Tolerance of Remedies in Disease

The application of Remedies to the cure of disease, is as old as the history of disease itself. Amongst the earliest nations and the most savage tribes of men, there have ever been some who have dedicated their lives to the relief of human suffering; and who by the magic influence of charms and incantations, or the illusory armament of intangible substances, known as drugs, waged eternal war with every species of mortal disease. Like every art, the treatment of disease by means of these remedies was at first of very dubious advantage; earth, air, and sea were painstakingly sought for the latent “Panacea” and no substance so gross or loathsome but human stomachs were ready to receive in the vain hope of a cure.
Accordingly the earlier Materia Medica was burdened with substances for the treatment of disease, and if Hippocrates can be called the Father of General Medicine, certainly Dioscorides may justly be termed the Father of Materia Medica. Since that time, however, the object of the profession generally has been rather to curtail than add to the Materia Medica, to investigate the modus operandi of such drugs as are of real utility, and not to search every department of natural science for new remedies. And there can be no doubt that a knowledge of the action of remedies is infinitely superior to any acquaintance with their mode of administration. The former, in fact, ought in every case to precede the exercise of the latter.

Amongst the many great facts which the science of medicine has disclosed there is none more remarkable than the comparative tolerance of remedies in different diseases. That certain diseases
should generate a condition of the system, capable of sustaining the fullest use of certain remedies altogether intolerable in other states, is purely a phenomenon not less striking than important to the medical practitioner. And as this tolerance is best exhibited in certain conditions of the system, known as inflammatory and the multitude of diseases originating with inflammation, I have deemed it right to antedate the subject proper by a short synopsis of the prominent features of the morbid condition—Inflammation. It consists of congestion of nerves and vascular irritation. Determination of blood towards the affected part or, according to others, attraction of blood to the part. Obstruction of the vessels most affected by atomic enlargement of the capillaries; by production and adhesion of white corpuscles in the vessels. Dis- tension of arteries and capillaries before
The obstruction causing increased effusion of serum, lymph, pus &c.
Emptiness of the veins beyond the obstruction, causing increased absorption, hence loosening &c. Impeded & arrested circulation at the obstruction causing a reduction or abolition of vital properties, hence the death of the part, and its removal by ulceration & suppuration or its decomposition by gangrene. Increased circulation of blood around the obstruction causing impalpation of vital properties; hence spasm, pain, sympathetic irritations, increased secretion.

The constitutional effects of inflammation are—extension of the excitement to the heart & arteries causing inflammatory fever. Change in the whole blood by increase of albumen from the inflamed part, and by diminution of the excitants in the inflammatory fever. Exhaustion ensuing after the excessive excitement, or the effusions of inflammation. Depression, sometimes with partial irritation, from the
Presence of pus or gangrenous matter in the blood, or retention of fermenting matter. The external signs by which these changes are recognized are "Redness, Pain, Heat & Swelling." This definition has been objected to by some on the ground that these characters are not observable in internal inflammations. But though these conditions are not palpable to our senses, we have no reason to doubt their occurrence, and the symptom of pain during life and the redness and swelling that are often observable in internal organs, that have been inflamed, after death, show that at least three of these conditions are present. Some physicians affirm the existence of latent inflammations without the presence of any of these symptoms, but I am not satisfied that these cases are well authenticated nor do I think it possible that Nature should allow such serious mischief to proceed without any tokens. At all events, such cases are seen-
tially chronic in their character so that the neighbouring parts became gradually accommodated to their presence.

We shall now discuss:

1st. Those remedies which as they are most powerful have ever been esteemed the most useful and effectual in their influence over diseases; viz. Bloodletting, Mercury, Antimony, Opium, &c.

2nd. Of the Toleration of those remedies in various diseases and the probable explanation of such Toleration.

3rd. Of the alleged producing Intolerance of Remedies formerly borne with impunity or benefit.


1st. Bloodletting. The most familiar of the effects of loss of blood is syncope. The influence of posture; and the first sensations and appearances of the patient in this state, appear to denote that the
brain is the organ the function of which is first impaired; the respiration suffers as an immediate consequence; and the action of the heart becomes impeded as an effect of defect of stimulus, first from a deficient quantity of blood, and secondly from its deficient arterialization; the capillary circulation also suffers; and if the state of syncope be long continued the stomach and bowels become paralyzingly affected. From the state of syncope the system usually recovers itself spontaneously, if the cause by which the syncope was induced be continued. The principle by means of which this recovery is effected may, without involving any hypothesis, be deminated reaction.

