infective arthritis; that pus is not produced, and that the inflammation is apt to flit from joint to joint.

Arthritis associated with Lesions of the Alimentary Canal.—In some rare instances there may be evidence that a micro-organism has been absorbed from the alimentary canal and carried to the joints, so that an infective arthritis is set up, as in the cases of dysentery in which a coliform organism has been isolated from the joints (Salle). Apart from these exceptional cases the arthritis associated with lesions of the alimentary canal may, perhaps, be assumed to be toxic and due to the action of poisons, usually of microbic origin, absorbed from the alimentary tract. Oral sepsis is well known to be an antecedent in some cases of a disease closely resembling, and often said to be, rheumatoid arthritis; the joint changes are usually chronic rather than acute. But occasionally attacks of acute arthritis are seen in patients who have pyorrhoea alveolaris or suppuration draining into the mouth. I have seen recovery follow removal of such an infective focus. Acute arthritis in association with the common disorders and lesions of the stomach and intestines is extremely rare. According to Salle,⁸ dysentery is accompanied by some degree of arthritis in about 4 per cent. of the cases. Ulceration of the rectum has in some instances been noted to be associated with acute arthritis, which has been observed to disappear when the bowel condition was cured (Wallis²³).

Considerable interest attaches to the association of appendicitis with arthritis, for it has been interpreted in two different ways: it has been thought that the appendicitis is a manifestation of rheumatism (Grant²⁴), and conversely that the joint manifestations are secondary to absorption from an inflamed vermiform appendix. The association is undoubtedly rare, but it is worth bearing in mind.

Similarly there is considerable scope for discussion as to the relation of the association of arthritis with the various forms of colitis. The French school regard mucous colitis as a manifestation of the arthritic diathesis, on the grounds that the subjects of mucous colitis have a hereditary or personal history of joint affections. On the other hand, arthritic lesions may follow in the wake of colitis, and may be explained as due to the absorption of intestinal toxins. This arthritis is commonly chronic, an acute form is rare. I have seen two cases in which acute arthritis was associated with colitis, but in both instances the two conditions were probably independent of each other and due to some common infection. Both began with fever, at first thought to be influenza.

In one, a woman aged 50, widespread peripheral neuritis was first observed, then oedema of the legs, and then arthritis and severe mucous colitis with the passage of intestinal sand. Recovery was very slow, the movements of the joints being much impaired for more than a year after the other symptoms had disappeared.

In the other case, a man aged 32, sore throat and multiple arthritis first appeared, accompanied by constipation; this was followed by diarrhoea and the passage of blood and mucus from the bowels. About a week later a large round worm was discharged from the bowel. After a long convalescence he recovered completely.

In conclusion, acute arthritis may be a manifestation of various diseases; but whilst some fevers are so constantly characterized by obvious cutaneous changes as to be grouped together as the exanthemata, the occurrence of arthritic changes are less constant in well-recognized diseases. I do not know if it has ever been suggested from a teleological point of view that the object of cutaneous rashes is to give warning that the individual is infectious; but the same spirit of final causes might urge that the reason why certain diseases, such as acute rheumatism and in some instances scarlet fever, affect the joints is that, by limiting movement, rest for the heart may be ensured. Teleological explanations though attractive are dangerous, and this one will not stand much criticism.

The other point on which I wish to insist is that a weakness in resistance on the part of the joints, whether inherited or acquired, may determine inflammation in the joints in certain persons when attacked by an infection or disease which in ordinary persons is not characterized by arthritic manifestations. This probably accounts for the rare form of arthritis exceptionally seen in hemiplegia and paraplegia.

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EXPERIMENT AND OBSERVATION IN MEDICINE.*

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IN selecting a subject for the presidential address, it is sometimes the practice to take one definite subject and to follow it out fully, but in other cases a retrospective view is taken, recalling some points of interest that have occurred in the president's own career, or a general survey of the progress of medicine or some branch thereof. It is my intention to take the latter line, and to put in order some of the reflections that have from time to time engaged my attention.

