

**The history and therapeutical value of arsenic in skin diseases / by
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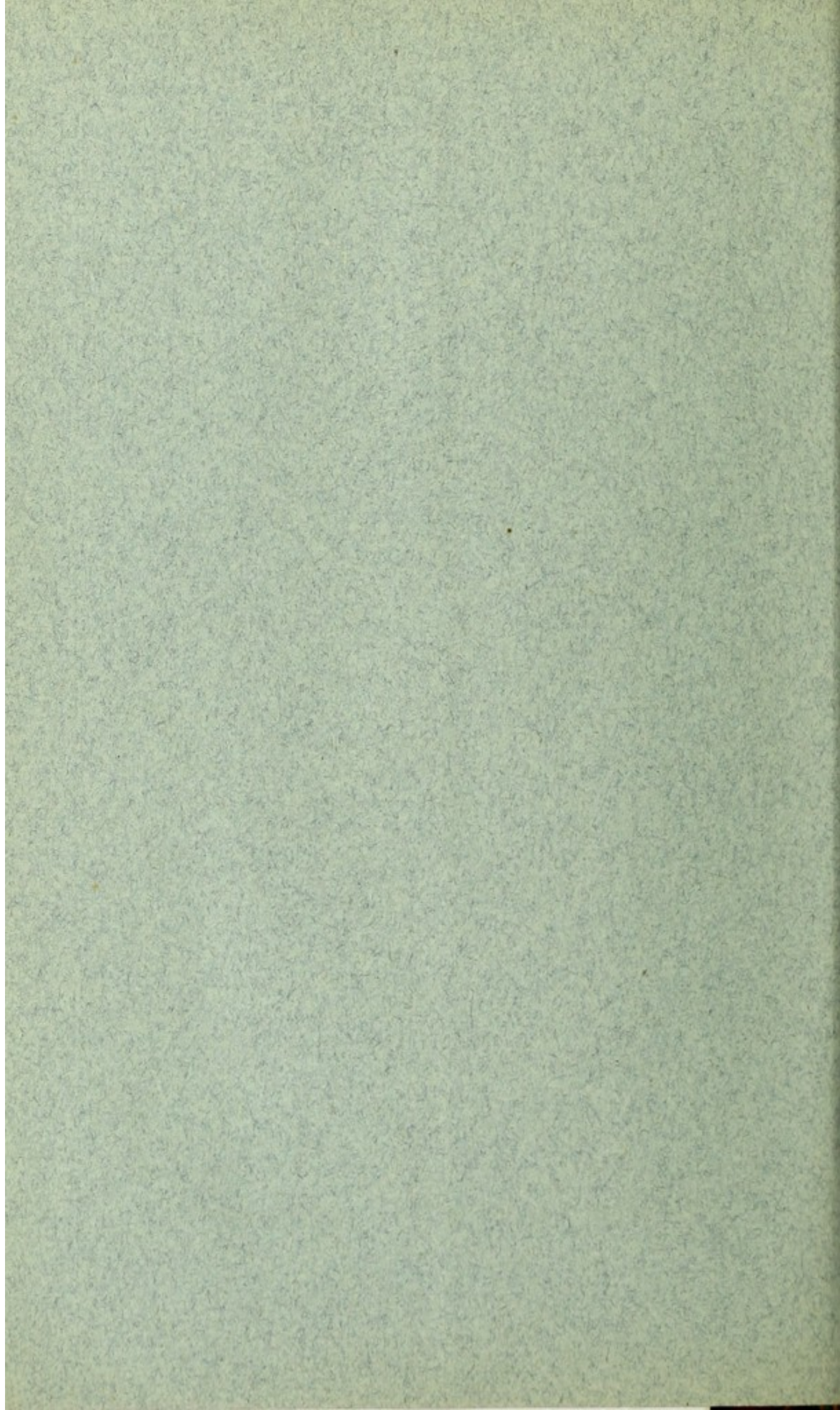
THE HISTORY AND THERAPEUTICAL VALUE OF ARSENIC IN SKIN DISEASES;

BY

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THE HISTORY AND THERAPEUTICAL VALUE OF ARSENIC IN SKIN DISEASES.¹

GENERAL HISTORY.

It is always of interest to study the history of any method of cure by any drug, and it is especially interesting in the case of arsenic, from the alternate excessive confidence in and excessive suspicion of it at different periods. From a study of these different periods we shall be able to perceive the mistakes that have been made, and see the necessity of arriving at a rational theory for its use. We shall see that it was the purely empirical knowledge of the early and even the comparatively late physicians that led them to take exaggerated views about it; but I desire here to base whatever conclusions we may arrive at as far as possible on a physiological basis.

Dioscorides² used arsenic as a remedy internally for asthma and inhaled for spasmodic cough, and his remarks were copied by Pliny, Galen, Coelius, and other great physicians of the Roman empire, who prescribed it for ulcers of the lungs and intestines, and asthma, but after their decline it seems to have fallen into disuse in Europe.

However, the Arabian physicians derived a knowledge of it from them, and Rhazes and Avicenna gave it for diseases of the skin, such as scabies, lepra, and herpes, for the diseases of the

¹ Read before the Medical Society of London on April 5th, 1880.

² Harles, *De Arsenici Usu in Medicina*, p. 49, 1811.

lungs, as asthma, spasmodic cough, and spitting of blood, piles, and malignant ulcers.

From the Arabians, Paracelsus adopted it and tried to bring it into use as a medicine, but the prejudices against it, owing to its frequent use as a poison, were so strong, that this attempt was used as one of the arguments to prove him a charlatan.

