power in causing the changes which ensue in the matter supposed to be under its sway, it is certain that no phenomena at all comparable with those which characterise every particle of matter that lives, whether it be high or low, simple or complex, have been manifested by any form or state of matter which is not living.

All attempts to show that life, vitality, in any living particle, is capable under any circumstances of being converted into, or made to take the form of, heat, light, electricity, or other form or mode of motion have so far signally failed. Indeed, the manifestation of various forms or modes of energy in living things appears to be a direct result of a certain rearrangement of the atoms of living matter, the rearrangement being effected by the operation of vital power upon the material particles with which it is temporarily associated. The change in position and relation of the atoms is no doubt accompanied, though not caused, by chemical action, and in many cases by the evolution of heat, light, or electricity. In the present state of our knowledge, as it seems to me, this is the nearest approach to an explanation that, in strict accord with known facts and reason, can be advanced, and, indeed, the only way in which the rearrangement of the particles, which undoubtedly takes place, can be accounted for.[2]

I submit, then, that so far all the facts adduced and the arguments founded upon them establish the conclusion that the living matter which is directly concerned in the development and formation of the most complex and highest organism, organ, or tissue, be it vegetable or animal—man, an eye or a brain cell—exhibits no special characteristic which would enable us to decide what particular organism, organ, or tissue was about to be produced, or to distinguish it from living matter from which some low and comparatively simple organism, organ, or tissue of the most passive and unchanging kind would be evolved. The results of the influence of life power on matter cannot, in fact, be foreseen. The results may be observed and the resulting structures subjected to investigation, but the power itself is not demonstrable and cannot be isolated. It stands by itself among natural agencies. Its origin is unknown and the means by which it is communicated to non-living particles undiscovered and perhaps undiscoverable. That vital power is transferred without loss is quite certain. Nothing is added to the weight of the matter when it becomes living—nothing taken from it when it ceases to live. Vital power in many cases undergoes certain modification as regards its special characters, probably at a time when it is least active and perhaps at a time when it appears to be in a dormant state, the modification in power being evidenced in the departure from the characters, properties, and action of the tissues and organs formed.

I claim, then, vital power—vitality—as the agency upon which the composition, characters, minute structure, and action of all tissues and organs in every living organism directly depend. In the absence of vital power not a structure characteristic of any living form in nature could have existed. It is the wonderful operation of vital power which distinguishes all living from all non-living. Vital power effects the separation from one another of elements in combination in the various substances which constitute the pabulum of the living, rearranges these elements, and determines their new position, so that new combinations resulting in the formation of particular compounds are occasioned. Such analytical and synthetical operations are of a special kind and are always proceeding, slowly or quickly, in every particle that lives, and many of the products as regards properties, composition, and action—predetermined, as it were foreseen—are inimitable and obtainable only from organisms in a living state or that have lived.

These general conclusions will be further strengthened by observations which will be advanced in the next communication, "On the Interstitial Circulation of Living Organisms in Health and Disease."

(To be continued.)

[2] Seeing that energy is indestructible, while life—vitality—ceases without undergoing conversion into any form or mode of motion, and cannot, therefore, be indestructible in the same sense as that in which matter and energy are held to be indestructible. It cannot, however, be said to be impossible that some life may be destructible and some indestructible, but in this case the supposed destructibility or indestructibility must be due to a potency which can be perpetually multiplied without any addition to, or change of, or subtraction from, any material forces or properties associated with the particles concerned.

THE ACTIVE PRINCIPLE OF INDIAN HEMP: A PRELIMINARY COMMUNICATION.[1]