The peculiar effect of General Blood letting is, at first merely to diminish the quantity of the circulating mass by the amount abstracted; afterward lessening especially the proportion of red corpuscles. It is true that the whole amount of solid ingredients, in relation
Some believe that it is owing to the greater facility by which tadpole corpuscles escape from the vessels they being in the middle of the current.
to the liquid, is diminished; but the albumen and fibrine suffer less than the coloured constituent, probably because they are more readily supplied from the tissues and food, though the processes of digestion and absorption.

Indeed, in inflammation, the proportion of fibrine, according to Andral, even increases up to a certain period, notwithstanding the loss of blood. But as the red corpuscles are probably the most stimulating ingredient, the effect of the bleeding is chiefly to diminish the excitant properties of the blood, even in inflammation.

2. Mercury, classed by Stahl and amongst the Catalytic Remedies, tends most powerfully to check the general blood-injuries of inflammation. Its action, though less immediate is not less powerful than that of antimony. It seems to act by diminishing or liquifying the fibrine of the blood, and by stimulating the absorbents to increased action. Thus
causes absorption of effusions, the disintegration and mineral of lymph production of the viscosity of the blood, beside exciting a general antiphlogistic effect upon the general system.

2° Antimony much resembles Mercury in most of its effects, being however more rapid in its action, it is preferred where a sudden and powerful impression is desired. It has also a sedative influence on the heart and circulation. In Bright and Pneumonia, both rapid and fatal inflammations, Antimony is far preferable to Mercury. But in Chlorosis where there is generally no immediate danger to be dread, and a subsequent diffusion, Mercury is best, being in time to lessen or to prevent this result. Its effect varies according to the amount of dose, in doses of a sixth or an eighth of a grain repeated every two hours it produces diaphoresis over coming the and state of the skin and clearing the capillaries by restored secretion. Quarter of a grain similarly repeated, not only
prove diaphoretic, but also occasions nausea
and herts a sedative influence on the gener-
al circulation. In the dose of from half
a grain to a grain, repeated every two
hours, a still more truly antiphlogistic
influence, resembling the mercurial, seems to
be safest; opposed to general exaggeration of
arterial tone, limiting local deposit, fa-
vourable to absorption, and so finding
its points normal tissue and function.

4° Opium. No remedy is of more essential
value in the treatment of disease than
opium. As a remedy for inflammation it
invariably follows the use of the lanced
or the use of evacuants, or is combined
with them. In this way it tends to keep up
the sedative influence which the previous
bleeding has exerted on the disturbed cir-
culation, at the same time diminishing pain
and restoring the irritated nervous system
hence its influence in all nervous diseases
when there is preternatural irritability.