When we compare the advances made in the strict sciences with those made in medicine, we must admit that, brilliant as are the latter, they cannot compare with those of the pure sciences. We have to remember that medicine is not only a science but also an art, and it is with the latter that most of us are chiefly concerned, and art is long. The laboratory worker is concerned with science, but the clinician is almost wholly concerned with the art or practice of medicine. Much of this distinction in results is due to the nature of the material we deal with. The personal equation of the patient is so variable, there are so many difficulties in the way of making adequate controls. The human factor is a variable and not a constant, and so the equation never works out accurately.

"Science is measurement," but measurement with the accuracy of a chemical balance or a Kelvin electrometer is impossible to apply to clinical methods. We can, it is true, count pulses and respirations, and record temperature and weight, and these observations are very useful. But other measurements, such as sphygmographs and haemomanometers, have many sources of error, and the error of experiment bears such a large proportion to the actual measurement as to render the latter of dubious value.

And our observation, as a rule, does not take the form of measurement, but of signs that have not an absolute value, but only a relative one. A resonant note in one person would be a dull one in another. The note elicited over the lung of a thick-set, muscular, or fat subject would, if heard over the lung of a thin patient, suggest disease. There is a great variability in the standard of resonance in different patients, and for each patient it is necessary to have a standard of normal resonance. I believe that in the early stages of phthisis, where the signs at each apex are exactly the same, there is a danger of overlooking the signs, owing to our habit of comparing the resonance of one apex with the other, instead of relying on a standard of absolute resonance.

In all scientific operations the element of control is largely represented. Two substances of exactly the same composition, weight, and appearance can be placed side by side, one experimented on and the other retained as control, and the two can be compared at every stage. This can be done in testing urine and laboratory work, but in treating patients it is very difficult. The scientific method of study would be to have two patients exactly

*Read at the annual meeting of the Staffordshire Branch of the British Medical Association.

alike, having the same disease and the same stage and virulence of the disease, and one should have the proposed treatment and the other left alone as a control. But many difficulties present themselves against carrying out this course. (1) No two persons are alike in appearance or constitution, and so the test would be somewhat invalid. It is impracticable to catch the disease at the same stage, and to be sure that it is of the same virulence. Even with the most careful opsonic tests, we could not be assured that both cases would run exactly the same course if left alone. (2) If the proposed form of treatment or any other would be likely to do good, it would not be justifiable to leave the control patient alone, if the disease were of great severity or danger. (3) The *vis medicatrix Naturae* upsets our calculations. Many worthless drugs owe their reputations to the fact that the patients on whom they were first tried got well in spite of them. The old argument, *post hoc, ergo propter hoc*! Parenthetically, we may remark that many a practitioner also owes his reputation to the same sequence.

About ten or fifteen years ago there was a great "boom" in pharmacology. Each useful drug was to have its action in health studied carefully. Experiments were made of a very comprehensive and exact character, firstly on animals, and finally on the experimenters themselves. Great expectations were aroused that they would put medicine and therapeutics on a sound and scientific basis. If we knew exactly how they acted in health, and then observed what happened when they were exhibited in disease, the net result would surely indicate their influence on disease processes, independently of the *vis medicatrix Naturae*. This work has done much to amplify our knowledge and to make more exact our trains of thought, but it has not quite realized our expectations. Many drugs only show their potency in disease. Antipyretics reduce a temperature abnormally raised, but have no action on the normal temperature. Anodynes and analgesics relieve pain, but have precious little effect when there is no pain. So all drugs that have a specific action on certain diseases often do not show anything analogous to this action in health.

While there is abundant evidence of the old empiric attitude among us, yet there has also been abundant evidence of the rise of a more critical spirit, amounting in many physicians to scepticism. I was once handed a textbook by Marshall Hall which was represented to me as a type of thought and practice well worthy of study and imitation by a young physician. I found in this book that everything was cured by mercury, antimony, and bleeding. Moreover, each disease had its proper number of ounces of blood to be extracted. While the ranges at either end of the scale were very far apart, yet many of the indications for different diseases in the scale differed only by 2 oz. of blood that required extracting. Everything was nicely out-and-dry. Pneumonia required, perhaps, 30 oz. of blood extracted, and bronchitis only 28. It is wonderful that, with every disease having its treatment expressed so exactly in ounces of blood, and with such a limited pharmacopoeia as mercury and antimony any one ever died. I am afraid that the young physician saw more of the humour than the value of this excellent work. The sublime and artless credulity of this system of therapeutics smacks very strongly of the Chinese medicine of the present day, which appears to be a kind of organo-therapy gone mad—each disease has its cure in a certain organ of a certain animal.