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Introduction.—The want of uniformity in the preparations of Indian hemp has so often led to serious consequences in practice that many practitioners have discarded the drug as worthless or dangerous. Others, finding it of benefit in certain diseases, have expressed a hope that some means of standardising it would be discovered or the active principle of the plant isolated. Of the two conditions, the isolation of the active ingredient is the more important and its use is more likely to lead to uniform results in treatment. Quite recently such a pure active product has been obtained and the mystery which has hitherto enveloped Indian hemp seems in a fair way to being cleared up. Many points still need investigation, the most important from a medical point of view being the gradual change which cannabis compounds undergo by keeping. Both by practical experience and scientific experiment it has been shown that the active ingredient gradually loses its power, and at present we know of no means of preventing this. A very interesting case of this loss of activity is described by Thomas Smith.[2] He found that cannabin, which, when freshly prepared, produced a narcotic effect in doses of two-thirds of a grain, after exposure to the air for three years became absolutely inert.[3] In India, it is said, dealers in this drug refuse to buy the old crops after the new ones are gathered, and after two years the crops are publicly burnt in the presence of an Excise officer. The cause of this growing inertness is probably due, as Leib Lapin[4] suggests, to the oxidation of the active ingredient. He mentions experiments in support of this view, but these are not sufficiently convincing. Age, however, will not account in all cases for the uncertainty of commercial preparations. More often it is due to the more or less inert natural products from which these preparations are made. That the physiological activity of the hemp plant varies with the locality in which it is grown is well known, and it has been suggested that the gánjá of Bombay and the Central Provinces, which is "infinitely inferior" to that of Bengal, finds its way into European pharmacy. "There is also good reason to believe that the Indian hemp merchants, who deal with the drug in the first instance as an article of excise consumed locally, are in the habit of supplying to the European drug exporter or his agents samples for which, owing to the partial or complete loss of activity, they can no longer find a native market."[5]

Natural products.—The principal natural products obtained in India from the hemp plant, excluding the fibre, oil, and seed, are known as charas, gánjá, and bháng.[6] *Charas* is a resinous exudation found on the leaves, young twigs, immature fruits, and bark of the stem, and is regarded, and with justice, as the most active preparation of the hemp plant. It is gathered by rubbing the flower-tops between the hands, or by men, naked or wearing leather coats or skins, running through the fields; it is then scraped off and made

[1] Suggested by Dr. Walker's letter in the British Medical Journal of Nov. 7th, 1896, p. 1382. The experimental part of this communication was read before the Cambridge Philosophical Society on April 19th, see their Transactions, vol. ix., part iii., p. 149.

[2] Pharmaceutical Journal [3], vol. xv., p. 853.

[3] O'Shaughnessy also found that the extract which he himself brought from India did not produce in England the effects which he anticipated (Pharmaceutical Journal, vol. vi., p. 71). This may have been due, in part at least, to the age of the preparation. Christison (Watt's Dictionary of the Economic Products of India, vol. ii., p. 123), on the other hand, states that he used for some years an alcoholic extract sent to him from Calcutta twenty years before, and which was still as powerful as ever to relieve pain and obtain sleep. Casiccia (Rivista di Chimie, Medicina e Farmacologia, July, 1883, p. 326; Virchow's Jahresberichte, 1883, Band i., p. 438) also quotes a case of poisoning with 2 grammes (30 gr.) of a very old extract.

[4] Ein Beitrag zur Kenntniss der Cannabis Indica. Dissertation, Jurjew, 1894, p. 66.

[5] Imperial Institute Journal, vol. ii., No. 15, p. 105 (March, 1896).

[6] This account has been compiled from Watt's Dictionary of the Economic Products of India, vol. ii., p. 113 et seq., to which the reader is referred for further information, and from a private letter from my friend Mr. John Stephenson, I.M.S. A good account is also given in Flückiger and Hanbury's Pharmacographia, p. 493.

into cakes or pills. Most of the substance is prepared in Kashmir and is imported into Northern India (the Punjab principally and the North-West Provinces) from there. It varies considerably in activity, being adulterated to a great extent with powdered leaves and other substances. *Gánjá* is composed of the "female flowering tops with the resinous exudation on them." After gathering, these are exposed to the heat of the sun and then left over-night to the influence of the dew; afterwards they are pressed into shape by the stamping of native men. Both gánjá and charas are cultivated products and are chiefly used for smoking. *Bháng* comprises the mature leaves, and in some parts of India the fruits and very young twigs also, but not the stems. By trituration with sugar and water a beverage is made which is known as haschish or bháng. It is the least injurious form of cannabis and the one most frequently used. It is often prepared from wild plants growing around the native huts; consequently it is inexpensive and the greater part probably escapes duty. Various other preparations and natural products are known, but with these we are not concerned.