In fact Opium may be adminis-
terad wherever pain is found at least in most
cases.
Under the second division of our subject we have to consider the tolerance of these and other remedies in various diseases and the probable explanation of such tolerance. It is well known that the same disease requires a very different treatment in persons of vigorous constitution with a plethoric circulation and healthy blood, from that which would be suitable in the feeble, the anemic, and those in whom the blood is depraved or putrid. An amount of depletion which might be essential in the former would prove highly dangerous if not fatal in the latter. Since, it is necessary to take into consideration the various circumstances in which the patient may have been exposed previously to the commencement of the disease, age is not without its influence. Infancy is more impresrible than manhood, and therefore requires more caution in the use of remedies. Though more rapid in the curative processes, it is yet most readily depressed below the point of reaction. The nervous system at this age
is peculiarly susceptible, and frequent calls are made for remedies addressed to the support of that system. This fact is often fatally overlooked in the advanced ages of infantile diseases. Old age also demands caution. Though less susceptible than middle life, it is not capable of supporting excesses of any kind, and should therefore, as a general rule, be treated with much reserve. As the blood is made less rapidly, it should be more sparingly abstracted; and greater care should be observed not to give medicines in over-doses. Even stimulants in excess are less safe than in earlier life, because there is generally some failing in the organization, especially in the brain which may cause it to give way under any considerable excess of arterial action. It also has its peculiarities. Woman is to be treated in all respects more delicately than man. During menstruation, peculiar care is required in the use of remedies, not to interfere with that process; and as a general rule, unless
Treatment is improperly required, it should either be suspended or moderated. Pregnancy also calls for certain cautions. Though it usually tolerates bleeding well, especially when advanced, it contraindicates perturbing treatment, such as the use of violent emetics and cathartics. The sanguine temperament bears depletion better than the phlegmatic or nervous. Individual peculiarities or idiosyncracies require a careful attention. The practitioner should listen respectfully to the representations of his patients as to any peculiar susceptibilities which they may possess, and, in the absence of such representations, should himself make inquiries upon the point. He will thus be spared many awkward, and sometimes even fatal accidents. Thus, death has resulted from the use of a moderate dose of colomel, which might have been avoided by a previous knowledge of the extraordinary susceptibility of the patient to the mercurial impression. Remedies which ordinarily produce no unpleasant effect woul-
sick, act with greatest violence in some individuals. Hereditary tendencies must not be overlooked. In a doubtful case, the scale may often with great propriety incline towards one or other side, according to the known constitutional habits of the parent. The son of morbid parents should, under certain circumstances, be treated very differently from one in whom no morbid hereditary tendency could be suspected. Climate has a modifying influence over the effect of remedies. Rather bleeding or general stimulation is so well borne by the inhabitants of hot countries as by those of temperate or cold latitudes; while the influence of calomel as a cathartic is perhaps in general better borne, in consequence of the less susceptibility of the liver. The habits of the patient are of the highest importance, and should always be investigated. Exhaustion from sexual excesses, debility and depredation of the blood from inflammation or from bad food and air, depletion from glutinous indulgence of the appetite; intemperance in the use of alcoholic
dimpls; and the influence of occupation and trade, should be taken into account in presenting. In persons accustomed to excessive eating and drinking, it should be recollected that rest and total depression often follow the abstinance consequent upon attacks of illness against which it is necessary that the practitioner should be on his guard. In such instances, particularly in those of drunkards, it is often necessary to support the tone of the nervous system by the continued use of stimulating drinks, even while the abstraction of blood from the arm is rendered necessary by an acute and dangerous attack of inflammation. Previous disease generally leaves a debility which renders the patient less able to bear depleting or depressing measures. But there is another point of view, in which this influence is to be considered. Peculiar diathesis, such as the rheumatic, the febrile, the tubercular, &c. often have a wonderfully modifying influence upon accidental diseases, upon which they are apt to impose more or less of their own character. Coincident influences
often greatly modify the morbid results of particular causes. Of these, perhaps, the most important are miasmatic influences, and that of epidemics. Without attending to these, the practitioner must be liable to make most fatal blunders. It is well known that the diseases of miasmatic regions assume a character, or less analogous to that of the peculiar fevers by which they are infected. From arising from other causes, and from the ordinary phlegmasias, occurring in the autumn and winter, except generally the remittent aspect of the proper miasmatic fever, and, like it, require less depletion than in other situations, and often yield (most happily) to quinine. Epidemics are notorious for their quality of imparting something of their quality of imparting some thing of their own nature to all other co-existing diseases. Now sometimes the epidemic influence conduces to a cleanly or vigorous state of the system, sometimes to an asthenic, feble, or typhoid condition. In the former case, diseases ordinarily of a fiible character assume a
degree of energy and elevation which requires depletion; in the latter, inflammatory complaints, which usually yield most readily to copious bleeding, sometimes become so protracted as to forbid evacuation, and how to procure the support of active stimulation. This latter effect was frequently witnessed in this country during the prevalence of our great typhus epidemic. Dr. Ward firmly believes that inflammatory diseases in general are less tolerant of bloodletting since the Cholera first visited over this country in 1832.