Among the physicians of the sixteenth and seventeenth centuries, only two are recorded as making use of it; Wirth, about the year 1570, for asthma, and Jean de Gorris, chief physician to Louis XIII. of France, in ulcers and many other diseases.¹

But though it was neglected by the physicians of the time, it was largely used among the people in Germany, France, and Italy, and prescribed by quacks. Lemery, the chemist, in 1675, says it was much used in France for quartan fevers, and Sperling, in 1685, attests the frequency of its use in Styria and Bavaria.²

In the year 1700, Adrian Slevogt published a treatise on arsenic, in which he recommended it and justified its use on medical grounds. His conclusions were supported by Frick of Ulm, in his book on poisons, 1710, but equally strongly opposed by Stahl and Wedel. Slevogt³ summed up the controversy in his book on the subject in 1719, in which he gives statistics of his great success in quartan and tertiary fevers. It still continued much in vogue among quacks,⁴ and Ackermann mentions a family who made use of it as a family secret against intermittent fevers, herpes, and melancholy with good results, but only two physicians of repute, professors at Vienna, named Plencitz, father and son, gave it systematically, and with invariable success for forty years in intermittent fevers even during an epidemic. Their success, however, did not prevent opposition, and even the great Linnæus declared it ought not to be used as a medicine, and eventually the disastrous failure of an arsenical febrifuge when used by Prof. Stoerk again made it once more unpopular.

In this country arsenic had long been used as a quack⁵ remedy

¹ Harles, p. 58.

² *Diss. de Arsenico*, Wittenburgh, 1681.

³ Slevogt, *De Arsenico*, Jena, 1719.

⁴ Harles, p. 70.

⁵ Desgranges, "Sur l'Arsenic," *Journal Générale de Médecine*, vol. xxx. 1807, p. 254.

in ague and intermittent fevers, and a preparation of tartarised arsenic, called in the Pharmacopœia of Edinburgh "solutio mineralis arsenici," was well known as a remedy even against certain cutaneous diseases. One of these quack remedies, known as ague drops, which seem to have been identical with the fever drops spoken of by Neumann as much used in Berlin, was analysed for Dr. Fowler of Stafford by a chemist named Hughes, and found to be a saline solution of arsenic. He¹ published a pamphlet in 1786 entitled *Arsenic in Ague, Headache, and Intermittent Fevers*, in which he gives the prescription called after his name, and describes several cures due to his remedy.

Fowler's Solution—Original Prescription.

Solutio mineralis.

Recipe arsenici albi in pulverem subtilissimum triti.

Salis alkalini fixi vegetabilis purificati, singulorum grana sexaginta quatuor.

Aquæ fontanæ distillatæ libram dimidiam.

Immittantur in ampullum florentinam qua en balneo arenæ posita, aqua lente ebulliat, donec arsenicum perfecte solutum fuerit. Deinde solutioni frigidæ adde.

Spiritus lavendulæ compositi, unciam dimidiam.

Aquæ fontanæ distillatæ libram dimidiam, plus vel minus, adeo ut solutiones mensura libra una accurata sit, vel potius pondere, uncizæ quindecim cum dimidia.

$$\text{℥j} = 4 \text{ grs. } \text{℥j} = \frac{1}{2} \text{ grs.}$$

Nevertheless much opposition was raised against Fowler on account of the supposed danger of the drug, so much so that Willan² thought it necessary in the *London Medical Journal* to declare that he had seen the best results in seven cases under his care. Dr. Pearson and Sir George Baker³ also gave their testimony, and the former substituted a solution of his own for that of Fowler. The greatest opportunity of attesting the success of

¹ *On the Effect of Arsenic in the Cure of Ague, Intermittent Fevers, and Periodic Headaches*, London, 1786.

² Willan, *Lond. Med. Journ.* 1787.

³ Pearson, Bradley's *Med. and Phys. Journal*, London, 1806.

arsenic in fever was given to the army surgeons, of whom Dr. Jackson, in St. Domingo, Dr. Winterbottom,¹ in Sierra Leone, and Macleish,² in Corsica, universally approved of it even in preference to quinine.

Even before the acknowledged success of arsenic in intermittent fever, it had, like all other remedies, been attempted in cancer. In France, Lefebure Justineau, whose prescription became a family secret among the Earls of Arundel and Salmade, had invented various preparations.³ In America, Rush in his *Medical Enquiries*, and in Sweden, Roennow and Ohdel, all published cases of cancer cured by the internal use of arsenic. Dr. Simmonds, of Manchester, in the year 1796 published a book on the use of arsenic in cancer, in which he declared it to be a specific, and in articles constantly contributed to the medical press quoted cases in which he had been successful. From our present knowledge of cancer it seems that it was rather to an error of diagnosis than to the action of arsenic itself these cures must be attributed, for when used in skilled hands such as those of Desgranges it was valueless. The popularity that had been acquired by arsenic after its introduction by Fowler for intermittent fever caused it to be tried in England for various diseases, and Dr. Alexander, of Halifax, professed to have cured angina pectoris, epilepsy, and convulsions from worms, Dr. Jenkinson rheumatism, and Dr. Ferrier whooping cough, and John Hunter himself, owing to a report of its successful use among the natives of India, is said to have recommended it for hydrophobia.⁴

The early medical history of America has not been sufficiently noticed, and the authors on the continent of this date refer to Anglo-American physicians as if there were but one school of medicine for the two countries. Whether this was so or not it cannot be affirmed, but there is no doubt that arsenic was used in America very shortly after Fowler introduced it in this country. Dr. Rush, of Philadelphia, who has been previously mentioned, was the first, as far as can be ascertained, to rely on arsenic as a remedy chiefly in cutaneous, cancerous, and scrofulous diseases.

¹ Winterbottom, *Medical Facts and Observations*, vol. vi. 1795.

² Macleish, Duncan's *Annals of Med.* vol. ii.

³ Harles, p. 109-112.

⁴ Harles, p. 82.

He was supported by William Currie, also of Philadelphia, who strongly advocated its use in intermittent fevers, and by Prof. Barton,¹ who seems to have been to Rush what Pearson was to Fowler, and who gave it in the form of pills combined with opium. After Barton's time the remedy came into regular use in the United States.