We have advanced considerably beyond that stage. Pharmacological researches have carried our knowledge very far. We can define with certainty the precise action of many drugs, but we cannot tell the how and we cannot tell the why. We know that curare causes paralysis by paralyzing the end-plates of the muscles, but we do not know how it does so, what precise anatomical or chemical changes take place. We know that strychnine exalts the anterior cornual cells of the spinal cord and that physostigmine depresses them, but here, again, we cannot tell how they do it, and what relation between the chemical structure of the alkaloid and that of the cell protoplasm causes this action. I do not know of any observations that have been made showing anatomical changes in the nerve cells as the result of the action of these powerful drugs, though such changes have been shown in the case of alcohol.

Another point of interest is, Why do plants elaborate out of their simple food—carbon dioxide, water, and ammonia—these highly complex alkaloidal poisons? What can be the item in the scheme of natural selection that results in the elaboration of these substances, and how does it come to pass that they should have such a powerful action for good or evil on our bodily functions? It is very difficult to understand how in a purely mechanical theory of natural selection this wonderful symbiotic relation should come to pass. Why does the nux vomica produce strychnine and the belladonna elaborate atropine? What can it have to do with the plant's economy? Can it be some form of protective device to prevent them being eaten up by animals? and, if so, how does it happen that atropine has no poisonous effects on rabbits? Who so likely to eat them up as this voracious rodent? If this were so, one would expect poisonous plants to flourish much more than non-poisonous ones. And yet one finds that the plant least harmful to animals, and one on which they feed more than any other—the common meadow grass, *Lolium perenne*—is the most widely distributed of all plants. The action of natural selection in plants is more concerned with effective reproduction and distribution of reproductive products than with the security of the individual plant from injury or destruction.

One can scarcely compare the elaboration of the poppy alkaloids to the pungent odours and taste developed by certain moths, or the protective colouring assumed by other and more innocent lepidoptera to resemble their more nauseous relatives. The teleological doctrine in its old frank statement finds little favour now, but it is difficult to escape it in this context. We know that the strawberry does not don its crimson luscious receptacle for the benefit of our palates, but to attract birds to devour it and its contained achenes, so that after passing through the alimentary canal, the hard, dry, indigestible achenes may be deposited with a good dollop of fixed nitrogen in a favourable position, and giving them a wide distribution.

The lovely hues and exquisite odours of the violet and rose are not for the gratification of the lord of creation, but simply to attract the lowly insect, who is an efficient agent in securing fertilization, and especially that more potent agent, cross-fertilization.

All these gratifications derived from the floral world which we enjoy have been evolved by the pure mechanical agency of natural selection. But the evolution of the alkaloid-producing power appears to be on quite another platform. So far it does not seem practicable to compare etiologically or teleologically the plants producing these powerful principles with those that do not, and to have regard to the great variety of these substances that are produced, and to account for them merely on the theory of the survival of the fittest.

It is also remarkable how few really useful drugs and powerful alkaloids are derived from the animal kingdom. With the exception of cantharidin, there does not appear to be one drug derived from it, except vehicles. The matters relating to organo-therapy, toxins, antitoxins, and vaccines, of course, do not come in this category. The relation of these to the organism producing them is easily understood.