Having considered most of the modifying influences viz. Age, Sex, Temperament, former diseases, hereditary tendencies, Climate, Habit, Previous disease, Diathesis, Pleuropneumonic influences, to which the patient may be exposed previous to the attack of disease, we shall now consider the "tolerance of the remedies apportioned in special diseases, and first then of blood-letting. That there is a far greater tolerance of blood-letting in inflammation than in health, cannot
I think for one moment be doubted. It might be urged against this statement that no one ever bleeds in health and that we have no proof. A healthy person that has lost blood by accident faints with the loss of less amount of blood than he would do if labouring under an inflammation. We see many a one faint from a small wound of the finger and with a comparatively small loss of blood, this may in part be due to nervous shock, but certainly not entirely. The best authority on the effects of loss of blood is Dr. M. Hall who states that persons in health and of moderate strength will generally faint if bled in the recumbent posture, on taking 15 oz. of blood. He has known 70 oz. to be taken in the sitting posture, in the tendency to apoplexy, without syncope! But the case is an extreme one. In cases where there is some doubt as to whether they are inflammatorv or not, bloodletting, like Divining in Intermit
not for might be used as a test, if it was inflammatory, syncope would not be so easily produced, as it would be, if it were non-inflammatory. I must admit that this test would certainly not be practicable in most cases, for it would be a dreadful mistake to sacrifice that most important fluid, for merely establishing a diagnosis, and generally speaking, inflammation gives tokens of its presence soon enough.

The loss of a sufficient quantity of blood will always produce syncope, but the amount requisite for this effect varies greatly in different individuals, and in different diseases. In plethora and inflammation, more is required than in health; in anaemia and asthenia, or tedious affections, less; the difference probably depending upon the more or less stimulant quality of the blood. The nature also of the tissue inflamed has some influence upon the tolerance of the loss of blood. It is well known that posture has great effect, when lying down, an individual
will bear a greater loss than when sitting and in this position than when standing. This partly owing to the effect of gravitation, favouring or otherwise the pressure upon the brain; partly, to the greater amount of blood required to support the increased muscular action in the two latter postures.

The tolerance of blood letting varies so much in different diseases, that Marshall Hall was led to construct a table or scale to show the amount of blood that can be drawn before syncope is produced, and which I take the liberty of inserting here.

I. Augmented Tolerance
Represented by the mean quantity of blood which flows before incipient syncope.

1. Concomitant of the Brain
2. Tendency to Apoplexy

II. Inflammation of Membranes
1. Arachnites
2. Pleuritis

\[3 \times 1 - 1\]
3. Peritonitis
4. Inflammation of the Synovial Membranes and Fibrous Juxtactions of the Joints

III. Inflammation of the Parenchyma of Organs
1. Inflammation of the Substance of the Brain
2. Pneumonia
3. Hepatitis

IV. Inflammation of the Serous and Viscous Membranes.
1. Erysipelas
2. Bronchitis
3. Dysentery

But these are mere approximations, and the numbers are liable to very great diversities. Much depends upon the rapidity with which the blood is drawn. When it flows in a full stream, through a large orifice, faintness is induced by a much smaller quantity than when it is taken very slowly, or by small and repeated portions. The quantity of blood to be drawn, in any particular case, must vary not only with the tolerance
of the individual or the disease but with the particular object to be accomplished. When strong determinations of blood of the brain, or the lungs, threaten death from cerebral or pulmonary apoplexy; or when violent inflammatory spasm puts life in immediate danger, as in some cases of laryngitis; or when inflammation of extraordinary violence attacks some vital organ, the bleeding may often proceed till symptoms of approaching syncope appear. But in ordinary cases of vascular irritation or inflammation this is seldom necessary. It is usually sufficient, in these cases, to produce a sensible diminution in the force of the pulse; and it is safer to bleed a second time, if requisite, than to abstract too much at once. Bleeding to absolute syncope in fixed affections, is injurious, independently of the mere quantity of blood lost. The explanation of the increased tolerance of bloodletting in inflammation, according to Dr. Williams, is found in the in-
creased susceptibility of the heart and tenacity of the arteries, which maintain a sufficient force and tension to preserve the circulation, especially through the brain, even when much blood is lost. In asthenic or diseased, on the other hand, the arteries being frail, and ill-fitted to transmit the blood, a smaller loss is felt, and syncope may result. The variations between inflammations occupying different seats must be referred to the hearts strength and the arterial tone being less augmented in some than in others, and are therefore indications of more or less phlegmic character of the inflammation. The quantity of blood in the whole system will affect the heart's action and arterial tension in a similar way; and no doubt the more stimulating quality of the blood may contribute to the same results. Antimony or tartar emetic. It is a very curious thing that although, when administered in a considerable dose, its first effect
is usually sickness followed perhaps by purging, a repetition of the same dose is in the majority of cases, at length borne without any further purging. The stomach comes to tolerate the medicine, and then its beneficial influence upon the disease is no less marked than when nausea and itching takes place. Some patients do not vomit at all; others, the majority in fact, vomit two or three times, and then Tolerance is established. Although patients suffering from inflammation are less easily nauseated than others, yet after the disorder has been subdued, they have often continued to take 12 or 18 pr. daily without nausea, or even loss of appetite.