In Germany, where arsenic had been first studied and successfully tried, it had, as we have seen, fallen into complete discredit, and was entirely abandoned by the profession. At the commencement of the present century, however, it was re-introduced into legitimate practice by Oberreich,² who used it in a great variety of diseases. Whether his advocacy would have been sufficient to have brought it into general use may be doubted, but the increasing price of quinine, owing to Napoleon's continental system, gave rise to an imperative demand for some cheaper febrifuge. Heim, in his book on arsenic in fever, drew attention to this remedy, and described the good effects he had procured from it. The great extent to which it was now used indiscriminately is proved by a proclamation of the King of Prussia in 1810, which, after describing in the preamble the value of arsenic in intermittent fevers, proceeds to make regulations as to its sale by druggists, and forbids its use except when prescribed by a medical man. The solution which was legalised by this proclamation was practically the same as Fowler's. Hahnemann, in his studies on *Materia Medica*, experimented with arsenic, but he gave it in such infinitesimal doses that, as Harles³ justly remarks, he could get no really good from it. In the year 1811, Harles, a Bavarian, summed up in his treatise, *On the Use of Arsenic in Medicine*, all the early history of its use, from which the foregoing sketch has been largely derived. Besides working out the earlier history of the drug, he describes its general physiological and therapeutical effects, and gives directions and warnings for its use, based on experiments by himself and his friends, which he gives at great length.

¹ Harles, pp. 85, 87.

² *Ibid.* p. 114.

³ *Ibid.* p. 113.

About the same time as the value of arsenic was universally recognised owing to the labours of Fowler in England and Harles in Germany, Brera¹ adopted it at his clinique at Pavia. He prescribed it chiefly for the fevers of North Italy, and in the year 1806 published in his *Clinical Observations* a sound estimate of its use and a complete refutation of its opponents. His pupils, however, in consequence of his recommendations and success, fancied it a specific not only in fever, but in nearly all other diseases.

It is in France that the history of arsenic is most instructive. After its general use in the tenth century it fell into discredit among physicians, though much used by the people themselves and by quacks. The successful revival of its use by the English and Americans, the Germans and Italians, could not long be neglected in France, and it was an army doctor who had practised in America and travelled in England, Louis Valentin, that first made it known in France by articles in the *Journal de Médecine*. The first book that appeared on the subject was by Dr. Fauves, published at Paris, 1804, under the name of *Clinical Researches on the Effects of Arsenic in Intermittent Fever*, but Dr. Fodéré, physician to the military and civil hospital at Martigues, was the first to use it in large quantities. In 1809 he described the success he had had in more than 300 cases of intermittent fever by means of arsenious acid, which he had first used in spite of himself, owing to the lack of quinine.

Dr. Niel, first physician to the hospital of Marseilles, declared he knew no febrifuge equal to arseniate of soda, and Desgranges, in a remarkable article in the *Journal Générale de Médecine* in 1807, describes the practice with this drug in England and America, and confirmed the results from his own experiences. In spite of the testimony of so many eminent physicians, and the universal success they had reported, Deidier, Peyrilhe, and Thibaut violently opposed its introduction, and were enabled once more to procure its disuse. Yet all did not acquiesce in its rejection, and both Cazenave in 1833 and Trousseau in 1837, in articles in dictionaries, assert its therapeutic value, but without any appreciable result. It was reserved for Boudin,² physician general to the

¹ Harles, p. 99. ² Boudin, *Traité des Fièvres Intermittentes*, 1842, p. 250.

French army in Algeria, to finally re-establish it in practice, in consequence of his success with it in the prevalent fevers there. In 1842 he published his first treatise, and in 1845 presented to the Academy of Medicine a new memoir, in which he stated he had cured 3,000 intermittent fevers with arsenious acid, without a single case of failure or a single accident. This statement created great excitement, and was followed by an equal amount of support and detraction. It is unnecessary to mention the names of all who joined in the discussion that ensued, but in the end its value in fever was generally recognised.

It will be seen from this short history that arsenic suffered many vicissitudes before it was recognised in general medicine. Though prescribed by Galen and Cœlius, it was neglected in the middle ages, and when re-introduced, probably from the Arabians, soon again became unpopular. The cause of this unpopularity is to be found rather in its having been recognised as a typical deadly poison than from any accidents in its therapeutic administration, but this was strong enough to completely banish it from the domain of medicine. At last, at the commencement of the eighteenth century, it was for the first time properly tested by Slevogt, but his researches were not able to make it generally popular in the face of violent opposition based on its alleged poisonous properties. All through this time, it had been universally used as a quack remedy in fever and ague throughout Europe, and it was from one of these quack remedies that Fowler of Stafford derived the solution which bears his name. His success was soon followed up by other English physicians, and arsenic became once for all an established English remedy. It was equally quickly re-established in Germany, where it had fallen into discredit after the death of Plencitz, and in Italy mainly through the authority of Harles and Brera. In France the labours of Fodéré, Desgranges, and others seemed to have been equally successful, and at the beginning of the nineteenth century it seemed to be thoroughly recognised, yet it once again, owing to the violent opposition based on the old suspicion of its dangerous character, was rejected. It was not till the discussion raised by the memoirs of Boudin was over that it took a permanent place in French practice.

SPECIAL HISTORY IN SKIN DISEASES.

The foregoing history of the use of arsenic in general diseases, especially in intermittent fevers, shows clearly the alternate periods of belief in, and fear of it as a medicine, and must be understood to comprehend the history of its use in skin diseases. It will have been noticed that up to the time when its action was first physiologically examined, each period of excessive popularity was followed by a period of equally excessive distrust. But after the commencement of the eighteenth century, the re-actions seem, with two notable exceptions, at different times in Germany and France, to have become less and less marked, and by this time its value in general medicine, especially in fever, appears to have been justly estimated. The history of its use, and of the process by which the modern estimate of its general value has been gradually arrived at, will be of assistance to us in trying to steer between the equally excessive use and disuse of it in skin diseases, and in trying to arrive at a fair estimate of its value in this special department.

