An Address

ON

THE DRUG HABIT.

DELIVERED AT A MEETING OF THE PHARMACEUTICAL SOCIETY,

BY

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THE food customs of mankind should not be regarded as random practices adopted to please the palate, or to gratify an idle and vicious appetite. They are more probably the result of experience and instinct which supply important wants in the animal economy. The natives in many different countries of the world use herbs containing caffeine or one of its allies in the form of a decoction or infusion, although such herbs possess neither characteristic taste or smell. Caffeine is obtained most readily from tea, which may contain anything from 3 to 5 per cent.; other plants are coffee from Arabia containing caffeine, cocoa from South America containing theobromine, kola from Central Africa containing both caffeine and theobromine, guarana paste from Brazil, Paraguay tea from the Argentine, and there are many others.

Stimulants in some form would appear to be even more essential to the exigencies of life under modern civilization. Caffeine, which is universal, is a powerful cerebral stimulant, but its action in banishing sleep and its effect on the heart effectually prevent it from being taken in excessive doses. Chronic poisoning by tea and coffee is not very uncommon and may occur when six or seven grains of caffeine are taken daily. The sufferer is tremulous, shows loss of self-control, and exhibits fits of excitement and depression; he has a haggard appearance and loses his colour. Cardiac symptoms are often first noticed. A renewed dose of the poison gives temporary relief. Such patients abandon their tea or coffee without much difficulty when they are assured that it is the cause of their trouble, and a true "craving" never exists.

TOBACCO.

Tobacco smoking is universal; the following table gives the composition of the smoke from the cigarette and the opium pipe:

Analysis of Tobacco and Opium Smoke in Conditions approximating to those which occur in Smoking.

	100 grams tobacco burnt as cigarettes.	100 grams dross opium containing 7.35% morphine.
HCN ...	0.080	0.010
Pyridine ...	0.146	0.147
Nicotine ...	1.165	—
NH ₃ ...	0.360	0.395
CO ...	410 c.cm.	0
Morphine ...	—	0.016

Chandoo opium smoke contains 0.1% morphine.

Ordinary Virginian tobacco from which cigarettes are made contains weight for weight nearly twice as much nicotine as Manila cigar tobacco. But when these two are burnt during smoking the smoke from the cigar contains more than twice the amount of nicotine in that from the cigarette. During the slow combustion of a cigar, as in ordinary smoking, immediately behind the lit end is an area in which the water and other volatile substances in the tobacco condense; during the act of smoking, a large portion of the nicotine at the seat of combustion is destroyed (50 per cent.), and the nicotine which finds its way into the mouth of the smoker is derived from the hot gases passing through this hot moist area in which the rest of the nicotine has condensed. The smaller the moist area behind the point of combustion, the less likely is the smoke to contain volatile toxic bodies. A thin cigar or a cigarette will yield fewer of these products than a thick cigar, for the thin cigar or cigarette obviously permits a relatively greater cooling.

The nicotine from the smoke of one cigar should correspond with the nicotine from that of twelve to eighteen cigarettes. In practice it seems as if even less nicotine than this reached the circulation unless the cigarette is smoked to the very end. Experiments we made some years ago on boys showed that the Manila cigar caused a con-

siderable rise in blood pressure in five or six minutes, followed by collapse, representing respectively the stimulation and depression of nicotine on nerve cells. No such effect could be obtained with cigarettes. The blood of cigarette inhalers, however, contains carbonic oxide—perhaps 5 per cent. for a man who smokes twenty cigarettes a day—and the vertigo, tremors, nausea, anaemia, and loss of memory for recent events are all symptoms which occur in chronic CO poisoning. The cigar smoker, on the contrary, absorbs a considerable amount of nicotine, and true nicotine poisoning may follow from excess.

Some tolerance can be acquired to both nicotine and CO. Nicotine tolerance is brought about by destruction of the alkaloid in the body of the addict; since the alkaloid reaches the circulation slowly and in minute quantities the tissues are able to deal with it. CO tolerance is known in animals, and is due to an increase in the number of red blood cells and percentage of haemoglobin.

The pleasure of smoking is no doubt partly due to the stimulating and later narcotic properties of nicotine, though there are other factors like rhythm and sight to consider. The habit is rarely very strong, as most of the nicotine is destroyed during combustion. A smoker never forms a very strong "craving," but were he to inject his nicotine the tale might be different.

ADDICTION DRUGS.

