The question arises whether cells which have undergone a reducing nuclear division are "inclined" in plants or in animals to self-fertilization or fertilization from chemical stimuli. Such a phenomenon in cancer would presuppose that a sexual change is signified by this reducing division, similar to the sexual and asexual phases in the life-cycle of certain sporozoa and dependent on intrinsic and extrinsic (environment) forces. Parthenogenesis brought about in some way might explain by reinforcement the wonderful power of mimicry of original structures seen in metastases. It has long been known that parthenogenesis occurs in certain animals, and it has been shown in some cases to result from the lack of separation from the egg-nucleus of the second polar body, or to follow on the re-fusion of this body with the egg-nucleus. As stated by Professor Farmer in his kind reply to my letter of inquiry¹ parthenogenesis has been shown to occur in consequence of chemical stimuli, in cases where the egg-nucleus evidently possesses the reduced number of chromosomes. On the other hand, Dr. Bashford believes that the heterotypic mitoses are the expression of a terminal phase in the life-cycle of the cancer-cell.

Fig. 1.—Part of a section of a glandular carcinoma of the rectum, showing a somatic and heterotypic mitosis in two cells of a gland. Both figures show the "metaphase" stage, the figure being viewed from one of the two poles of the spindle. In the somatic figure nearly the whole of the thirty-two chromosomes are shown; in the heterotypic figure nine thick curved chromosomes are seen in the section.

A second structural change that links malignant processes is afforded by the morphological transition of cells of sarcomatous to those of epithelial form. Many sections of an "adenocysto-sarcoma" of the breast (removed by Mr. C. Whipple at the South Devon Hospital from a woman, aged 52) show that the columnar cells of the intracystic growths pass by gradual transition into large sarcomatous elements. Again, in a huge diffuse melanotic sarcoma of the liver (in another woman, aged 52, under the care of Mr. W. L. Woollcombe), the hepatic capillaries were stuffed with pigmented cells, varying from the size of small endothelial to that of large sarcomatous elements. A pigmented mole over the seventh right intercostal space showed similar pigmented cells in the cutis; the thyroid gland in this case was the seat of an adenoma. Though such a mole may be considered to be sarcomatous or again to be epitheliomatous, I regard it as a primary endothelial tumour, on the same grounds that Raymond Johnson and Lawrence regard "parotid tumours" as endotheliomata.

Similarly, H. D. Rolleston and O. Grünbaum note as follows in a "perithelioma" of the cheek: "Striking features are the transition from cells of a sarcomatous type to cells resembling columnar epithelium and the villous or papillomatous arrangement," despite the use of selective epithelial

stain.² This is not "metaplasia," defined by S. G. Shattock and C. A. Ballance as the transformation of one normal tissue to another, but is akin to true "heterology" (Virchow). It appears to be the reverse of that which is seen in those tumours in which epithelial and sarcomatous elements are formed from "indifferent" tissue.³

Not only may such changes as calcification, pigmentation, vascularity, etc., be faithfully transmitted from primary to secondary growths, but pigment appears in the neighbourhood of certain pigmented secondary deposits (for example, in or between the liver cells). This cannot be explained by the wandering of pigmented sarcoma cells, comparable to the wandering of pigment cells in fishes, but may be an excretion. It even appears in some sections as if the cells of a secondary deposit and those of the organ exert mutual action on each other's shape. Again, carcinoma can convert adjacent normal tissues to stroma. Both phenomena suggest that environment does influence the "germinal" cells of these growths, chemically or otherwise, despite the tendency of Jensen's experiments to magnify the potentiality for growth and reproduction inherent in "epitheliomatous" cells in the mouse.

Fig. 2.—A to G are from the same series of sections as Fig. 1 (glandular carcinoma of rectum). A is a somatic mitosis, metaphase, and 25 of the 32 chromosomes are seen; in B, C and D, the spindle is cut longitudinally; in E, F and G it is cut transversely at about the middle. In B to G the mitoses shown are of the heterotypic kind, the chromosomes being few, thick, and irregularly shaped. In some cases they are evidently ring-shaped, and in E one of the chromosomes shown is branched, being Y-shaped in section. G is probably a multipolar mitosis, the chromosomes showing a tendency to form three groups, but the spindle-threads were not distinct. H and I are from a sarcoma in fascia of thigh, H being a beautiful example of a somatic mitosis, whilst I is heterotypic, the section showing only 4 curved chromosomes. J is from a carcinoma mammae, heterotypic metaphase, showing four thick bent chromosomes; above is seen the resting nucleus of an adjacent cell. The drawings were made with uniform high magnification.