I now intend to give, first, a brief history of the use of arsenic in skin diseases, in order that we may see and avoid the extremes to which partisans on either side have been drawn; secondly, a description of the physiological action of it as at present accepted; and thirdly, the results of personal experience. In conclusion, I hope to be able to draw some reasonable inference as to the particular class of skin diseases in which it may be prescribed.

In the history of the general use of arsenic, it was noticed that it was in common use among quacks as a remedy against ague and fever, even at the time when it was in greatest disfavour among medical men, and this was also the case as regards skin diseases. Two remarkable instances of this may be mentioned, one in Germany and one in England. Ackermann gives the prescription kept as a secret by a family of surgeons for many years, which they declared to have been most successful in the treatment of herpes. An Edinburgh *Pharmacopœia* of about 1775, gives a prescription under the name of *solutio mineralis arsenici* which was used among the people to cure leprous diseases.

Besides this popular use I have only been able to discover three distinct references to its early use by medical men. In 1784 Dr. Adair, who had practised in the West Indies, states in a communication to the *Medical Commentaries of London* that he had used it internally with opium in the form of pills in cancer, elephantiasis, and yaws. According to Desgranges, who speaks on the authority of Dr. Valentin, Rush of Philadelphia used to prescribe it for darts and other serious affections of the skin, seemingly without success, but also without any ill-effect. Oberreich¹ who wrote on arsenic in the year 1803, speaks in exaggerated terms of it as being the most efficacious remedy in a large variety of different diseases, including herpes and cancerous ulcers.

These individual experiences had no widespread effect, and until Dr. Thomas Girdlestone of Yarmouth contributed his well-known letter to the *Medical and Physical Journal of London*, in April, 1806, no actual case of cure by means of it had been recorded. He says, that "although I had frequently used with success the arseniate of potash in mesenteric, and many other scrofulous affections, yet your old acquaintance Mr. B. was the first patient on whom I tried the effects of this medicine in lepra. You remember that he had laboured for fourteen years under that disease, tried repeated salivations, many physicians and every quack medicine, without any effect, and was at last cured by small and repeated doses of arseniate of potash. It is now several years since his cure was completed, and my experiments and success have extended to some hundreds of cures of lepra, lichen, prurigo, psoriasis, tinea capitis," &c.

Another early case is reported in the *Medical and Physical Journal* of 1807, by T. Y., who gives the notes of his own case. He says: "I had had severe psoriasis diffusa since 1880, had tried every known remedy without avail, local and constitutional, when I began arsenic as recommended by Girdlestone. Began three drops twice a day, increased to seven, in six weeks I was quite well." Its use in skin diseases seems to have become known immediately, for in 1807, Dr. Bardsley of Manchester gave his

¹ Harles, p. 114.

experience of Fowler's solution, and in 1812, an American physician, Dr. Redman Coxe, narrated a cure of lepra of fourteen years date cured by arsenic.

Nevertheless Willan in the first edition of his great work on cutaneous diseases makes no mention of it, but it must soon have been recognised in English practice, for Biett, who was the first to use it at the celebrated Skin Hospital at St. Louis, is said by Cazenave to have introduced it from the London hospitals. Bateman in his edition of Willan, published in 1819, speaks of Fowler's solution being extremely beneficial in inert cases of lepra, owing to its tendency to support the strength, and to stimulate the cutaneous vessels.¹

In a monograph on arsenic by Mr. John Marshall, 1817, he says that Dr. Browne, senior physician to the Sea Bathing Infirmary at Margate, gives arsenic in skin diseases, but always limits the dose of 5 \mathfrak{m} . of Fowler's solution, twice a day, beginning with 3 \mathfrak{m} ., and his reason for not giving more than 5 \mathfrak{m} . is because of the deleterious effects he has witnessed when the drug has been pushed.

In France Fodéré used it with success in some dartsous affections, as well as in intermittent fevers, but it was not a recognised remedy in skin diseases till Biett, as has been already stated, introduced it at the Hospital of St. Louis in 1817. By the year 1820, he had invented the arseniate of ammonia, which he gave in addition or in alternation with the solutions of Fowler and Pearson. He seems, according to Cazenave's article on arsenic in the year 1833, to have used it not only in lepra and psoriasis, but also in eczema, impetigo, and urticaria tuberosa with success, and to have tried it, but without avail, in porrigo, acne, sycosis, and lupus. Rayer, whose first work was published in 1826, mentions arsenical preparations for chronic cases of almost every disease, but in his introduction he says that "for his own part he ardently hopes that experiments of another description, put to the same test, may cause these violent remedies to be superseded by external medicines, more rational, more immediate in their effects, and less dangerous."² In his later edition, trans-

¹ Page 33.

² *Traite de Maladies de la Peau*, Paris, 1826.

lated by Dr. Willis in 1835, he says that arsenical medicines are most frequently and most successfully employed in certain chronic and obstinate forms of eczema of the scrotum, margin of the anus and labia; they ought never to be used in exanthematous, and but rarely in chronic bullous inflammations, occasionally in lichen, and sometimes in spite of much abuse, with success in prurigo, pityriasis, psoriasis, and lepra.¹ Cazenave in his article in 1833 said that marvellous effects resulted from the administration of arsenical preparations, not only in lepra and psoriasis, but also in eczema and impetigo, though they failed in porrigo, acne, and sycosis. In his *Manual* on diseases of the skin published in 1853, he repeats even more emphatically his former opinion. Devergie, Hardy, and Bazin all largely recommended arsenic, the two latter chiefly in darts affections.