It is a strange and happy circumstance that so many of these powerful active principles have the power to cure disease and mitigate symptoms. The theory has been advanced in more remote times that wherever there was an endemic disease, there grew a plant that cured the disease. Wherever nettles abound, there alongside grows the dock, ready at hand for the cure of the unfortunate stung by the nettle. In fenny country, where rheumatism is prevalent, there grows freely the willow, yielding salicin. Where malaria abounds, there the cinchona grows, accessible for the relief of the sufferer. I am afraid that the cinchona does not adapt itself to the would-be users quite so well as this, but I believe in some parts of South America the disease and the cure grow side by side. But I am afraid, as far as our present knowledge goes, instances like these (even if we take them for granted) could not be multiplied very much. There are very few indigenous plants that we use, and I believe the ground has been fairly well covered. If one reads Bentley's *Botany* (where the known therapeutical

use of each plant is described along with its anatomical features), one is surprised to find how many of them have been extensively employed for various ailments, most of them without success. Most of our knowledge of these things has been derived from the careful observation of keen-witted natives, many of whom have been accustomed to use plants found in their district, and to use them successfully for many generations before the advent of the European. It would almost appear that we have reached the limit, and that we are in possession of almost all the facts relating to the galenicals and the preparations derived from them. Very few serviceable additions of this description to our *Pharmacopoeia* have been made during recent years, the only notable one being the Malayan plant that was reputed to be of such value in the cure of the opium habit, but of which we have heard very little since the first boom.

Our advances in recent years have been along the lines of the products of the chemical laboratory and those of the pathological laboratory. I suppose drugs of the former class far outnumber the galenicals, and every week new ones are being introduced and disturb our breakfast tables. When they are all reviewed and added up, they resolve themselves into one or other of the following groups: Antipyretics, anodynes, anaesthetics, diuretics, antiseptics, hypnotics, and purgatives—not a very large field, I am afraid. Each new one professes to be an improvement on its predecessors in that class. Take the phenetidine group—phenacetin, lactophenin, citrophén—all acid esters of phenetidine, but of increasing complexity. It was held that as the acid radicle advanced in complexity, so the drug increased in its analgesic power. It has occasionally happened that conditions that failed with phenacetin have yielded to lactophenin, but the fact remains that phenacetin still is the most popular of the three.

So in the sulphonal group: it was held that the more ethyl groups there were, the greater the hypnotic effect, and that therefore sulphonal, or diethylsulphondimethylmethane is exceeded by trional (diethylsulphonethyl-methylmethane), and this, again, exceeded by tetronal (diethylsulphon-diethylmethane). But the fact remains that sulphonal, with its two ethyl groups, is still the most popular, and that trional is more popular than tetronal, the latter being seldom used. Possibly the greater cost, in the absence of very marked difference in effect, has something to do with the relative frequency of use.

The want of correlation between chemical affinities and pharmacological affinities is very marked. The halogens, Cl, Br, and I, are, of course, closely related chemically and so are their compounds, but the pharmacological and therapeutic properties of their compounds are very different. Methyl-morphine has very similar action to morphine, while methyl-strychnine has quite an opposite action to strychnine. The chlorine derivatives of methane, however, have similar actions. Monochloromethane is an anaesthetic, but is little known. Dichloromethane had a great vogue twenty years ago, when it was brought into prominence by Sir Spencer Wells. Trichloromethane still shares with ether the position as premier anaesthetic. Tetrachloromethane has earned itself recently an unenviable notoriety as a profound anaesthetic in the hands of hairdressers—much too profound!

The old adage, "Of making many books there is no end, and is much weariness to the flesh," applies also to organic compound breeding. They are very many, their full names very much exceed that of a royal personage; their therapeutic activity exceeds that of any other drug hitherto introduced. If our credulity were equal to the claims put forward by their introducers, our whole time for months might be occupied in experimenting with one week's output in new drugs. Perhaps this is the origin of the expression, "It is a drug on the market." The only difficulty is to sift the wheat from the chaff, and the danger is to overlook a few valuable grains of wheat, owing to the abundance of chaff and its capability of concealing.