Historical.—The first European to investigate with any degree of scientific accuracy the action of Indian hemd was O'Shaughnessy[7] (1839). He used an alcoholic extract made by boiling freshly prepared gánjá with rectified spirit in a Papin's digester and evaporating the spirituous extract to dryness on a water bath. The substance thus obtained was very active; half a grain produced a distinct effect, and one and a half grains O'Shaughnessy regarded as a large dose. The estimated yield from fresh gánjá was 20 per cent. The process was subsequently modified by Robertson[8] (1846). He used a percolation apparatus, and extracted the drug with distilled alcohol. A green product was obtained, which he stated (probably erroneously) to be six times stronger than O'Shaughnessy's brown extract. The resin in a state of comparative purity was next obtained by T. and H. Smith[9] (1846). They digested bruised gánjá in successive quantities of warm water until the liquid came away colourless, then in sodium carbonate solution for two days at a moderate heat. The residue was next pressed, washed, and dried and then extracted with rectified spirit. The spirituous extract was now treated with milk of lime, filtered, and the excess of lime precipitated by sulphuric acid. A little animal charcoal was added, the mixture agitated, and filtered. Most of the spirit was now distilled off, water was added, and the remaining spirit allowed to evaporate gradually. The residual resin was then washed until free from acidity and bitterness and afterwards dried in thin layers. The yield was 6–7 per cent. Thus obtained the resin, to which they gave the name of *cannabin*, was extremely active; two-thirds of a grain produced narcosis and one grain decided intoxication. De Courtive[10] (1848), independently of Messrs. Smith, also isolated an active resin. This was obtained by extracting the leaves of Algerian hemp with spirit at a moderate heat, precipitating with water, re-dissolving the precipitated resin in alcohol, and evaporating. The yield was 9–10 per cent. Five centigrammes (about two-thirds of a grain) produced a distinct effect. Smaller quantities of a similar though less active product were obtained from plants grown in France.[11] Personne[12] (1857) controverted the results obtained by the brothers Smith. By distilling hemp with water he obtained an oily body[13] which he subsequently separated into two distinct compounds—*cannabene*, a liquid with the formula $C_{18}H_{20}$, and *hydride of cannabene*, a crystalline solid[14] with the formula C_6H_{14}; the latter body is physiologically inactive. Arutinianz believed[15] that he had obtained the hydride of cannabene, but as he concludes, according to Lapin, as to the identity of the two from the percentage of carbon present, this is doubtful. Personne attributed the effect of cannabis in great part to the cannabene he obtained, but on totally insufficient grounds, and he further states that by distilling Smith's resin with soda-lime at 300° C. (=572° F.) the residue was rendered inert. Considering the heroic treatment we may, perhaps, not question this, but as the dose given (from 0·2 to 0·5 *centi*gramme) would be inadequate to produce any effect proof is wanting[16] Messrs. Smith[17] themselves had shown that the activity of the resin was not due to any very volatile compound by exposing it to a temperature of 180° F. (82° C.) for eight hours freely to the air: the product was still as active as before. Vignola[18] (1895) has recently shown that Personne's cannabene is an impure sesqui-terpene. The pure substance he obtained by distilling in a current of steam, extracting the distillate with ether and subsequently purifying by repeated distillation from metallic sodium. It was then found to have the formula $C_{15}H_{24}$, and appears to be the same body as was obtained by Valenti[19] in 1880 from ordinary hemp. Moreover, Roux[20] proved by researches on animals that the ethereal oil was inactive, whereas an alcoholic extract was a decided intoxicant.