In Germany the use of arsenic has not been so extensive as in France and England, for Hebra, the distinguished dermatologist of Vienna, has, since 1840, taught rather the value of external instead of internal remedies, and the necessity of placing the latter on some scientific basis. He says: "I set not the slightest value on any remedies except those which (after repeated trials, and when I am accurately acquainted with the complaint) I find to produce a favourable change in its course, or, in other words, to cure the patient. I never attribute therapeutical powers to a medicine, unless I observe its employment to be invariably and constantly followed by some change in the morbid products, and by the termination of a disease in a shorter time than when it is allowed to undergo spontaneous involution."² Yet he gives it in psoriasis, remarking that arsenic has a decided curative action, and can make this affection undergo involution for a time, if not permanently, and also in lichen ruber with good results. On the contrary, he denies its value in eczema, and says, in strong language: "I cannot concede to arsenic the undefined blood purifying and eczema curing powers which are attributed to it by English and French physicians."³ Neumann and the other German writers adopt pretty nearly Hebra's views.

¹ Page 85.

² *Hebra on Diseases of the Skin. New Sydenham Society Trans. Vol. ii. p. 89.*

³ *Ibid. Vol. ii. page 143.*

Though the science of dermatology had taken deep root in France in the early part of the century, chiefly, or I might say entirely, due to the labours of the St. Louis physicians, yet it had not done so in this country ; for, after the death of Bateman, who carried on Willan's great work, nothing of any importance was published on the subject till 1842, when Mr. Erasmus Wilson's work on diseases of the skin appeared. In this early edition, not very much mention is made of arsenic ; under the head of eczema, it is included among several other remedies as a suitable one for the chronic and obstinate forms. Its action is described in a footnote in the following words : " Arsenic, when it acts on the nervous system, performs the part of an alterative but when its effects are directed upon the membrane of the kidney, viz., by counter irritation, by exciting inflammatory action in the interior, and thus determining from the surface." ¹ In lepra also Mr. Wilson had used it, but he does not strongly urge its adoption, as its action is only incidentally mentioned in a footnote. In his lectures delivered before the Royal College of Surgeons in 1871-2-3, Mr. Wilson points out that in eczema there is no medicine more harmless, more certain in its effect, and more successful than arsenic. The good qualities as well as the dangerous effects are again referred to when dealing lepra, but it will be sufficient for me to say that Mr. Wilson strongly advocates its use in this disease.

No Englishman, and probably no man who ever lived, used arsenic to such an extent as Hunt. He not only gave it in every single disease of the skin, but states in the ninth edition of his book, published in 1871, that it is a perfectly harmless drug, and that after thirty years' observation he has rarely known it produce any unpleasant effects on the system in a degree incompatible with perseverance in its use. He adds : " There are few medicines less likely to do harm than arsenic." ² Modern English dermatologists do not however go to the excesses of Hunt. Dr. McCall Anderson ³ recommends it both in eczema and psoriasis, and Dr.

¹ Page 172.

² *Guide to the Treatment of Diseases of the Skin*, 1871, 9th Ed. p. 18.

³ *A Practical Treatise on Eczema*, London, 3rd Ed. 1874 ; *On Psoriasis and Lepra*, London, 1865.

Tilbury Fox in cases of the latter in which "the scaliness is well-marked, and the disease in other respects typical."¹ Mention must also be made of Dr. Bulkley, the eminent American dermatologist, who in his monograph *On the use and Value of Arsenic in the treatment of diseases of the skin*, has given a clear and practical summary of his experience with it.

PHYSIOLOGICAL EFFECT.

From this short history, it will be seen how much the internal use of arsenic has been regulated by more or less empiricism; how that its success in one disease has caused it to be tried in all; and how its known poisonous property has often caused its therapeutical value to be denied. But more recent observers have investigated its physiological effect on the various organs of the body, and it will now be my endeavour to consider their results.

The fortunate absence of ill results even when taken in large and increasing doses is clearly seen in the arsenic-eaters of Styria. In the year 1851 Tschudi first drew the attention of the profession to the existence of this habit, the objects for which it was taken, and the result. It seems that the young peasants, both men and women, take it to improve their personal appearance, and also, according to Wurmb, to make their respirations deeper and easier. To all appearance they achieve their object and apparently meet with no inconvenience even when they are taking large doses, unless they suddenly stop using it, which causes sickness, burning pains in the stomach and other symptoms of poisoning very speedily followed by death. Tschudi was opposed, especially in England, where Taylor, Pereira, and Christison openly stated their disbelief, but his assertions have since been verified by many German physicians, and by Dr. Craig MacLagan of Edinburgh. From the analogy of its effects on man it is not an uncommon custom for coachmen, especially in Vienna, to give it to their horses to make their coats more glossy and to fatten them.

Before discussing the effects of arsenic on the various parts of the system it will be well to draw a distinction between the effects

¹ *Skin Diseases*, London, 3rd Ed. 1873, p. 268.

of poisonous and therapeutic doses, since it is owing to the want of such distinction that such opposite conclusions have been arrived at as to its physiological properties.

In this paper it is proposed to examine only the effects of small and therapeutical doses.

M. Lolliot, in his extremely able physiological study on arsenic, discusses, first, its action on nutrition, respiration, circulation and the nervous system ; and secondly, its elimination by the skin, the mucous membranes, and the liver and kidneys. This arrangement seems to be exhaustive, and will here be followed.

1. *Nutrition*.—The increase of appetite caused by arsenic is so noticeable as to have drawn the attention of the earliest investigators, and Harles attributed it to an increase of irritability of stomach and intestines. Biett and Cazenave noticed the fact and believed it was due to the same cause, as did Dr. George Harley, who, amongst his deductions from experiments on animals, states that arsenic has “a specific action on the digestive canal.”¹ But certain German investigators Schmidt, Sturzwage, and Brett-Schneider, proved by experiment that arsenic had a direct action on nutrition by diminishing oxidation, and these results were confirmed by Claude Bernard and by Professor Sée. The former, after explaining the action of carbonic oxide on the coloured corpuscles of the blood, says that arsenic acts in a similar manner. “It fixes,” he writes, “upon the blood corpuscles, but does not entirely suppress their action ; it only tends to diminish the activity of the perpetual exchange carried on by their means between O and CO₂, a state of things which, when confined within proper limits, is not wholly incompatible with health, and under such circumstances produces, as a natural result, a certain degree of obesity.”¹ Arsenic, therefore, in consequence of this combination with the coloured corpuscles, prevents them from receiving the due amount of O in the lungs, and therefore diminishes oxidation in the tissues and prevents wasting. Its final action on nutrition in the decrease of the temperature and diminution of urea is due to its action on the digestive organs.