The figures which accompany this paper are from cases under the care of Messrs. R. H. Lucy, W. L. Woollcombe, and C. E. Russel Rendle at the South Devon Hospital, to whom I express my thanks for the material obtained on removal during operations. I am greatly indebted to Mr. F. Cavers for his beautiful and exact drawings, some of which are here reproduced.

REFERENCES.

- ¹ *Nature*, February 25th, 1904, p. 392. ² *Trans. Pathol. Soc. Lond.*, vol. liv, p. 353. ³ The "blastomata" of C. P. White, *Lancet*, February 15th, 1902; and of H. Snow.

THE TREATMENT OF INEBRIETY BY ATROPINE.

By C. A. McBRIDE, M.D. TORONTO, L.R.C.P. AND S. EDIN.

As doubt is sometimes thrown on the efficacy of all short-term systems of treating inebriety, a few notes on the subject based upon a lengthy and somewhat wide experience, may be of interest, especially as I have come to the conclusion that in the majority of cases long periods of detention are wholly unnecessary, and that a complete recovery, with absence of all craving for stimulants, may generally be expected after a course of treatment lasting six weeks.

The advantages of a short-term system, if efficient, are so obvious as not to call for enumeration. The question, of course, is whether the treatment results in permanen

recovery. As to this, there is, to my mind, no doubt whatever, assuming that the drugs be not only rightly selected but rightly employed.

The essential element of the treatment I have found successful is the administration of atropine. This is most conveniently given hypodermically, using the sulphate. In my opinion this drug has a specific action, and, although probably by itself insufficient to eradicate a craving for alcohol or other narcotics previously administered, it is, in the great majority of cases, essential to the treatment. Along with atropine it is my practice to administer at the same time strychnine, and I consider it also of great importance to exhibit regularly a bitter tonic, usually a fluid extract of cinchona bark. The cases to be mentioned subsequently will indicate the method of treatment. I may here say generally that the drugs used must at first be given in small doses which subsequently are increased; that their exhibition must be conducted personally by the medical attendant in charge of the patient and not deputed to others, and that the drug should be pushed until a distinct physiological effect is produced. In an adult where there is no delirium or serious complication, the doses I am in the habit of administering are as follows:

1. Atropine sulphate commencing at $\frac{1}{320}$ gr. three times a day, increased gradually during the first week until the pupils are affected and the mouth becomes dry. In most cases $\frac{1}{80}$ gr. will be the maximum dose.

2. Strychnine nitrate given at the same time subcutaneously in doses beginning with $\frac{1}{80}$ gr. and rising to $\frac{1}{20}$ gr. in the majority of cases.

3. Fluid extract of red cinchona bark given every three hours in ordinary doses by the mouth.

It will be obvious that in the administration of powerful drugs of this kind considerable judgement is required, and that in many cases it is needful to modify the above treatment. Auxiliary methods of treatment are also of great value, amongst which may be mentioned attention to the general health of the patient, the use of warm baths, special dietary, and regulated exercise. In cases where there is delirium, or when maniacal symptoms are threatened, as is only too common in cases of acute alcoholism, other remedies may be required. Even at the risk of somewhat lowering the strength, it is generally advisable to administer a brisk purge at the commencement of treatment, in order to remove imperfectly eliminated waste products. Bovril containing plasmon may be administered freely and frequently.

To illustrate the application of the remedies I have selected four cases, each one being typical of a different class of inebriate.

CASE I.

E. M., aged 45, entered for treatment August, 1895; of cadaverous appearance, slight physique, markedly nervous, general health bad, suffering greatly from insomnia. He was a heavy smoker. The attacks of alcoholism were periodical, and lasted about a fortnight. During the two or three months' intervals he had no desire for stimulants. While transacting his ordinary business he would suddenly be seized with an uncontrollable desire for them, and rushing from the room would disappear for a time; he would be found later in the back room of some low inn, where he had been drinking large quantities of whisky. During the debauches he would talk quite rationally, but afterwards could remember nothing of what had occurred. Prior to the beginning of treatment the patient was found by his friends, after having been in hiding for three days, commencing a fresh debauch.

Finding the patient hypersensitive to the effect of strychnine, I did not push this drug beyond $\frac{1}{80}$ gr. three times daily. In combination with this I gave atropine sulphate, commencing with $\frac{1}{320}$ gr., and gradually increasing the doses until the eyes and mouth were affected; this strength was maintained for a fortnight, and the drug withdrawn two days later. The patient was also given every three hours a mixture of red cinchona bark, gentian, and capsicum. The above strength of strychnine was maintained until the twenty-eighth day, when it was gradually reduced to *nil* at the end of the fifth week. The capsicum in the mixture was only administered during the first fortnight, and the simpler mixture continued during the remainder of the course. The patient lost the craving for stimulants on the third day; on the next day the insomnia disappeared; his general health improved with marked rapidity, and he left the sanatorium at the end of six weeks enjoying excellent health.