Nothwithstanding the investigations of O'Shaughnessy, Smith, and De Courtive it was thought that cannabis might contain some alkaloidal principle. Preobraschensky[21] (1876) obtained nicotine from a specimen of haschish obtained in Turkestan and from the flowering tops of the plants. As cannabis preparations are usually smoked in combination with tobacco, Dragendorff and Marquiss[22] suggested that the nicotine was derived from admixture with this substance—a supposition proved by Siebold and Bradbury[23] (1881) and Kennedy[24] (1886). Although Kennedy failed to obtain nicotine he was of opinion that an alkaloid was present, and Siebold and Bradbury also isolated a varnish-like base which they termed *cannabinine* and which gave alkaloidal reactions. The substance had an odour of coniine, but was not identical with it. Only two grains were obtained from ten pounds of drug. Arutinianz[25] and Masing,[26] on the contrary, obtained no alkaloid. In 1883[27] Hay discovered an alkaloid which produced tetanus in frogs and to which he gave the name of *tetano-cannabine*. It was present in very small amount and its elementary composition was not determined. His results led him to believe that other alkaloids were present, but these do not appear to have been isolated. Denzel[28] (1885) also obtained a tetanising alkaloid from hemp, but Warden and Waddell[29] (1884), working on large quantities of material, obtained no such compound. It is only fair to state that the process employed was slightly different to that of Hay, and a cat instead of a frog was used to determine its effect. A nicotine-like substance was obtained, but this proved to be physiologically inert

7 On the Preparations of the Indian Hemp or Gunjah; Calcutta, 1839. Also, Transactions of the Medical and Physical Society, Calcutta, 1839; Journal of the Asiatic Society, vol. viii.; Bengal Dispensatory, 1842, p. 579; Provincial Medical and Surgical Journal, 1843, pp 343, 363, 397. The leaves of European hemp had previously (1821) been examined by Tscheepe (Chemische Untersuchung der Hanfblätter, Dissertation, Tübingen).

8 Pharmaceutical Journal, vol. vi., p. 70.

9 Ibid., vol. vi., p. 171 (see also p. 127).

10 Journal de Pharmacie et de Chimie [3], tome xiii., p. 427. Comptes Rendus, tome xxvi., p. 509.

11 Other investigations are also recorded about this time. Foy (Journal de Pharmacie et de Chimie [3], tome xiii., p. 350) extracted haschish with water, alcohol, acetic acid, white and red wines, butter, lard, and olive oil, but did not succeed in adding much to our knowledge. Martius (Gmelin's Handbook of Chemistry, Cavendish Society's edition, vol. xvii., p. 447) obtained a shining clear brown resin.

12 Journal de Pharmacie et de Chimie, tome xxxi., p. 46.

13 Bohlig (Pharmaceutisches Centralblatt, 1840, p 519) had previously obtained an oily compound with similar physiological properties from European hemp.

14 Personne gives the formula in the old notation—$C_{36}H_{20}$ and $C_{12}H_{14}$. The formula of the last-named body is erroneously given in most books as $C_{18}H_{22}$. Personne gives the percentage composition C. 84·02; H. 15·98, which more closely approximates to C_7H_{16}.

15 Chemischen Untersuchungen des Indischen Hanfs. Dissertation, St. Petersburg, 1881. Quoted by Leib Lapin, p. 25.

16 Personne appears to have fallen into error with regard to the activity of Smith's resin. This is stated to produce a distinct action in doses of 0·05 centigramme. It should have been *gramme*. The dose of residue given, therefore, was too small to produce any effect, even with the original substance.

17 Loc. cit., p. 173.

18 Gazzetta Chimica Italiana, vol. xxv., i., 110. Abstracted in the Journal of the Chemical Society, vol. lxviii., i., 623.

19 Ibid., vol. x., p. 479. Abstracted in the Journal of the Chemical Society, vol. xl., p 284.

20 Bulletin Général de Thérapeutique, Dec. 15th, 1886, p. 492. Curiously enough, Roux states that an ethereal extract produces insignificant results.

21 Pharmaceutische Zeitschrift für Russland, 1876, p. 705. Also Dissertation, St. Petersburg, 1876. Quoted by nearly all writers.