One of the most remarkable transformations in medical practice in the last ten years has been the decline in the use of alcohol. The statistics of the large London hospitals, the Metropolitan Asylums Board, and the London County Asylums are a most convincing record of the fact that a great change has come over the practice and

convictions of the medical officers of these institutions, who number among them—if not entirely composed of—the best elements of our profession, the best type of professional efficiency, and to whose opinions we look up with the greatest respect, and whose practice may be fairly taken as a standard representing that of the profession of the nation at large. In the London County asylums, while the patients and staff had gone up from the year 1885 to the year 1906 from 8,107 to 19,457, the wines and spirits had gone down from 1,902 gallons to 250 gallons, and the beer from 255,486 to 1281 gallons. This is not the practice of a few cranks, but the outcome of the increasing conviction among all classes of the profession of the uselessness and harmfulness of alcohol; as the result, not of preconceived prejudice, but of added knowledge due to careful experimental work, carried on under the finest modern scientific conditions, and better clinical observation, from which the obscuring bias of ages has been put away. The International Congress of July, 1909, gave evidence of the great amount of work that had been done, with the desire, not of fortifying a position, but of ascertaining the truth, and recent research in immunity and kindred subjects has given to these workers a very potent instrument for unravelling these mysteries. The work has been slow in method, sparing no pains to gain accuracy in result, but the accumulation of facts has been sure, and the facts have been marshalled with unerring fidelity and relentless energy, and it is now clear to us that alcohol is a narcotic and not a stimulant, that it is a protoplasm poison of the first order even in very dilute solution, and even under such circumstances leaves indelible marks and lowers the immunity index of the individual.

Bias has to some extent hindered the revelation of the laboratory being transferred to the bedside in all its fullness. There are many human traits in our clinicians which I need not specify more particularly, but which have in the past caused the frequent and almost universal exhibition of this drug, and, even with recent illumination, we must expect a certain clinging to this old idol for a time. The foundations of society still depend on the free exhibition of alcoholic beverages at social gatherings. Till recently the passing of the wine denoted the merriment. Perhaps this does not obtain to the same extent now. But even now it is regarded as social heresy of first order not to offer your guest what you consider a powerful poison. You are not obliged to offer him opium, hashish, or cocaine, but if you do not offer him alcohol you are a social pariah. With this spirit still prevailing, it is hopeless to expect the revelations of the laboratory to be transferred very readily and universally to the bedside. In the laboratory observations are so exact that bias and sentiment have no place, but in clinical work sentiment and fashion are bound to influence us to some extent. Observation cannot be so accurate without the control element.

The scope of the physician has been inevitably narrowing during recent years, and the process is likely to continue. At one time he had it all his own way, and the surgeons were merely only the descendants of the barber-surgeons. The gold-headed cane and other symbols were no doubt the important elements in the physician's armamentarium. But in spite of all the humbug, there were doubtless many able clinicians in those days, all the more so because they were dependent on their native wits, and not on the aid that modern instruments and researches give.

With the introduction of anaesthetics and antiseptics a great change took place, and since then the surgeon has continually encroached on the ground hitherto occupied by the physician.

In more recent years, with aseptic methods and improved technique, the advance of surgery has been enormous, and much of it has been at the expense of the physician. McGill used to preface his lecture on the surgical treatment of intestinal obstruction with the remark, "Formerly the treatment of intestinal obstruction was left to the physicians, and the result was that the patients nearly all died." The same may be said of many other things that have now been relegated to the surgeons in like manner, and many other cases that in the physician's hands received only palliative treatment, but with surgical treatment the cure has been complete. This has not been

due to the relative capacities of the two classes, but to the limitations that have been imposed on the physicians. Each year the surgeon invades some branch of the physician's work, and this is as often due to the physician's improved method of diagnosis as to the improved technique of the surgeon. In fact, the chief reward the physician gets for increased precision in diagnosis is to get his territory raided and that class of case annexed. It will be but a short time when most of the diseases of the stomach (formerly regarded as sacred to the physician) will be treated by the surgeon, and I look forward to the time when the diseased lobe of the tuberculous lung will be removed. With this very much diminished field, with the prospect of a still further rapid contraction of the field of work, what is the outlook of the physician? However narrow his work may be, there is, of course, still some scope for research and acquiring greater precision of diagnosis, but if the *clientèle* is reduced severely, the income necessarily becomes narrowed, especially as the physicians' fees bear such a small ratio to the fees obtainable for operations. Treatment by drugs, whether galenical or synthetic, is likely to be restricted. There are, however, certain lines of advance which he can reasonably develop.