In 1901, when I last heard of this man, he was still perfectly well, and there had been no return of his troubles.

CASE II.

W. B., aged 45, entered November, 1896; married. At the time of commencing treatment he had been drinking to excess for five years. His nervous system was completely shattered and the heart's action weakened; he was very emaciated and anaemic.

Treatment was as follows: Strychnine injections were administered four times a day, commencing with $\frac{1}{80}$ gr., and sulphate of atropine,

commencing with $\frac{1}{320}$ gr. At the end of the second day the desire for alcohol had completely disappeared. On the morning of the third day I was, however, compelled temporarily to withdraw the atropine as the man began to develop symptoms of delirium tremens; these I met with a hypodermic injection of $\frac{1}{4}$ gr. of morphine, which sent the patient into a sound sleep lasting ten hours. After regaining consciousness the delirium had quite disappeared. The atropine injections were resumed upon the following day and continued as in Case I: the strychnine was rapidly increased, so that by the fourth day he was receiving $\frac{1}{20}$ gr. each injection, and this strength was continued for twenty days, when it was gradually reduced to nothing at the end of the fourth week. The rest of the treatment varied but little from that in Case I.

The patient was so satisfied with the results that during the two years following his admission he was the means of inducing a number of men from his native town to undergo treatment. I may state that most satisfactory reports regarding this patient have recently come to hand—that is, September, 1903.

CASE III.

A. B., aged 32, married, one child, entered for treatment May, 1891. He was anaemic, of slight build, highly nervous, but there were no signs of visceral disease. He had been drinking to excess for about three years.

Entering under compulsion, and consequently refusing treatment, it was with difficulty that I succeeded in inducing him to submit to treatment by allowing whisky at frequent intervals. He was able to take this stimulant for two days, but on the morning of the third he could not bear its odour, and although he made persistent efforts to drink a glass of whisky and soda was quite unable to do so. Being an intelligent man, he recognized that some change had taken place, and decided to go through with the treatment. From that time on to the completion of the courses he gave me no trouble, but, on the contrary, became intensely interested in his progress towards recovery. The hypodermic treatment consisted of four injections daily of strychnine nitrate and atropine sulphate, commencing with $\frac{1}{80}$ gr. and $\frac{1}{320}$ gr. respectively. In conjunction with this he received every three hours a mixture of red cinchona bark, coca,* gentian, and capsicum. The strychnine was rapidly increased so that by the third day he was receiving $\frac{1}{20}$ gr. each injection, this strength being maintained for twenty-one days, when it was gradually reduced to *nil* at the end of the fourth week. The atropine was slowly increased until the usual physiological symptoms appeared on the fifth day, and this strength was maintained until the thirteenth day, when it was gradually reduced and finally discontinued on the sixteenth day. The coca and capsicum in the mixture were only administered during the first fortnight and the simpler mixture continued during the remainder of the course, which lasted altogether five weeks. During the whole course of treatment he resided with his wife at a neighbouring inn. Here he had every facility for indulgence in his former habits and enjoyed entire liberty after the fourth day. He rapidly gained in strength and flesh, his appetite for food returned during the first week and remained excellent throughout; he slept well, thoroughly enjoyed the daily exercise prescribed, and left for home in good health.

I met with this gentleman about three months ago, and ascertained that ever since the treatment thirteen years ago he had retained a strong aversion to all alcoholic stimulants. I may add that about seven years ago he passed through a severe financial crisis, owing to the worries of which he became very depressed. At this time he was in a strange country, separated from all his friends, and in the heart of a heavy drinking community. I naturally asked him whether, under this great trial, he felt any inclination to resort to stimulants; his reply was that he never once thought of them. Prior to his treatment his family physician had informed me that he would not live two months longer unless something was done to check his heavy excesses.

CASE IV.

C. H., aged 50, married, a commercial traveller, was treated May, 1891. He began drinking at the age of 20, but did not drink to excess till he was 35. Though a man of exceptional ability, his drinking habits had brought him so low as to cause him to sell his furniture to obtain money for drink. He had been unusually fleshy, but at this time the flesh hung upon him loosely, and there was considerable enlargement and tenderness in the hepatic region. The heart's action was weak, but there were no lesions; the mental faculties, even during sober periods, were enfeebled. The man was a nervous wreck, the slightest thing throwing him into either tears or excessive laughter.