It is sometimes said that civilization is responsible for the craving for narcotic drugs; that men weary of the strain and anxiety involved in the fight for existence, and that anything that gives them relief from their cares and anxieties is seized with avidity. Those who are addicted to the use of narcotics in civilized communities are rarely the phlegmatic and the dull, but rather those possessed of quick perception, acute sensibility and other higher attributes of mind which go to make up the qualities of high breeding and culture. These people are so highly reflex, so easily responsive to external impressions, that the associations set loose by any ordinary stimulus cause such a complexity of cerebration that the ordinary affairs of life become a burden. In them mental activity quickly gives rise to fatigue, depression, and distress.

The higher faculties of mind, such as those concerned with choice, attention, judgement, and control, are the last to develop in man. They are not completely formed till the age of 15 or 16, and the nerve cells in the brain which are associated with these attributes of mind are the most delicate and by far the most sensitive to narcotic poisons, so that they would be influenced by narcotics before other cells, such as those associated with movements and sensations. It is therefore not difficult to understand why narcotic drugs are so esteemed by such people. In narcotism they shut out contact with reality and drift along knowing little of the reactions of mastery and defeat. They are sheltered by the inhibition of the higher centres. The very acuteness of their intellect is their undoing; they exaggerate the everyday trifles and inconveniences of life out of all proportion to their significance, and life becomes for them oppressive and anxious. Perhaps in a few special instances persons possessed of such vivid sensations may benefit by a narcotic, which limits these conflicting impulses by allowing a freer play of the higher mental faculties; certainly the records of De Quincey and Coleridge suggest such a possibility.

Increased nervous sensibility would seem to be an effect of civilization and wealth. An attempt was made some years ago to compare this sensibility in different nations by estimating the number of women who employed anodynes during normal parturition. The figures obtained were for the United States 70 per cent., Great Britain 50 per cent., and for Spain and Russia 5 per cent. The figures are interesting in view of the prevalence of addiction in the States. The morphinist is not a mental defective, and drug addiction does not lead to insanity or serious nervous diseases needing custodial care, but it makes the habitué more dangerous to society: it diminishes his usefulness to the community and injures his career. The addiction commences as a vice, like smoking, but the developed craving becomes a disease.

There seems to be agreement on the point that the addict is generally a psychopath before he acquires the habit (Rhein, McIver, and Price), while some authorities,

like Block, boldly assert that normal persons never become drug habitués.

The neurotic, having indulged on a few occasions with his narcotic, is so delighted with its effect in giving him some immunity against the stresses and worries of life that he desires, naturally enough, to repeat the panacea, and so the habit is formed, weak at first, but growing with each successive dose, and before he knows of his fetters he is a prisoner. It is not difficult in most cases to recognize in society those who are addicted to drugs. The chief characteristics of drug addicts are plausibility and disorderliness. They are full of schemes for the benefit of others, but, owing to luck always being against them, none of these fructify. They are late for appointments owing to the faults of others, and have no regard for time. In everything they are casual and slack to the extreme limit. Rules of ethic become so blurred that they are hardly regarded, and they lie for the sake of lying. When under the influence of the drug they can work and write, though after a somewhat disjointed and slovenly fashion.

OPIMUM.

Opium, or one of its derivatives, is the commonest addiction drug. Those who indulge in opium may be divided into three groups: the opium eater, the opium smoker, and the injector. The opium eater is uncommon amongst Europeans, possibly on account of the constipation, the delayed absorption, and the difficulty in obtaining the large supplies necessary. It is not unusual for the opium eater to consume half a pint or more of laudanum in the twenty-four hours, twenty drops being a liberal dose for a normal man.

The general use of opium eating in India led to the appointment of a Royal Commission in 1895, which reported that moderate indulgence led to no injurious effect and did not shorten life, but that, on the contrary, it tended to ward off sickness and lessened the discomfort consequent on poor food and malarial and other diseases. Sir W. Roberts, the Medical Commissioner, said: "The evidence laid before the Commission showed that in some districts of India the local consumption of opium bore a close relationship to the greater or less prevalence of malaria in the localities." Opium is still taken in the Fen districts of England as a popular remedy to "ward off the ague." The Commission were frequently told that people who were well off and had plenty of good food tolerated the opium habit with impunity, whereas the poor with an insufficient supply of food suffered from it. On the other hand, they were often told that opium ameliorated the lot of the underfed man and enabled him to live longer and better with a scanty diet. In India the opium habit is mainly a habit of middle life and advancing years. This is in marked contrast with the Western morphinist, 70 per cent. of whom, from recent American statistics, are said to be under 30. With one exception, the Commissioners recommended that nothing should be done in the way of restricting the Indian growth and exportation of opium.