The most reasonable notion of the action of Antimony is that it chiefly acts by diminising the tenacity of the vascular system; and in addition to this it possesses a catalytic power over the blood-constituents, reducing their plasticity and thickness, and so rendering them less able to keep up adhesive attraction. (Williams)
There can be no doubt that the immediate influence of a nauseating dose of Quatara imits is upon the vagus nerve and its allies. Through this influence it produces sickness, depression of the heart's action, muscular relaxation, and retarded breathing. No nausea is produced until a portion of the medicine has been absorbed into the blood and carried by it to the nerves. Some assert that the tolerance of the constitution is contemporaneous with the inflammation, but this is mere asserting for several observers. Christians, Maclay, and Williams to, have seen the tolerance of the medicine continued after the inflammation has been subdued. Dr. Christian has met patients in whom the medicine is not tolerated at all. Arseny is acts most subsceptibly in inflammations of vascular paramephynema and complan membranes; such as the lungs, the bladder, the mamma, the air passages, the cellular membrane and skin, and the joints. It is less effectual in inflammations of viscous mem
and would be unsafe in inflammatory affections of the intestinal canal.

Mercury—Like the preceding remedies, this is an especial tolerance of this drug in inflammation. Its influence is most marked over inflammations of the peritoneal membranes generally, as in peritonitis, pleurisy, also in Hepatitis and Diathes. If administered in the absence of such inflammation, the system is more readily affected, as shown by the constitutional effects of constipation of the bowels, fever of the blood and general incordination. There is a remarkable tolerance of the drug in Infancy and Childhood, but the reverse in adult age, this I apprehend is owing probably to the high state of functional activity of the secretory glands in general—the drug being eliminated chiefly by the salivary and intestinal glands as well as by the Liver—hence its value as a cholagogue. The tolerance varies in different constitutions, some persons being salivated by wonder
fully small doses, others requiring as much as a hundred grains without any sensible effect. In some individuals it produces symptom and in others painful symptoms. These cases are exceptional however and are due to idio- sympaties or peculiarities of constitution.

Opium. If a small dose of opium be continually repeated, the stimulant action may be maintained for some time, and the narcotic effect prevented. But whenever it is taken habitually, the dose will require to be gradually increased or the desired effect will not be produced, for the system is induced by degrees to tolerate the remedy in larger and larger quantities. Given in moderate doses, it powerfully relieves pain, and controls nervous irritability. Though it always tends to produce sleep, its analgesic effect may take place without its soporific action. Opium must be avoided in cases of acute inflammation within the cranium and in pr interval diseases where there is a
tendency to death by coma and apnea. On the other hand, it is, ceteris paribus, in cases where the tendency is towards death by asthenia, that the use of Opium, as a remedy for inflammation, is most permissible. It has a useful effect, often, after free bleeding, in cases of peritonitis, and of uterits. It probably does good in various ways: by quieting the nerves — by sustaining the regulating action of the heart — by keeping the inflamed parts at rest. In part in all cases of severe pain whether paroxysmal, as in the passage of hepatic or renal calculi, or continuous as from the shock of operation or external injury.

In tertianus, extraordinary quantities of Opium and other Narcotics are borne with impunity, and in Delirium tremens there is no remedy of equal power in quieting the excited brain in procuring sleep, the main object to be attained in Anasmatism, and which is the certain
preliminary to recovery. The tolerance of opium in fevers seems to be in proportion to, and in some way dependent upon, the amount of pain. Cannabis indica has been employed also with some success in the treatment of fevers. Given in large and repeated doses, there being a marked tolerance of the remedy, it was found in the hands of Professor Miller, to supersede all other remedies. The well-known intolerance of opium in children is probably due to their nervous system being so easily excited and impressed by all narcotic remedies.