Treatment was as follows: Three strychnine injections were administered precisely as in Case III. The atropine was commenced in the same way, but was temporarily withdrawn after two days' administration, as symptoms of delirium tremens appeared. Doses of whisky had been allowed periodically up to this time, and to obtain sleep 30 gr. of potassium bromide had been added to the final drink of the day. Although he slept off and on during the second night, the delirious symptoms remained. On the morning of the third day he was given $\frac{1}{4}$ gr. of morphine hypodermically; at the end of two hours the excitement had increased to such an extent that he was rapidly exhausting his remaining strength. Another $\frac{1}{2}$ gr. was injected, and after an hour and a-half had passed without the desired result another $\frac{1}{4}$ gr. was administered. This caused the excitement to subside in about ten minutes, so that he dropped into a deep sleep which lasted for about seven hours. Upon

* For some years now I have entirely omitted the use of coca, and believe that it played no useful part in the treatment of these earlier cases.

waking for a few minutes he took some bovril and I gave an injection of strychnine. Another quiet sleep ensued for about the same period as the first. During the few minutes he was next awake he was fed and treated as before; altogether he slept for twenty-four hours, at the end of which time the atropine injections were resumed and continued as in Case III. He found on regaining consciousness that the craving for stimulants was greatly lessened, and during the course of the next two days it not only disappeared, but was replaced by absolute aversion to alcohol. With the exception of some slight modifications incidental to the condition of the patient's system, the treatment varied but little from that in Case III during the remainder of the course. He returned home in what he was pleased to term "the pink of condition," his treatment having lasted five weeks.

During the second week he informed me that he had apparently been "living in a cloud," but he now felt as though "scales had fallen" from his eyes, and that he could not only think and see clearly, but that also his views on the use of intoxicants had been entirely reversed. His subsequent career proved that his recovery was complete. It may be added that three years after treatment he unintentionally took some brandy sauce when away from home; the effect was remarkable, in that he had hardly time to leave the dining room before vomiting. He remained well in January, 1904.

The four cases cited are typical of the majority, but I may refer to one extreme case that passed through my hands in October, 1895. It was a case of acute alcoholic poisoning in a man 30 years of age. He was a confirmed inebriate and not expected to rally from the unconscious condition in which I found him. I agreed to treat him in consultation with his medical adviser, provided consciousness was regained. The treatment was administered at his own home, and as the man had no idea that he was being treated for alcoholism, I purposely left the decanter and siphon within his reach. On the fifth day he ordered them out of his sight, remarking that their presence nauseated him. This may be scarcely credible, but I can vouch for the accuracy of the statement. It was not until his recovery was completed that he was informed of the reason of his treatment. When I last heard of the patient three years ago there had been no relapse to his former habits.

I think that the foregoing cases will fully illustrate the method of application.

I make no claim for originality in respect of the drugs used in this treatment of inebriety. The method of their application is, however, I believe, new, and I cannot find that the medical profession generally is aware of the specific action of atropine in combating inebriety. In the ordinary textbooks no mention is made of it. In Hare's *Therapeutics*, published in 1903, the value of strychnine and atropine is discussed. I may quote the following passages:

There can be no doubt that in most cases strychnine is beneficial, and that it markedly diminishes the depression of the period of withdrawal, and may even tend, as is claimed by Phelps (*Medical Fortnightly*, St. Louis, 1895, viii), to impair the appetite for alcohol. Though it has not in the writer's experience so valuable a property, no harm can be done by its use, especially in moderate doses. In many cases we must admit that its use is followed by most gratifying results.

Referring to the use of atropine, he says: "Its stimulating qualities are apparently of much service in many cases of alcoholism. Like strychnine, it appears to lessen the depression caused by the withdrawal. It seems to diminish especially the distressing epigastric and sinking sensations from which alcoholics suffer. . . . Clark (*New Orleans Medical and Surgical Journal*, vol. xxiii, p. 721) regards the combination with strychnine as almost a specific. He maintains that while strychnine acts as a nerve tonic the atropine has a special aptitude for decreasing the appetite for alcohol. Carter (*Medical News*, March 9th, 1895) also regards atropine as of special value. He declares that atropine given three or four times a day will produce a great distaste for alcohol in from one to five days; that whisky becomes repellent as regards both sight and odour, and that its taste becomes intolerable, producing nausea."

Hare also remarks further . . . "Atropine may indirectly lessen the craving for alcohol."