The pernicious nature of the habit of *smoking opium* was early recognized in China and India. In China the habit is traceable as early as the end of the seventeenth century, and by the year 1729 it had grown so common in some parts of China that it drew down an imperial edict severely prohibiting opium-smoking shops and the sale of opium for smoking purposes. In the year 1799 an edict, which was issued by the Governor of Canton, directly prohibited the import of opium. Sir J. B. Lyall, one of the Commissioners, in his Memorandum II attached to the Commissioners' Report, says of this edict: "It is a very strong denunciation of the opium habit as morally and physically degrading, and as ruinously expensive."

The amount of alkaloid absorbed in the smoke is very small, both because the amount of opium used in the pipe is small, and because most of the alkaloid in the opium is destroyed. Nevertheless, absorption is rapid and produces an immediate effect. After the first few whiffs there is a feeling of elation, followed in the habitué by delightfully languid ease and an exalted sense of superiority, and later by dreamy sleep. The smoker becomes a slave to the habit, and the evil is enhanced—at all events in the West—since for indulgence the devotee must prosecute his vice in the worst possible surroundings. This way of taking opium is the least objectionable, because the

amount of alkaloid taken is so small, because a strong craving is not formed, and because "cure" is relatively easy.

Pipe smoking is usually begun as a group indulgence, while morphinism is solitary and secretive. Both types of habitués commonly use opium with discretion and may indulge in the narcotics for years without apparent evidence of harm.

The dose has to be continually increased, but as the amount of alkaloid absorbed is so very small the craving never reaches great intensity as with those who inject the drug. The varieties of opium chosen by the smoker are not those which contain the greatest proportion of alkaloid. One average pipe of opium contains about three milligrams of morphine, and ten pipes only about half a grain. But the greater part of this is destroyed in the process of smoking, so that the amount absorbed is exceedingly small; this, no doubt, accounts for the comparative ease with which this habit is cured. Opium smoking obtained a distinct vogue in the United States until it was superseded by the infinitely more objectionable habit of injection. It is worth noting that before the war large quantities of morphine were sent yearly into China, often in proprietary packages, as a cure for the smoking habit; a cure it is, but it produces another vice infinitely worse.

In Europe and America the alkaloid is usually *injected* by the hypodermic needle; this is the worst and most pernicious form of taking the drug, and, however the habit has been formed, to obtain the requisite relief the devotee must be continually increasing the dose. The amount of morphine injected daily varies greatly; 15 grains is an ordinary quantity for a morphinist to use in the twenty-four hours, though the same person will double this dose in the case of any small imaginary trouble.

The Department of Health of the City of New York published in an important memorandum statistics and details, by medical experts, of nearly 8,000 cases of drug addicts during ten months. Five per cent. of these patients asserted that the habit resulted from medication during illness; this figure is obviously likely to be too high. Sixty-nine per cent. asserted that bad associations were responsible; this figure may be too low. Seventy per cent. of the patients were under 30; other authorities say that 90 per cent. occur in adolescence. Only 1,580 out of 2,800 received at the clinic were willing to accept treatment and withdrawal of the drug. Those treated were kept six weeks and discharged in good physical condition, "cured." In three months a large proportion had already relapsed in spite of all efforts made to assist them.

Much of the increase in drug addiction has without doubt been started in ignorance; opium smoking was regarded as a harmless pastime to be relinquished as desired; the employment of the "white snuff" cocaine served as a nerve stimulant and pick-me-up; and heroin was used as a substitute for morphine, with the idea that it was not an opium derivative. Much evidence is to hand that difficulty in getting alcohol leads people to try any substance which may have a "stimulant" effect. Sheer ennui, a luxurious life without serious responsibility, lack of exercise, over eating, fatigue, and dyspepsia are predisposing causes. A few take to morphine because it is accessible; of these, doctors and pharmacists form the majority: no doubt they think that their technical knowledge will save them from abuse.

The addict always finds it to his advantage to co-operate with the distributor of his drug, and almost never will he give information leading to the disclosure of his source of supply.

Withdrawal.

Addicts are held in addiction largely through fear. Prolonged indulgence often fails to give them pleasurable sensations; still they must go on in order to avert the crisis of withdrawal. Their horror of pain, both mental and physical, is an obsession, and contact with the responsibilities of the world, they feel, is not to be borne.