The field of physical therapeutics is one which is sufficiently large to occupy the whole attention of medical men practising in very large populations, but in smaller areas the *clientèle* would be too small, and in such cases the work is very aptly undertaken by the physician. Electro-therapeutics offers a very useful, though limited, field, especially in the relief of neuralgias and neurites, and other painful conditions when they are not caused by too gross a lesion. Even in the latter case much relief may be afforded. Paralytic conditions often meet with much better results with scientific treatment than when treated in the rule-of-thumb method with a small battery. Cataphoresis, or ionization, has also a good prospect in effectively carrying the medicament to the affected part without permeating the organism.

Radio-therapy is a field that may suitably engage the physician's attention, and requires skill of the highest order. It does not involve the mere turning on of the switch, but requires first-class specialized technique, and accurate observation and judgement. There are terrible potentialities for evil as well as for good in radio-therapy, and the work calls for specialized attention, not by druggists and other non-medical operators. The cure of lupus, rodent ulcer, tuberculosis of the skin, and other skin lesions by this means has come within the knowledge of most medical men. Recently much has been done in the cure of deeper lesions by means of filters which cut off the soft rays which do not penetrate and which injure the skin, but allowing the harder rays to penetrate the skin and permeate the diseased structures. Tuberculous glands, provided they stop short of suppuration, can be cured, and even after excision irradiation of the site of the glands effectively prevents recurrence. A case of this nature well illustrates this.

The son of a medical man came to me with glands in the neck which were caseating or even suppurating. I applied x rays for a time without lessening the swelling. I then advised that they be removed, and this was done, and the glands were found to be suppurating and adhesions formed, and some of the pus escaped into the wound. Previous to this, at the same operation, the other side was opened and some non-suppurating glands removed. Both sides were cleared out completely. The wound healed by first intention. Within a month the side that had not been irradiated relapsed and several glands enlarged. The other side that had been irradiated, in spite of the suppuration and the adhesions, never relapsed. Further irradiation of these glands cleared them up.

I believe that routine irradiation of the sites of malignant disease that has been removed would materially lessen the chance of recurrence.

Many excellent results have been obtained in Graves's disease, some of the cases doing remarkably well, others being intractable. There are at least two types of this disease, and it is those with a large feebly throbbing goitre, with proptosis and tremor and erythrim that seem to do the best. In ringworm, sycosis, and favus, x rays is easily *facile princeps*.

In radiography, too, the physician finds an excellent field of work. The chief trap he has to beware of is the temptation to buy every new piece of apparatus that is

going to revolutionize radiography and its allied spheres of work. If the surgeon or the anaesthetist will make a mental picture of the new gags that have been offered to him during the last ten years, he will realize a fraction of the number of new brakes that have been offered the radiographer during the last five years, at from ten to twenty times the cost of the gags. Each is going to beat all the others quite out of the field. So, too, the question of tubes is a constant source of anxiety to the radiographer. You can pay anything you like for tubes (on the high side), and a slight accident or misjudgement may consign it to the scrap-heap. A physician (failing a specialist in radiography) is the likeliest man to undertake the work. His work is much more limited in scope than the surgeon's, and as the radiographer's work is largely concerned in surgical diagnosis, and it is his business to make the diagnosis and return the patient to the surgeon for treatment, there is less likelihood of friction than if the radiographer were a rival surgeon to the one who sent him.

It is remarkable how large a proportion of the radiographic work I do both at home and at the hospital is kidney work. I estimate that I do more kidney work than all other forms of radiography put together. There have been great improvements in radiographic work recently in getting more rapid exposures. The use of the new accelerating screen has reduced the exposures very much, and has shown practically no grain in the radiograph; and this great reduction has enabled much more current to be sent through the tube, but not so much but that ordinary heavy anode tubes can be used, and the valve tubes have been so improved lately that no harm happens to the tube when this heavy current passes. Consequently, we are approaching instantaneous radiography without needing to use the very expensive tubes and costly interrupters. The more nearly they approach the instantaneous, the sharper the definition in chest and kidney work, when the breath can be held and movement arrested.