22 Pharmaceutische Zeitschrift, 1877. Abstracted in the Year-book of Pharmacy, 1878, p 248.

23 Pharmaceutical Journal [3], vol. xii., p. 326; Year-book of Pharmacy, 1881, p. 453.

24 Pharmaceutical Journal [3], vol. xvii., p 453.

25 Loc. cit.

26 Dragendorff: Die Gerichtlich-Chemischen Ermittelung von Giften, zweite Auflage, p. 240.

27 Pharmaceutical Journal [3], vol. xiii., p. 993.

28 Pharmaceutische Centralhalle für Deutschland, 1885, No. 46, p. 540.

29 Indian Medical Gazette, vol. xix., p. 259. I was unable to find the continuation of the paper, but an excellent account is given in the Pharmaceutical Journal [3], vol. xv., p. 594.

Jahns[30] (1887) also states that *tetanin* does not exist. More recently (1891) H. F. Smith[31] isolated an alkaloid resembling coniine from Indian hemp, but in such small quantity (0·75 milligramme per kilogramme) as to render it therapeutically unimportant. Still more recently (1895) Marino-Zuco and Vignola[32] prepared an alkaloid from various parts of "cannabis indica and cannabis sativa," but neither alkaloid possessed the characteristic action of cannabis compounds. Physiologically they were cardiac depressants, the alkaloid from cannabis indica being much the most powerful. The most recent investigators, Wood, Spivey, and Easterfield[33] (1896), failed to obtain any alkaloid from charas, and the bulk of evidence is therefore against the view that the effects of cannabis are due to an alkaloidal principle. In 1887 Jahns[34] obtained a crystalline base which he subsequently recognised as choline. He pointed out that chemically this body would explain the alkaloidal base obtained by previous observers, but it differs in crystalline form and solubility in ether from Hay's tetano-cannabine; physiologically, also, their action is different.

Of the more recent investigators Warden and Waddell[35] seem to have commenced upon the right lines. They argued that "as many of those addicted to the haschish form of intemperance obtain the intoxicating effects by smoking the plant in a pipe, it is to be expected that destructive distillation of the freshly prepared resin might yield up the active principle." They therefore made an alcoholic extract of the plant, added excess of caustic potash, and distilled. An amber-coloured oil came over, which, by exposure to the air or by the action of alkalies, rapidly assumed a dark brown colour. The oil contained ammonia, phenol, and other products of destructive distillation, and was "devoid of narcotic and irritant properties." One drachm administered to a cat produced no sensible effect. Leib Lapin[36] (1894) isolated a substance which he termed *cannabindon*, and which appears to possess the physiological action of fresh cannabis preparations. This he obtained by warming the plant with milk of lime and extracting with ether. The ethereal extract he treated successively with acetic ether, alcohol, petroleum ether (twice), and water, the precipitate being rejected each time. The second and third fraction obtained by precipitating with water contained impure cannabindon; this he subsequently purified. Last year, Cowan Lees[37] expressed a belief that watery extracts contained some active ingredient of cannabis. He describes good effects from the use of such preparations, but I am not aware that any scientific explanation has yet been given of them.

The most important results of recent years are those of Wood, Spivey, and Easterfield.[38] Working with charas they isolated from an ethereal[39] extract—(1) a terpene, boiling-point from 160° to 180° C., yield 1·5 per cent.; (2) a sesqui-terpene, boiling-point from 258° to 259° C., yield 2 per cent.; (3) a paraffin ($C_{29}H_{60}$?), melting-point from 63° to 64° C., yield 0·15 per cent.; and (4) a toxic red oil or resin ($C_{18}H_{24}O_2$), boiling at 265° C. under a pressure of 20 m.m. Hg., yield 33 per cent. As we should expect from its method of preparation the resin is extremely stable. It yields mono-acetyl and mono-benzoyl derivatives and is unacted upon by alcoholic potash, and, below 150° C. by hydriodic acid and phosphorus. It is insoluble in water, but soluble in alcohol, ether, benzene, and organic solvents generally. It appears to be the active constituent of the drug, and the authors have succeeded in isolating it from several cannabis preparations in the market—viz., from Smith's cannabine, 30 per cent.; Merck's cannabinon, 50 per cent.; Merck's ethereal extract, 26 per cent.; and Merck's cannabis resin, 26 per cent. As the compound contains at least one hydroxyl group the authors recommend the name *cannabinol* for it. Further investigations are being made upon its constitution, but as yet no further communication has been made.