The symptoms of withdrawal correspond almost exactly with stimulation of those tissues which morphine in medicinal doses depresses. The yawning, sneezing, nausea, vomiting, and mucous secretion result from stimulation of the medulla; the abdominal pains and diarrhoea from stimulation of Auerbach's plexus; the twitchings, cramps, circulatory troubles (rapid pulse, arrhythmia), and some-

times even convulsions, and collapse hardly distinguishable from surgical shock, are due to excessive stimulation of the cortical cells. A patient seen with these symptoms, even when in a state of collapse, on receiving an injection of his drug, exhibits a transformation almost miraculous; he becomes in a few minutes a relatively normal person. Whatever peculiar characteristic of mind or accidental incidents may determine the formation of the habit, when once it is formed the patient has a real disease, and he can only exist free from great physical and mental pain when he is under the influence of the drug to which he is addicted.

Strong alcoholic beverages taken for a long period of years in some people lead to a craving. It is not necessary that these people should ever have been intoxicated, but only that they should have taken daily libations of alcohol for some time in sufficiently large amounts to depress the central nervous system. The sudden cessation of this habitual alcohol, such as might occur in a man from an accident necessitating his stay in a hospital for a week, is sometimes responsible for an attack of delirium tremens, which is in every way comparable with the condition of a morphinist during morphine starvation.

The explanation I suggest to account for these withdrawal symptoms is that nerve cells after prolonged narcosis are, on reawakening, hyper-excitable. The contrary effect is an everyday axiom, that stimulation is followed by depression. But there is another explanation. Morphine and cocaine maniacs must be continually increasing the dose to get the necessary effect. This acquired tolerance is at least partly explained by the enhanced power of the tissues to destroy the alkaloid. On this we have decisive evidence. But it is also suggested that this acquired tolerance, this inability of cocaine, morphine and other drugs to produce their normal action on the brain, is due to some substance which neutralizes the effects of the poison. We know several such chemical substances which are elaborated by the body and neutralize poison; carbolic acid, the salicylates and camphor are so neutralized and rendered innocuous in the body by relatively simple chemical substances. Moreover, when there is a demand for some substance in the animal economy that substance is elaborated by the tissues. Valenti rendered dogs tolerant to morphine, and found that on suddenly stopping the drug the animal showed typical withdrawal symptoms. He alleges that injection of the serum from these dogs into normal dogs caused similar symptoms. This is mentioned because so much reliance appears to be placed on this work in America. Whether the lack of morphine is or is not the sole determining factor in the production of withdrawal symptoms cannot at present be decided, but it can be stated definitely that neither morphine nor any other drug causes antibody formation.

When once a habit is formed it becomes all but impossible for the addict to renounce it voluntarily, the craving is stronger than the controlling powers; it is the combination of association-memories and an abnormal brain. Few would hesitate to employ opium for the relief of physical pain; why not, then, for the alleviation of mental suffering? The answer must be that there is no such thing as moderation in the habitual employment of narcotics in such people. The craving becomes so intense that the sufferer is unhappy—indeed, almost in agony—unless he is continually under the influence of his drug. Craving is rarely obliterated by a short-time treatment, and unfavourable circumstances will cause it to spring to the surface months after the cure.

HEROINE.

Heroin was brought to the notice of the profession in 1898, but it was not much used until 1912. About this time it was employed in the United States, and to a smaller extent in Europe, as an addiction drug and substitute for morphine. Sometimes it was taken by injection, and sometimes as a snuff like cocaine. Both here and in America the public had little difficulty in obtaining any supplies they required of this proprietary substance. It was even much vaunted as a cure for morphinism.

The addict often prefers heroine to morphine. The average morphine addict has perhaps one or two stools weekly, whereas the bowels of the heroine addict are almost normal. The heroine addict does not exhibit so much pallor and emaciation; the symptoms are less pronounced and withdrawal is easier. Heroine is not

necessary to the physician, it has no advantages over codeine or morphine, and its use might be forbidden without harming a single genuine patient. The amount consumed varies from 8 to 20 grains daily, and considerable tolerance is attained.

Codeine does not commonly lead to addiction, and only one or two cases of a codeine habit have been recorded.

COCAINE.

Coca leaves have been used from time immemorial by the Indians in the west of South America as a stimulant and narcotic, and the habit survives to the present day, especially in Peru. The Indian takes his coca leaf in much the same way as Europeans employ tea or coffee—as a stimulant in mental and physical fatigue. It is asserted that natives who chew the coca leaf are able to perform long and rapid journeys with less fatigue and without feeling the pangs of hunger and thirst. Attempts by Europeans in the Alps and elsewhere to simulate these effects have not been successful. It may be that there are other constituents in the freshly gathered leaves which are absent from the dried leaves.