There is one sphere of work for the physician that is full of promise. Much has been done in the past, but over a somewhat limited sphere, but in the larger sphere the results are not sufficiently developed to justify conclusions. I refer, of course, to antitoxin, toxin, and vaccine-therapy.

This is work of an eminently scientific nature. It consists of the searching out of the means which Nature has provided, ramifying into all her secrets, and adopting her own methods. We have hitherto, in using galenicals and synthetic products, been guided by rule of thumb and pure empiricism. By trying every conceivable and inconceivable drug we could lay our hands upon, a few have been found useful and have been retained. But by studying the principles that underlie the *vis medicatrix Naturae*, work has been done in recent years which has shown in the large number of diseases that are of bacterial or parasitical origin the actual processes adopted by the organism and its constituent tissues in the warfare against bacterial invasion. They have been carefully studied, and the very weapons themselves have been taken from Nature's armoury and by the resources of the laboratory reinforced a thousand-fold, and used with greater precision and independently of the resisting power of the patient, which is an ever-changing variable.

The antitoxin treatment of diphtheria rests on sound experimental evidence, backed by extensive and irrefutable clinical results, and there can be but little advance in this direction. The antitoxin of tetanus rests on the same sound basis, but clinical success is hindered by the rarity of the disease and the fact that supplies of fresh serum are not always available at the earliest moment. But, except in the case of the vegetable ferments, abrin, ricin, etc., the other antitoxins have not proved very serviceable. Certainly pneumonia, typhoid, and streptococcal and staphylococcal antitoxins have not. There seems to be evidence that certain bacteria do not part with their toxins to the culture fluid, but only yield them when in contact with the cells of their host, when they readily pass out and manifest their toxic effects.

In these cases it is necessary either to inject living bacteria in small and increasing doses into the serum-producing animal, and get from them an antibacterial serum, or to kill the bacteria and inject an emulsion of them into the patient. The latter is the favourite process

at the present moment, and has great promise of success. The toxins are liberated from the dead bodies of the bacteria and stimulate the formation of numerous receptors or side-chains in the cell, and some of these latter are thrown off into the blood stream as antitoxin, and in a position to seize upon and unite with and neutralize the toxin molecules, not only those that have been artificially introduced, but those that are being constantly produced by the invading germ.

In many cases the diagnosis is very difficult, and in others the strains of what is apparently the same bacterium are very numerous, and though their effects may appear the same, the species or variety is not the same. I suppose the strains of streptococci and staphylococci are as numerous as the varieties of *Rubus*, and the distinction of the colours, "aureus," "citreus," "albus," etc., which their cultivations show, do not by any means represent their numbers. Antitoxins of the cocci have failed partly because of their infinite variety. The stock antitoxin did not come from the same strain as the disease. So the practice of using polyvalent serum resulted, making antitoxins of every conceivable strain of coccus, mixing them together like a plum-pudding and throwing them at the patient, hoping that one at least might hit the mark; like firing a shot gun at a grouse, hoping some of the pellets will go home.

But in this, as in other diseases, vaccines have proved more useful than the antitoxin, but even here there is the difficulty in getting the right strain. There are also cases where a strange organism is found, or one that has been regarded as non-pathogenic is in a particular case found to be pathogenic. In fact, we must recognize the possibility, or even the probability, that natural selection is frequently producing new species, causing new diseases, or very definite modification of recognized disease. We do not know when any given germ attains its specificity for the first time—certainly not all of them in prehistoric times.

In all these cases where the stock vaccines do not appear to be of avail, the practice is to take some of the diseased organ or its secretion or contents, make pure cultures of the germ, and use one or more of these cultures as vaccines, giving back to the patient vaccines from the exact organism that has attacked him. This is a method of precision as keen as could be attained and the most scientific in its practice, and, *a priori*, most hopeful in its outlook. It is comparable in all its details for scientific spirit and method to the best work in chemical or physical research.