As previously mentioned, all samples of charas are not of the same quality. From a second sample of this substance, undoubtedly inferior to the first, Easterfield and Wood were only able to extract 15 per cent. cannabinol.[40] Another sample of charas sent to me by my friend, Surgeon-Lieutenant John Stephenson, I.M.S., and obtained in the cantonments at Peshawar, was of intermediate quality. Various other preparations of cannabis indica (Merck's, Bombelon's, Denzel's, Gastinelli's, &c.) are known, and even largely used, but as these have not added much to our knowledge of the chemistry of this body I shall not mention them further. By oxidising cannabis resin with nitric acid Bolas and Francis[41] (1868) obtained a crystalline substance oxy-cannabine ($C_{20}H_{20}N_2O_7$), but the physiological action of this compound was not determined. Flückiger[42] failed to obtain it.

Personal experiments.—The substances isolated by Wood, Spivey, and Easterfield were passed on to me for pharmacological investigation. Owing to the pressure of other work this investigation is not yet finished but as soon as time permits it is hoped to complete it and give a full account of the pharmacology of this drug. The present experiments are of a purely personal character and are merely to establish the activity of cannabinol and introduce it into therapeutics. The experiments themselves I intend to comment upon at some future time.

I was under the impression that I had taken a small dose of impure cannabinol some time previously without any effect, when, on the afternoon of Feb. 19th last, whilst engaged in putting up an apparatus for the distillation of zinc ethyl, I took from 0·1 to 0·15 gramme (from 1½ to 2 grains) of the pure substance from the end of a glass rod. It was about 2.30 P.M. The substance very gradually dissolved in my mouth; it possessed a peculiar pungent, aromatic, and slightly bitter taste, and seemed after some time to produce slight anæsthesia of the mucous membranes covering the tongue and fauces. I forgot all about it and went on with my work. Soon after the zinc ethyl had commenced to distil — about 3.15 — I suddenly felt a peculiar dryness in the mouth apparently due to an increased viscidity of the saliva. This was quickly followed by paræsthesia and weakness in the legs, and this, in turn, by diminution in mental power and a tendency to wander aimlessly about the room. I now became unable to fix my attention on anything and I had the most irresistible desire to laugh. Everything seemed so ridiculously funny; even circumstances of a serious nature were productive of mirth. When told that a connexion was broken and that air[43] was getting into the apparatus and an explosion feared I sat upon the stool and laughed incessantly for several minutes. Even now I remember how my cheeks ached. Shortly afterwards I managed to collect myself sufficiently to aid in the experiment, but I soon lapsed again into my former state. This alternating sobriety and risibility occurred again and again, but the lucid intervals gradually grew shorter and I soon fell under the full influence of the drug. I was now in a condition of acute intoxication, my speech was slurring, and my gait ataxic. I was free from all sense of care and worry and consequently felt extremely happy. When reclining in a chair I was happy beyond description, and afterwards I was told that I constantly exclaimed, "This is lovely!" But I do not remember having any hallucinations: the happiness seemed rather to result from an absence of all external irritation. Fits of laughter still occurred; the muscles of my face being sometimes drawn to an almost painful degree. The most peculiar effect was a complete loss of time relation: time seemed to have no existence: I appeared to be living in a present without a future or a past. I was constantly taking out my watch thinking hours must have passed and only a few minutes had elapsed. This, I believe, was due to a complete loss of memory for recent events. Thus, if I walked out of the room I should return immediately, having completely forgotten that I had been there before. If I closed my eyes I

[30] Fischer, B.: Die Neueren Arzneimittel, dritte Auflage, p. 222, footnote.

[31] American Journal of Pharmacy, 1891, p. 386.

[32] Gazzetta Chimica Italiana, xxv., i., p. 262; Abstracted in the Journal of the Chemical Society, vol. lxviii., i., p. 631.

[33] Transactions of the Chemical Society, vol. lxix., p. 541.

[34] Archiv der Pharmacie, 1887, p. 479; quoted in Dymock, Warden, and Hooper's "Pharmacographia Indica," vol. iii., p. 338; also Pharmaceutical Journal [3], vol. xvii., p. 1049.