¹ *Times and Gazette*, Nov. 1861.

2. *Respiration*.—I have mentioned the improvement in respiration noticed in the Styrian arsenic-eaters, and it is an acknowledged effect produced by it as shown in the diminished oxidation in the tissues. Lolliot attributes this to the diminution of the quantity of CO_2 exhaled and consequent great freedom of the respiratory movements. It is now acknowledged that muscular fatigue is shown by an increase of CO_2 , and therefore when CO_2 is decreased, muscular action is proportionally made easier. But it must also be remembered that the less O there is in the blood, the greater is the stimulation of the respiratory centre, and as a direct result breathing is improved.

3. *Circulation*.—The bright colour observed in arsenic-eaters has been attributed to a paralysis of the vaso-motor nerves, thus permitting a greater flow of blood. After the injection of arsenic into a vein, a marked fall of general blood-pressure has been noticed by Unterberger. Arsenic, at least in small doses, has but little effect on the heart, though Fowler and some other observers have stated that it increases the beats of the heart. Cazenave and others deny this, and say that arsenic only acts on the heart in poisonous doses.

4. *On the Nervous System*.—The action on the nervous system is very obscure, but there can be no doubt that in small doses it may produce headache, and in larger and prolonged doses some symptoms of paralysis. This seems to indicate that the central nervous organ is implicated and most probably through the influence arsenic exerts on the blood.

Elimination.—Having described the direct physiological effects of arsenic on the system, its various modes of elimination must now be mentioned. It is eliminated by the skin, the mucous membranes, the liver and the kidneys. That it is eliminated by the liver and kidneys has been proved by its discovery in the bile and urine. The various phenomena, such as conjunctivitis, bronchitis and diarrhoea, &c., after its use, prove as conclusively its elimination by the mucous membranes.

Its elimination by the skin is for our purpose of more importance, and will be discussed at greater length. It has been

found both in the serum of a blister by M. Chatin and in the sweat of patients undergoing arsenical treatment for psoriasis at St. Louis by MM. Bergeron and Lemattre by means of Marsh's test. Besides these direct proofs we must now proceed to notice the physiological effects of elimination by the skin when given in small doses. It has been observed by Christison and others that an increase of perspiration followed by violent itching and sometimes by eruptions, soon affect those who have taken arsenic. The itching may occur over the whole body or on particular parts, such as the hands, feet, and face, but is only temporary unless there is an eruption. M. Imbert Goubeyre has written a monograph on arsenical eruptions, dividing them into papular, vesicular, &c., but this seems an exaggerated account, for such eruptions are of rare occurrence. Nevertheless, though positive eruptions are rare, brown staining of the skin is often observed. It has been said that these stains generally appear after psoriasis, but they are probably more common then, rather because the arsenical treatment has been prolonged than for any peculiarity in the disease. Boils and Carbuncles also occasionally result, and as they originate in the deeper portion of the corium, they are a further proof of the passage of arsenic through the skin itself. Before leaving the subject of elimination, I must mention the important experiments on arsenic by Drs. Ringer and Murrell, published in the *Physiological Journal*. They found that when frogs were poisoned by arsenious acid in a certain number of hours desquamation of the epidermis was produced. Further experiments were made by Miss Nunn, who states that "the general effect of arsenious acid on the epidermis is to cause a degeneration and partial solution of the protoplasm of the cells, whereby (1) the whole epiderm becomes loosened from the subjacent derm (2), the cells of the malpighian layer become incoherent, so that the whole layer collapses and its well known architectural features become obscured, and (3) the intermediate layer separates from the malpighian layer below and at times from the corneous layer above."¹

¹ Vol i., 1878-9, page 248.

THERAPEUTICAL EFFECT.

Having considered the physiological action of arsenic on the system, and the modes by which it is eliminated, especially by the skin, I shall now pass to the more practical part of my paper and mention the various diseases of the skin in which it is recommended, and the results of my own experience.

Psoriasis is the disease of all others that arsenic has been prescribed for, from the time that Girdlestone gave it first up to our own day. It must be acknowledged that it would be absurd to doubt the curative effects of arsenic in this disease, for all writers on dermatology agree in praising it, but at the same time there are cases in which not only arsenic does no good, but really does great harm. Why this is the case it is difficult to explain. It seems as if the drug in these cases acted more on the vessels themselves through the medium of the vaso-motor nerves than on the blood. The following case is an illustration :—

CASE I.—H. M., a female, aged 34, who appeared in good health, applied at St. Mary's Hospital on July 3rd, 1879. She had several well-marked patches of common psoriasis both on her arms and legs, also a few on the trunk. This was the fourth attack. The patches were not markedly hyperæmic, but there was an abundant formation of scales. She was ordered 4 m. of Fowler's solution in water, three times daily, and no local application.

July 10th.—A few fresh patches have appeared during the week; the old patches about the same. Ordered not to wash, but to continue the medicine for fourteen days.

July 24th.—The patches were much worse, more intensely hyperæmic and very painful. She was then ordered local applications and the arsenic was discontinued.

In this case arsenic was fairly tried alone and undoubtedly did harm. I could mention other cases that have come under my observation in which a similar result took place, but it is sufficient to have noticed the fact.