While much of this work will lie in the hands of the pathologist, the final utilization will rest in the hands of the physician; and it is to this line of vaccine-therapy that we must look as the most promising line of the future that will redeem the physician from the somewhat secondary place to which I fear public opinion has relegated him, as compared with his brilliant colleague the surgeon.

ON FEVER CAUSED BY THE BITE OF THE SANDFLY (*PHLEBOTOMUS PAPATASII*).

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Definition.

A NON-FATAL, three days' fever, with a week's convalescence and certain sequelae, due to the bite of the *Phlebotomus papatasi*.

Distribution.

It is known to exist in Egypt, part of Austria, Malta, and in Italy; and it will probably be found widely distributed.

Symptoms.

These are local and general.

Local.—The bite is followed by intense itching and irritation of the part, which persists, and which is followed by the formation of a raised lump with a small watery head, and with a surrounding zone of inflammation. As the flies bite at night, sleep may be prevented for some hours.

General.—The illness begins with a feeling of tiredness, loss of appetite, malaise, headache, aching in limbs, chilliness, disinclination to do things; rigors are uncommon;

vomiting takes place sometimes. The temperature rises sharply to 101° or 104° F. (less in recurrent attacks). There is a disordered digestion, furred tongue; constipation is marked, occasionally there may be diarrhoea; the hands and feet are hot, the pulse is bounding and increased in rapidity. Blood pressure is probably raised from the beginning. Later there is well-marked anaemia and rapid loss of weight.

Special Symptoms.

There is a tendency to inflammation of synovial and pleural cavities, and to neuritis and headache. The micro-organism is probably not got rid of easily, and months after an attack chill or exposure to wet may bring on another attack of fever, accompanied by effusion into synovial or pleural cavities, or neuritis.

Blood Examination.

I have failed to find any organism.

Residence.

Newcomers are more affected by the bite of these insects, both immediately and more remotely, than those who have been in the country for years.

History.

For many years these symptoms had been noted, but were variously attributed to other causes and described under the name of dengue, influenza, malaria, and Egyptian fever, but upon careful observation the above diseases will be found to have different clinical symptoms, the nearest being influenza. There is, however, usually the definite history of the bites, and an absence of catarrh of the air passages. It differs from malaria in that there are no definite stages of the rigor, and no parasites to be found in the blood.

In dengue fever the severe rheumatic pains in joints, bones, and muscles, with injection of the eyes and slow, tedious convalescence, help the diagnosis.

Influence of Season.

The fever is prevalent during the hottest and driest part of the year, from April to November, when the flies are most prevalent.

Etiology.

Bite of the sandfly, *Phlebotomus papatasi*.

Incubation Period.

About four days. Three days' fever in cattle is well known in Egypt; and it is possible that the disease may be conveyed from them to human beings, as the flies are found in large numbers in the vicinity of dwellings and stables.

Habitat.

I could not find the larvae, but they will probably be found in latrines, human and other excrement, which is cast so freely round villages. From the nature of the fly it is manifest that, wherever the larvae may be found, the eggs must be laid in moist material, and the breeding time of the fly is during the hot, dry months of the year, beginning in April. For some years past it has been noticed that rooms nearest to the rough latrines of the Arab servants were the ones most infested. Last summer there were a large number of native workmen engaged in altering a premises. No latrines were provided; they used the desert, and sand-flies swarmed. The banks of the Suez Canal, alongside of which the sweetwater canal runs, are favourite haunts of the sandfly.

Description of the Fly.

It is said to be called by the natives "akhl-uskut," silent eater. This is hardly true, as the fly makes a high-pitched noise similar to that of the *Culex* mosquito, only much higher pitched. The fly is light brown in colour, so small that it can pass through the meshes of a mosquito curtain. The wings are held up away from the body, and are covered with hairs. The head is joined to the body by a narrow neck. The eyes are very large and prominent. The proboscis is about twice the length of the head, and contains a fine stilett. The antennae are three times the length of the proboscis, and are covered with hair. The body of the fly is of the same colour—light brown—and hairy. The thorax gives the impression of humpback. The abdomen is narrow, but when the fly is fed it becomes very prominent and darker in colour from the ingested