In Europe the addict employs the alkaloid cocaine only. This he either takes by the mouth, injects, or uses as a snuff. Formerly coca wines, snuffs, and lozenges were universally sold, but now the hypodermic injection has superseded the other methods almost entirely. When cocaine is sniffed up the nostrils as a powder it is absorbed very rapidly, and produces its effect even more quickly than when injected.

Cocaine acts differently from morphine; it first powerfully stimulates the brain, causing mental excitement and restlessness; the flagging nerve cells are whipped into activity and lassitude and fatigue pass. But this is accompanied by clouding of associations, and a marked depression of the central nervous system always succeeds the stage of excitement. Cocaine fascinates by the rapidity with which it relieves exhaustion and dispels gloom and by a delightful sense of mental and physical vigour. Morphine acts not by stimulating, but by depressing sensory nerve cells in the brain, so that fatigue and mental and physical pains are assuaged.

Tolerance can be acquired to cocaine like morphine, but it is less definite and slower in formation; still there are several cases on record in which 100 grains were taken daily. The prognosis in such addicts is better than with morphine; the abstinence symptoms are less severe and the cocaine can be cut off at once. Cocaine compared with morphine is relatively unimportant, and it may be doubted whether there is any case of cocaine addiction not associated with opium habituation.

INDIAN HEMP.

Indian hemp (*Cannabis indica*) is hardly taken as a narcotic in Europe, but in India different preparations of the dried flowering tops are made into a drink, are eaten or smoked. For smoking the crude drug is generally mixed with tobacco and the fumes drawn through water. Sometimes the devotees will sit in a circle, and a pipe is passed round, each person taking a few whiffs. Hemp is also used in the East in the preparation of sweetmeats and as a seasoning in cookery. In former times hemp preparations were used as substitutes for opium, but the drug keeps badly, and its unreliability is responsible for its disuse. Hemp intoxication differs from that produced by morphine in the preponderance of pleasant hallucinations and the active motor restlessness.

The Royal Commission on Indian Hemp in 1893 advocated control and restriction; its report aimed at suppressing the excessive use and regulating the moderate use within due limits. Total prohibition was regarded as neither necessary nor expedient.

PREVALENCE OF THE DRUG HABIT.

In this country narcotic drug addicts are as yet comparatively few, but in the United States the position has become serious. Even before the war Dr. Wilbert, of the United States Public Health Service, estimated that there were 175,000 addicts in the country; his figures were based apparently on the importation and sale of opium through trade channels. In a Government report it is estimated that 90 per cent. of the opium and cocaine entering the U.S.A. is used for other than legitimate medical purposes. Austria, it was estimated, only used

half a grain of opium per head per annum, Italy 1 grain, France 3 grains, and America 36 grains; Dr. Copeland, M.O.H. for New York City, puts this figure at 40 grains.

To some extent fashion or opportunity determines the type of drug used: in New York heroine is used almost entirely; in Chicago morphine is the common narcotic, and in cities with a large coloured population cocaine is in vogue.

The vast majority of cases of opium smoking, heroine and cocaine sniffing are acquired socially, though it is agreed in America that the largest single factor in the production of the morphine addict is professional medication.

Treatments for morphinism I am not considering, but it is generally agreed by those best fitted to give an opinion that the proper treatment, besides custodial care, consists in (1) the gradual withdrawal of the drug, in about ten days; (2) intensive purgation; (3) the administration of atropine or hyoscine. By this treatment the patient may be discharged in six weeks in good physical condition, and apparently a normal man without craving.

But can we cure a character, convert weakness into strength, so that temptation disappears? Perhaps proper education of the higher faculties of mind, like self-control, may do much, but simply to control conduct so that choice cannot be exerted is to court disaster. True temperance is dependent on self-control, not on control by others. Perhaps if children were taught something of the realities of the life into which they must presently enter, and received more vocational guidance, they would be in a better position to combat the difficulties and temptations to which they must presently be subjected, certainly in a better position than by a system of education apparently devised to fit a life of cultured leisure.

ALCOHOL.

It would hardly be fitting to conclude without a brief word on *alcohol*. Fermented beverages, and more especially beer, have formed from time immemorial the national drink of Great Britain. The introduction of the caffeine beverages did not oust them, and, although their popularity has not waned, the amount consumed is steadily diminishing before legislative restrictions and the attacks of the abstainers. England was once a drunken nation, and Mr. Lecky tells us that in 1688, 90 gallons of beer a head were consumed per annum: at the beginning of this century this had diminished to 30 gallons. Now it must be very much less and the percentage of contained alcohol smaller.