[35] Pharmaceutical Journal [3], vol. xv., p. 575.

[36] Loc. cit.

[37] Brit. Med. Jour., 1895, vol. i., p. 300.

[38] Loc. cit.

[39] Alcoholic and petroleum-ether extract also (Easterfield and Wood). Proceedings of the Cambridge Philosophica Society, vol. ix., p. 144.

[40] Private communication. Macnamara (1872) determined the amount of resin in various samples of gánjá—Dr. Prain's report on the Cultivation and Uses of Indian Hemp to the Indian Government. Abstracted in the Imperial Institute Journal, March, 1896.

[41] Transactions of the Chemical Society, vol. xxii., p. 417 (1869).—Chemical News, vol. xxiv., p. 77.

[42] Pharmacographia (1874), p. 494.

[43] Zinc ethyl takes fire on contact with air and consequently must be distilled in an atmosphere of carbon dioxide.

forgot my surroundings and on one occasion I asked a friend standing near how he was several times within a minute. Between times I had merely closed my eyes and forgotten his existence. Another peculiar effect was the occurrence of lucid intervals. They seemed to come on suddenly, sometimes but not always as if the result of an effort of the will. They lasted a variable time, being shorter when the symptoms of intoxication were most marked. In them I could converse in a fairly rational manner and even direct the work of the laboratory to a certain extent. But even in my sanest moments I was deficient in will power. I offered no resistance to being pulled out of the chair and made to walk the laboratory floor, and when asked if a medical man might be sent for I objected, but had no power to say "No." At one time, although walking rapidly, I felt cold and had to adjourn to an adjoining room where a fire was burning. I stood before it and thought how strange things were. I had a hazy notion of having been rational once and I wondered if ever I should be rational again. I was devoid of feeling, fearless of death, and even insensible to the feeling of others: if the friend by my side had died I think I should have laughed. About 5 o'clock a medical man was sent for. I had now been rational for nearly half an hour, but as soon as he appeared I again fell into an acute delirium and performed the same antics I had performed before. I knew I was acting foolishly, but I could not help it. Gradually I became calmer and then I told him what I had done. I could not have been devoid of reasoning power, for when he suggested an emetic I argued that it would do little good, as most of the substance must have been absorbed; I was too happy to be disturbed in that way. I told him I was getting better, but soon afterwards I again lost control. At 6 o'clock I had two cups of coffee and then feeling somewhat better walked home. The street seemed longer than usual and its lamps almost interminable, but although I had looked across the quadrangle previously this was the only illusion of distance that I noticed. The fresh air and exertion revived me. I ate a good dinner, afterwards read a little, and retired to bed at 11 o'clock without having experienced any symptoms of sleepiness. I quickly fell asleep and woke at 7 A.M. My memory had not quite returned to normal, but otherwise I was quite well. At 11.30 slight tenesmus and relaxation of the bowels occurred.

Although these notes were written immediately after the experiment many things which happened are not recorded; of many of them I have not the slightest recollection. I am told that early in the intoxication I drank water frequently, even out of my hand, but I have no remembrance of it. During the action of the cannabinol my pulse rose from 60 to 90 per minute, sensibility as determined by pinching was blunted, and my appearance was described as "ashy pale." The pupils were dilated somewhat,[44] but throughout reacted to light and accommodation. At no time do I remember having had hallucinations; no unpleasant after-effects were experienced, and the drug appears to possess no constipating action.