In order that we may judge honestly whether arsenic really can be said to cure psoriasis, it must be given alone, without combination with any other drug. This, I think, is very important, as arsenic is often given with iron, and when a cure is effected it is difficult to know which drug is to be credited with the success. Another point is the local treatment, for every one will admit that local applications alone will, if carried out properly and persevered in long enough, entirely remove all external traces of the disease. But can this be called a cure? My answer is, certainly not; for psoriasis usually relapses, and unless we prevent this occurring we cannot say the disease is cured. I have given arsenic by itself to a certain number of patients without any local application, and have carefully watched the effect in order that I might ascertain whether by preventing the formation of new patches and modifying the older ones, some idea might not be arrived at why, by its long continued use, relapses are prevented.

CASE II.—E. F., aged 23, applied at St. Mary's Hospital on August 14th, 1878, with psoriasis of the whole body. At my request her blood corpuscles were counted by my friend Dr. Henderson, by means of Dr. Gowers' instrument. The coloured corpuscles numbered 58 per square. She was ordered Fowler's solution m. v. and no local application.

August 21st.—Corpuscles 48 per square; eruption somewhat better.

August 28th.—Corpuscles 37·1 per square; eruption fading.

September 11th.—Corpuscles 37·3; eruption almost disappeared.

CASE III.—J. E., aged 13, applied on the same day with general psoriasis. Corpuscles 48·4 per square.

August 21st.—Corpuscles 42 per square: eruption much better.

September 11th.—Corpuscles 45·25 per square; rash much worse; did not attend last week; has taken no medicine.

September 26th.—Corpuscles 40 per square; has taken medicine regularly since last week; eruption nearly well.

These two cases were not selected for any special reason, except that they happened to come on the same day. It will be noticed that the improvement in the eruption coincided with a diminution in the number of coloured corpuscles, unaccompanied by increase or diminution of leucocytes. The second patient, J. E., having omitted to take her medicine, an aggravation of the eruption was found to coincide with an increased number of coloured corpuscles. In another case, L., a young girl, aged 13, the improvement coincided with a diminution of corpuscles from 51 to 46. She was not however long enough under observation subsequently to say whether the diminution would have continued.

These observations at first sight appeared to be opposed to the results of Dr. Gowers' experiments, for he found that arsenic like iron increased the corpuscles.¹ This is undoubtedly so in anæmia when first given, but if continued for any length of time, or administered in health, it has been proved by Drs. Cutler and Bradford that the number of both coloured and white corpuscles are diminished. We have seen that in large doses arsenic acts on the lower cells of the rete as a protoplasmic poison, and it seems to me therefore that it can fairly be argued that small doses in a much less degree may have a similiar effect in preventing the growth of the upper layers. Whether this action on the rete is brought about in consequence of the corpuscles being fewer in number, or because of the part arsenic takes in retarding oxidation, it is difficult to say, but I am inclined to suggest the theory that it is in one or both of these ways that arsenic acts beneficially in psoriasis. I have seen two cases of psoriasis rapidly cured by sudden but accidental loss of blood, and this was the common mode of treatment by the earlier physicians. Indeed Hunt, himself, who believed so exclusively in arsenic, always bled in severe cases, and says the eruption faded accordingly. Psoriasis usually attacks people who are in good health, and very often of a plethoric habit. From these remarks it would seem as if I thought that arsenic was a depressant; I would rather say that it is an economiser. I agree with M. Gubler when he says that

¹ *Practitioner*, July, 1878.

"arsenic is a contra-stimulant, and antipyretic, but not a tonic ; it is opposed to waste, but creates no strength. In preventing the organism from rapidly wasting away, it permits the reconstruction and storing up of fat whence the appearance of health."

After the acute attack of psoriasis has disappeared, I should recommend that arsenic be given in very small doses, but to be continued for a long period. I feel justified in giving this opinion from several cases I have seen, one of which I give the brief notes.

CASE IV.—Mrs. W. consulted me in June, 1878, for a severe attack of psoriasis. She was 40 years of age, and had had the disease since she was 12, with only short intervals free from the eruption. The extremities were particularly affected, especially the fronts of both knees. I gave her 5 m. of Fowler twice a day, and an ointment of chrysophanic acid. After about three weeks of this treatment, the eruption had nearly disappeared. I then gave her 2 m. of Fowler twice a day, and this she has been taking with hardly an interval since that time till January of this year. During this long period she has not had any relapse, and I cannot but believe this is due to the long course of arsenic she has had.

A noticeable point in this case is, that throughout this course there were no constitutional effects, and for my own part, I do not agree with Hunt, who says that to do any good arsenic must be pushed till "a pricking sensation is felt in the tarsi and the conjunctiva becomes inflamed ; at this crisis the disease is brought under arrest ;" though in this view he is supported by Dr. Begbie in an article in the *Edinburgh Medical Journal*, 1858.

My conclusions are (1) that arsenic sometimes relieves psoriasis in an acute state, sometimes aggravates it ; but what are the exact indications for its use, it is in our present knowledge of the etiology of the disease, impossible to say ; (2) that arsenic should always be given in small doses for a long period after the eruption has disappeared, to prevent a relapse ; (3) that it is never necessary during this course to increase the dose, so as to produce any physiological effect, such as irritation of the eyes.

I now pass to the consideration of another disease which in many of its characteristics is closely allied to psoriasis; I refer to lichen planus. There is some doubt, I know, in this country whether the lichen planus of Erasmus Wilson is the same disease as the lichen ruber of Hebra. The present is not the opportunity for discussing this question, but nevertheless it is important to remember that Hebra in a note to the English translation of his work mentions seven cases of the disease cured by arsenic. I have seen arsenic prescribed with apparently good results in this disease at the Skin Hospital, Blackfriars, but I must admit with the addition of the local application of tar, so that it was doubtful whether the arsenic or the tar did the most good. But a case under my own care is of interest, as no local applications were used.

