medical examiners; and every such nomination shall be made at least seven days prior to such appointment.

"SEC. 3. In the county of Suffolk each medical examiner shall receive, in full for all services performed by him, an annual salary of three thousand dollars,* to be paid quarterly from the treasury of said county; and in other counties they shall receive for a view without an autopsy, four dollars; for a view and autopsy, thirty dollars; and travel at the rate of five cents per mile to and from the place of the view.

"SEC. 4. Medical examiners shall hold their offices for the term of seven years from the time of appointment, but shall be liable to removal from office at any time by the governor and council for cause shown.

"SEC. 5. Each medical examiner, before entering upon the duties of his office shall be sworn, and give bond, with sureties in the sum of five thousand dollars, to the treasurer of the county, conditioned for the faithful performance of the duties of his office. If a medical examiner neglects or refuses to give bond as herein required, for the period of thirty days after his appointment, the same shall be void and another shall be made instead thereof.

"SEC. 6. The county commissioners in each county shall, as soon as may be after the passage of this act, divide their several counties into suitable districts for the appointment of one medical examiner in each district under this act; and when such division is made, shall at once certify their action to the secretary of the Commonwealth, who shall lay such certificate before the governor and council; but nothing herein shall prevent any medical examiner from acting as such in any part of his county.

"SEC. 7. Medical examiners shall make examinations, as hereinafter provided, upon the view of the dead bodies of such persons only as are supposed to have come to their death by violence.

"SEC. 8. Whenever a medical examiner has notice that there has been found, or is lying within his county, the dead body of a person who is supposed to have come to his death by violence, he shall forthwith repair to the place where such body lies and take charge of the same; and if on view thereof and personal inquiry into the cause and manner of the death he deems a further examination necessary, he shall, upon being thereto authorized in writing by the district attorney, mayor, or selectmen of the district, city, or town where such body lies, in the presence of two or more discreet persons, whose attendance he may compel by subpœna, if necessary, make an autopsy, and then and there carefully reduce or cause to be reduced to writing every fact and circumstance tending to show the condition of the body, and the cause and manner of death, together with the names and addresses of said witnesses, which record he shall subscribe. Before making such autopsy he shall call the attention of said witnesses to the position and appearance of the body.

"SEC. 9. If upon such view, personal inquiry, or autopsy he shall be of opinion that the death was caused by violence, he shall at once notify the district attorney and a justice of the district, police or municipal court for the district or city in which the body lies, or a trial justice, and shall file a duly attested copy of the record of his autopsy in such court, or with such justice, and a like copy with such district attorney; and shall in all cases certify to the clerk or registrar having the custody of the records of births, marriages, and deaths, in the city or town in which the person deceased came to his death, the name and residence of the person deceased, if known, or a description of his person, as full as may be for identification, when the name and residence cannot be ascertained, together with the cause and manner in and by which the person deceased came to his death.

"SEC. 10. The court or trial justice shall thereupon hold an inquest, which may be private, in which case any or all persons other than those required to be present by the provisions of this chapter may be excluded from the place where the same is held; and said court or trial justice may also direct the witnesses to be kept separate, so that they cannot converse with each other until they have been examined. The district attorney, or some person designated by him, may attend the inquest and may examine all witnesses. An inquest shall be held in all cases of death by accident upon any railroad; and the district attorney or the attorney-general may direct an inquest to be held in the case of any other casualty from which the death of any person results, if in his opinion such inquest is necessary or expedient.

"SEC. 11. The justice or district attorney may issue subpœnas for witnesses, returnable before such court or trial justice. The persons served with such process shall be allowed the same fees, and their attendance may be enforced in the same manner, and they shall be subject to the same penalties, as if served with a subpœna in behalf of the Commonwealth in a criminal prosecution pending in said court, or before said trial justice.

"SEC. 12. The presiding justice or trial justice shall, after hearing the testimony, draw up and sign a report in which he shall find and certify when, where, and by what means the person deceased came to his death, his name if known, and all material circumstances attending his death; and if it appears that his death resulted wholly or in part from the unlawful act of any other person, he shall further state, if known to him, the name of such person and of any person whose unlawful act contributed to such death, which report he shall file with the records of the superior court in the county wherein the inquest is held.

"SEC. 13. If the justice finds that murder, manslaughter, or an assault has been committed, he may bind over, as in criminal prosecutions, such witnesses as he deems necessary, or as the district attorney may designate, to appear and testify at the court in which an indictment for such offence may be found or presented.

"SEC. 14. If a person charged by the report with the

* This sum was changed to four thousand dollars by an act of 1890.