Having now for fully thirteen years used these remedies with a large measure of success, during which time I have treated several hundred cases, I feel justified in saying that a remedy is available which will prove of great value in the treatment of one of the most hopeless forms of disease.

The cases cited in this article refer simply to patients who have suffered from excessive use of alcohol. I have also used the treatment largely in the case of those who are suffering from the abuse of other narcotics, especially cocaine and morphine. I have never known unsatisfactory sequelae to result either in the case of these or alcoholic patients.

From an *a priori* point of view one would naturally think that recovery was impossible in a considerable number of cases. It is well known that alcohol produces extensive degeneration of the nervous elements in the brain and peripheral nerves, and as our present knowledge seems decidedly to indicate that very little repair of damaged nerve cells is possible

it is hard to believe in the complete restoration to mental vigour of patients who have for many years taken alcohol in great excess. Nevertheless, experience has shown me that many cases which are apparently most hopeless do recover under the treatment here recommended. I can hardly offer any explanation of this. I apprehend that in these cases the marked signs of mental deterioration are due to the effect of continued intoxication by alcohol retained in the body rather than to actual nervous destruction of tissue from alcoholic poisoning. No doubt some degenerative changes are present in most cases. The amazing recoveries which I have seen under the treatment here set forth make it perfectly clear to me, however, that the degenerative changes play but a small part in producing the obvious degradation and deterioration of the mental faculties.

I trust that the publication of these notes may result in this treatment having a careful and extended trial, but perhaps a caution is desirable lest the fate that sometimes follows the introduction of good methods of treatment should attend this and it become discredited by its wide adoption without proper precautions. Very considerable attention is required on the part of the physician. The cases are often exceedingly difficult to manage, and success is hardly likely to follow unless the treatment be carried out under proper conditions, and for this reason treatment in a sanatorium or other special institution is desirable in order to obtain the best results.

THE SO-CALLED "GOLD CURE" OF INEBRIETY.

By S. BACKWELL FENN, L.R.C.P. and L.R.C.S.Ed., etc.,
Medical Officer, Southport Hydropathic Hospital.

HAVING had the opportunity of treating many patients with, and watching the effects of, the so-called gold cure of inebriety for the last three and a-half years I esteem it a privilege and duty to testify to its methods and results. We are all only too familiar with the sad relapses occurring where the patient has been placed under restraint for six, twelve, or more months. Under these circumstances he is unable to procure the drink he craves for, and on leaving the retreat often immediately resorts to the prohibited stimulant and becomes its slave as before. The Americans have long recognized this, and institutions for the rapid cure of this disease abound in the new world, though it would appear that most of them work with secret or proprietary formulae. I am indebted to the Rev. Dr. Wolfenden for seriously calling my attention to the "gold cure" and inducing me to give it a trial.

The *modus operandi* of the "cure" is as follows: On entering the institution the patient is at once made thoroughly at home, and is given a glass or bottle of his favourite beverage if he wants it. No restriction is put upon his movements, and he can go in or out as he pleases between meals and the times for administering the medicines. A generous table is provided and, in some cases, extra nutrition is prescribed in the shape of soups, beef tea, oysters, etc. Before commencing the medicinal treatment the patient is thoroughly examined, and the presence or absence of organic disease ascertained. The "cure" then begins and consists of hypodermic injections, medicines given by the mouth and the administration of baths. The first are given four times a day and consist usually of a solution containing daturine sulphate gr. $\frac{1}{15}$ or atropine, gr. $\frac{1}{15}$ and strychnine sulphate gr. $\frac{1}{15}$, these doses being regulated according to the patient's condition. I have never seen an abscess or unduly sore arm from this frequent use of the needle. The medicine given internally is taken every two hours during the day and evening. This generally is a mixture containing chloride of gold and sodium gr. $\frac{1}{2}$, ammonium chloride gr. j, aloin, gr. $\frac{1}{2}$, fluid extract of viburnum m x and tincture of cinchona m xl . Should the patient suffer from diarrhoea I omit the aloin. It is found that small doses frequently repeated are better than larger ones at longer intervals.

If the patient from force of habit insists after the fourth or fifth day in taking alcohol, a little liquid extract of ipecacuanha is added to his medicine. The resulting emesis quickly induces him to abstain from his whisky. Should the medicine produce nausea, diarrhoea, or bilious symptoms I change the prescription accordingly. Tincture of capsicum, fluid extract of kola, and ammoniated tincture of valerian are drugs frequently used in addition to the above named. Special attention is paid to insomnia and neurasthesia, symptoms from which inebriates frequently suffer. The next, and by no means the least, important part