CASE V.—Mrs. G., a lady in fair health, aged about 50, consulted me last summer. The eruption which was situated on the inner side of the thighs and the outer sides of the fore-arms, consisted of flat-topped papules of a violet colour and slightly scaly. Some of the papules were close together, others scattered. The itching was very severe. I gave her 8 m . of the *Liq. Sodæ Arseniatis* after food, twice a day for a week, then three times a day. After regularly taking the arsenic in this form for one month the eruption began to fade. She still persevered with the medicine for another month, when hardly any trace of the papules was left beyond slight pigmentation. Since that time she has taken occasionally for a period of two or three weeks 4 m . of the same solution, twice a day, and has had no relapse.

Another case came under my notice in the summer of 1878. A young man, aged 22, a shampooer in a Turkish Bath had lichen planus on his thighs and buttocks. Though he believed that the bath had the power to cure any or all diseases of the skin, yet he admitted that he had suffered from his for many months. Under the influence of arsenic in the form of Fowler's solution in 5 m . doses, three times a day, he was entirely cured in a little more than a month. In lichen planus therefore my own conviction is, that arsenic is an invaluable remedy, since in the cases I have tried it I have never seen it fail.

In the acute varieties of eczema arsenic is by all admitted to be injurious, but in some of the chronic forms it is recommended by authors. I have never yet ordered it alone in chronic eczema, probably because I have always felt it would be unjustifiable to abstain from using local treatment at the same time. Under these circumstances it is impossible to speak with any degree of accuracy concerning its action. I must confess I doubt whether arsenic produces any specific effect in this disease, for I have noticed that when the local remedies are used with less energy, even though the medicine be taken regularly, the eruption is sure to be worse.

The value of arsenic in pemphigus has been more recently established, and, in consequence of Mr. Hutchinson's advocacy, it is now a generally recognised remedy in this disease.

In the *Medical Times and Gazette* of February 11th, 1854, cases under the care of the late Mr. Startin are reported, twelve of which were improved by arsenic, though they were not all cured. In the same journal for March 2nd, 1861, seven cases cured by arsenic are mentioned by Mr. Hutchinson; also another case in March, 1872. But it was as late as October, 1875, that Mr. Hutchinson's clinical lecture, entitled, "Can Arsenic Cure Pemphigus?" appeared. In this lecture he gives the notes of twenty-six cases, all of which were successfully treated by arsenic. Several other English observers have had similar experiences, but on the other side it must be said that Hebra in Germany and Tilbury Fox in England do not believe in it as a specific. The latter says at the end of a clinical lecture on pemphigus, "there is no specific for pemphigus. Arsenic is declared to be one, but it often signally fails to cure the disease, and I have seen quinine, in full doses, do much more good." I have myself lately had the opportunity of seeing a case under the care of Dr. Handfield Jones at St. Mary's Hospital, in which arsenic certainly did harm, and which was ultimately cured by quinine. On the other hand, I have seen cases in which the curative action of arsenic was undeniable. I recently read the notes of two such cases before the Harveian Society and I briefly recapitulate them :

CASE VI.—Mrs. S., a married lady, aged 42, first noticed the appearance of bullæ on the abdomen in the August of last year, when she was six months pregnant, and a short time later a few appeared on the right wrist. She was confined on December 12th, and immediately fresh outbreaks of bullæ appeared. I saw her on December 20th in consultation with Mr. Robert Walker, of Maida Vale, when I found the eruption situated on both arms and legs and over the body. The bullæ were arranged symmetrically in marked lines along the course of the cutaneous nerves. We ordered her 10 m. of Pearson's solution together with 10 m. of tincture of iron, to be taken three times a day. After taking this for a month all traces of the disease disappeared, and it has not since relapsed.

CASE VII.—A. L., aged 6, came to St. Mary's Hospital, in August, 1878. Has had constant attacks of pemphigus since the age of three. She had several times been ordered arsenic, but had not persevered regularly with it. Ordered 3 m. of Fowler with $\frac{1}{2}$ ʒ. of Vinum Ferri, twice a day. This she took till the attack subsided, but she constantly returned to the hospital in consequence of fresh outbreaks. In July, 1879, I gave her the arsenic without the iron in 3 m. doses, three times a day. When given alone it seemed to have a more rapid influence on the disease, and since last September she has not had a single relapse.

How arsenic acts in pemphigus is difficult to say. Whether it is through its effects on the blood or by its direct influence on the nervous system, I do not venture to offer a theory. I will now briefly mention one or two other diseases of the skin in which arsenic appears to act with benefit.

Chronic urticaria when unattended by intestinal irritation is greatly relieved and often cured by a course of arsenic.

Though an attack of zoster is not cut short by it, yet the severe pain in the course of the nerve which often lasts a long time after the eruption has disappeared, especially in elderly people, is greatly modified. This is mentioned by Trousseau in his *Clinical Medicine*.

Acne may be benefited by arsenic, but I have no evidence myself to offer on the subject. Dr. Bulkley says, "Of the value of arsenic in certain forms of acne, or rather in certain cases, I can speak with considerable positiveness."¹

Since arsenic has been found to be effectual in such different diseases as psoriasis, pemphigus, and urticaria, I cannot but think with Mr. Hutchinson that they must have some common cause, in spite of the variety of their external manifestations. Whether arsenic acts upon them all equally through the blood, or on the nervous system through the blood, or by some peculiar action on the epidermic cells themselves, cannot be positively determined with our present knowledge.

In conclusion, let me remind you that though arsenic is a valuable remedy in some, it is by no means a universal cure in all, skin diseases; but at the same time there need be no necessity for fear of ill results if the drug be given in moderate doses. It must also be borne in mind that some individuals have an intolerance for arsenic, under which circumstances I should advise that the various preparations be tried before the drug is abandoned; that it should *never* be combined with any other drug, even iron; that it should always be taken during or after food; that it should never be pushed to produce the slightest constitutional symptom; and that it should be continued to prevent relapses for a great length of time after all traces of the disease have disappeared.

I am indebted to Dr. Cheadle, of St. Mary's Hospital, for his kindness in allowing me to publish the notes of the cases that were treated in his clinique.

¹ *The Use and Value of Arsenic in Diseases of the Skin.* New York, 1876, p. 23.