About three weeks after the last experiment 0·05 gramme (⅘ grain) of cannabinol was taken (2.35 P.M.). No effect was felt for four hours; then symptoms similar to those I have described, but less severe, occurred. First, there was dryness, or rather sliminess, of the mouth and a peculiar taste. This was soon followed by weakness in the legs and intoxication. After dinner (7 P.M.) I sat in an easy chair and closed my eyes. A dreamy state supervened and visions of a grotesque character appeared. A regiment of soldiers was seen marching; their movements gradually increased to running, their legs went faster and faster, until finally the whole regiment was lost in a number of rapidly revolving circles. Then visions of ugly boys were seen; from slight ugliness greater ugliness developed, and this increased so as to become ridiculous. Similar hallucinations occurred in a friend. Accompanying—probably preceding—this dreamy state was a pleasurable tingling all over the body, sometimes and in some places (the cheeks especially) becoming almost painful. Time seemed long, but it did not pass with the same rapidity as on the former occasion, or rather I did not experience the same forgetfulness; external relations were more connected. Gradually I grew sleepier, and it was with difficulty that I kept my eyes open. I did not succeed in sleeping in a chair, and at 9 retired to bed. Sleep did not follow for some time and I awoke at 6 A.M. As before, slight relaxation of the bowels occurred. Much smaller doses (0·01 gramme, about ⅙ grain) produced no sensible effect.

A few months afterwards a non-medical friend complained of sleeplessness and at my request took 0·05 gramme (⅘ grain) cannabinol made into a pill with starch. He afterwards supplied me with the following account: "The pill was taken at 10.30, just before retiring for the night. I probably dozed a little at first, but I remember hearing the clock chime 11.30 and later 11.45. Almost immediately afterwards I began to see strange sights, which passed so rapidly that I had no time to examine them in detail. One that I remember was a bow-legged boy running with a chest of tea between his legs; another seemed like a procession of females in the distance, but on closer examination turned out to be coffins; these quickly melted away, leaving nothing but confusion. The clock struck 12, then 12.15. I remember nothing further until I awoke refreshed at 8 A.M. from a sound slumber." Cannabinol has been used in a few other cases as a hypnotic and with success, but at present I do not wish to enter into its uses as a medicine or even to recommend it as a therapeutic remedy. Considerable experience is always needed to establish the usefulness of any medicine, and this I have not yet been able to obtain. All that is claimed for this substance is that it is active—as active as any preparation yet made—and pure. Whether it will change by keeping or not time alone can tell. Perhaps when greater leisure enables me to complete the pharmacology of the drug I may be able to speak more definitely upon this point.

Of the other constituents of charas the terpenes are the most important. These have no peculiar action; they act as terpenes and in doses of 0·5 gramme (from 7 to 8 minims) are apparently without effect. It is possible that the good effects obtained by some physicians (Silver, McConnell, Bond, Edwards, &c.) in cases of menorrhagia, dysentery, &c., may be partly due to these constituents, but of this I hope to speak later. In conclusion, I express my thanks to Mr. Wood, Mr. Spivey, and Mr. Easterfield for the material with which they supplied me; to my friend, Mr. Stephenson, for samples of cannabis; and to Mr. Heath for notes of his observations during the time I was under the influence of the drug.

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[44] In the case of the Brothers Smith they were contracted (Pharmaceutical Journal, vol. vi., p. 173).

ON CERTAIN APPARENTLY ORGANIC TUMOURS OF THE ORBIT WHICH DISAPPEAR UNDER MEDICINAL TREATMENT.[1]

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I HAVE for a long time been familiar with the clinical fact that internal medication can in certain instances bring about the disappearance of orbital tumours. This is true, moreover, of tumours which exhibit features rendering differentiation from those of a malignant or certainly organic nature difficult, and but for the effects of treatment the distinction would perhaps be impossible without an examination of their minute structure. Just now I am thinking particularly of orbital growths occurring at about the middle period of life, when those of a malignant nature would be prone to arise. I propose to relate recent instances illustrative of this contention.

Panas of Paris, at the annual meeting in London of the British Medical Association in 1895,[2] brought forward a very valuable and instructive paper dealing with pseudo-malignant tumours of the orbit. He expressed the opinion that because dispersion of these growths followed the administration of iodide of potassium it was a mistake to regard syphilis as the only cause, and he believed that a "number of neoplasms thought to be lymphomas, sarcomas, or syphilomas ought to be attributed to the dyscrasia produced by some toxin." He spoke of a class of infectious tumours, the syphilitic being an example but not the only one. We are of course all familiar with the frequent impossibility of getting a specific history even in

[1] Read before the Sheffield Medico-Chirurgical Society, Oct. 22nd, 1896.

[2] Brit. Med. Jour., vol. ii. 1895, p. 955.