It has been clearly shown that as the difficulties of obtaining alcoholic beverages have become greater the consumption of drugs and truly noxious substances has become greater also. It is almost inconceivable to what lengths men will go to obtain something as a substitute for alcoholic beverages, and very few drugs or chemical substances—especially volatile chemicals—have not been used. This evil effect of prohibition has necessarily been more evident in America, where in past times most of the States have at some time, though generally only for a short period, adopted the principle of prohibition. Wood spirit (methyl alcohol) is one such evil substance; as little as a teaspoonful may cause blindness and an ounce death; several cases of poisoning have recently been reported from America. Methyl alcohol is oxidized in the body to formic aldehyde and formic acid, and it is to the production of these substances that the poisonous action is due.

Ethyl alcohol must be regarded as an addiction drug, though true addiction, in the same sense as morphinism, must be extremely rare. It is interesting to note that many authorities believe that habitual inebriety is not acquired, in the strict sense of the term, but that the inebriate starts life handicapped by imperfect brain development. That is to say, he takes alcohol in excess, just as he does everything else which is foolish and wrong.

It is notorious that morphine addicts rarely turn to alcohol; if they do, it seldom gives them what they seek, and they almost invariably return to narcotics. De Quincey says: "I do not readily believe that any man having once tasted the divine luxuries of opium will afterwards descend to the gross and mortal enjoyments of alcohol." Nobody questions the evils produced by alcohol in the intemperate, but for the vast majority moderation in alcoholic beverages produces pleasure and benefit. Ought we then to advocate prohibition? Would the benefits so accruing outweigh the disadvantages? Prohibition in other countries has led to

other and worse addictions and to industrial unrest, evils which appear to counterbalance the benefits. It is an axiom with lawyers that legislation for hard cases makes bad law; the plethora of these which we have experienced in recent times should make us chary in advocating yet another. Apart from this, prohibition is at present impracticable, as it would mean a loss to the revenue of over one hundred millions annually.

Plato says: "No one desires drink simply but good drink; nor food simply but good food." To the average man these add a little more joy and beauty to life. The position is perhaps summed up by Matthew Arnold, who says: "Wine used in moderation adds to the agreeableness of life."

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PYROGENIC THERAPY.

("PROTEIN SHOCK.")

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(A Further Contribution.)

THE paper published in this JOURNAL, vol. i, 1918, p. 195, described a severe febrile reaction which I obtained in 1916-17 with certain colloidal metals used intravenously; a reaction identical with that which certain American investigators had been producing at the same time by the intravenous use of suspensions of killed typhoid and coli bacilli (vaccines), and termed by them "protein shock." I found, however, that the full reactions following these particular metallic colloids could be produced by the protein used as the protective or coating to the metallic particles and in the same dosage. In an inert medium, such as gum water, the metallic suspensions were destitute of any fever-producing properties. In a recent examination of various well known metallic colloids the characteristic protein reactions were very marked, and so the clinical results would be questionable. When the metallic particles were suspended in an inert watery medium and injected in considerable quantity, the slight rise of temperature which sometimes followed was found to be quite capable of production by the water of the continuous phase.

"Protein shock" being rather an unfortunate expression,* I suggested "pyrogenic therapy" instead, chiefly in view of the fact that the reaction was produced by substances called "pyrogens" by Burdon-Sanderson. Moreover, the fever so induced is essential, as no benefit accrues without it. The view is, indeed, gaining ground that the high temperature, which is ushered in by a rigor more or less severe, is the crucial factor. Further reference to this will be made. In any case it is evident that some such distinguishing appellation is now needed, as "protein therapy" is a generic term applicable to uses of protein which are entirely different and distinct.

The cases in which the reactions were produced by the protein-protected colloidal metals were chiefly those of delayed resolution in pneumonias and pleurisies, with rises of temperatures to 100° and 101° F. for some considerable time. Recovery seemed complete at the end of the reaction; the temperature remained normal and the local lesions gradually cleared up. Some cases of acute pneumonia were then tried, but the results were by no means favourable. Certainly a fall of temperature soon occurred; but this proved to be a negative phase effect, as it always rose again to about the original level. These trials indicated that with a high temperature the defences

* In the first place there is no shock in the true sense, and, secondly, the reaction can be produced by certain non-protein substances.