Alcohol. There is no remedy that we have hitherto spoken of that will illustrate the law of Tolerance so well as alcohol. It is too well known that when taken in health habitually as a beverage, that the dose must be gradually increased to produce its desired stimulating effect, but at the expense of predisposing the system to disease. More and more ominous
In the attack of epidemic or malignant cholera, than those who have taken alcohol to excess. There can be no denying the fact that a host of diseases owe their predisposing if not their exciting cause to the over-indulgence of this drug (now may be allowed to call it so) and in this way tends to shorten life, but there are exceptions to this general statement. I know two or three old men who have been drunkards almost all their lives, yet nevertheless have most excellent health and their bodies in the highest state of physical perfection, making allowance for their last stage of existence decrepitude, and whose wounds, for they are continually being wounded in some way or other, Avant de se, heal most readily. But if alcohol be so generally delirious in health in the way I have mentioned, it is not the less remedial when employed as a therapeutic agent. It is principally of use as a stimulant or restorative in exhaustion from shock of
operation, and in fevers in which there is manifested great tolerance. Its tolerance is shown while there is great depression as from the profuse discharges of micturition, and also in Gripe which tends to exhaust the system, and to produce death by asthenia. But perhaps the tolerance of alcohol is best seen in Typhus and Typhoid fever where the type of the epidemic is of an asthenic character, there are some epidemics that wont tolerate the remedy at all. Of course the stage of the fever and the condition of the patient are to be carefully attended to.

We shall now briefly consider the third division of our subject viz. the alleged Intolerance of Remedies previously used with impunity or benefit. From the description we have given of Blood letting it might be supposed that we still advocated the views entertained with respect to that remedy during the early part of the present century, when blood letting in
Swiss and in inflammations generally, was the universal remedy. Since that time however, a revolution has taken place in medical practice, and nowadays bloodletting is almost entirely abandoned. The question arises: how is this to be explained? Two explanations have been put forward: one, that it is owing to improved diagnosis and pathology, rendering it apparent that bleeding never was the proper remedy for fevers and inflammations; the other, that a change has taken place in the types of such diseases, so that bloodletting formerly useful is inadmissible in the present day. With respect to the first theory, there can be no doubt that the improved means of diagnosis now at our command, by auscultation and percussion have enabled us to detect at an earlier period and to determine with more certainty, the existence of internal inflammations as, e.g., perniçiosa than our predecessors were able to do. But it must not be forgotten that internal inflammations are not diagnosed by physical signs alone, that
there always exists a constitutional element viz. Fever with high pulse, pain referred to the affected organ, and if the Lung be the organ affected, the character of the expectoration and other functional derangements,
symptoms purely as patent to the medical practitioners before the days of Cullen Lavoisier
as since. In fact we might almost always diagnose or predicate the existence of Pneumonia
without having recourse to physical diagnosis at all. There is no doubt that physical ex-
amination furnishes us with a strong confirmation in our diagnosis of pneumonia and
other internal inflammations. I think there is a preponderance of evidence in
favour of the second explanation, that the disease has changed its type. That such
a change has really occurred, is supported by the evidence of the oldest and best prac-
titioners amongst us, who have the most vivid remembrance of the time when blood-letting
was so much in vogue. Their observations go
to prove that Fevers were then of a more phthisic
and inflammatory type than they are now.
and that feeding was (not only well borne) but was almost invariably followed by beneficial results. Of this no unprejudiced person can have any doubt who peruses the admirable papers of Dr. Clinicon on this subject. Dr. Waton believes this change to have followed the first visit of Cholera in 1832. We believe that the T.W. has expressed it that there are waves of force through which the epidemic and asthmatic characters of disease prevail in succession; and that we are at present living in one of its adynamic phases, and that this is the main reason why bloodletting and other evacuants are not so much employed now, and why wine is so much used instead.

To conclude, the author regrets the imperfect manner in which the subject has been treated. It is not to his satisfaction, having put it together too hurriedly and left himself too little time for working the subject out as he would have wished. He intended to have made a series of experiments on the lower animals illustrating the subject of Tolerance. He has not adhered to the division of the subject to close as he would have liked, and must beg the candour of his reader.