education, perhaps the most important municipal activities are nursing, dispensary service and hospitalization. There may be a difference of opinion about the relative value of these, but the figures given perhaps fairly represent present day views. Certainly hospitalization, which a few years ago was considered of first importance, has been relegated to a secondary place.

It may be asked why the protection of the water supply does not find a place in this discussion. It might perhaps do so, but it is more properly a function of the state department of health to guard water supplies, though some of the larger cities have resources sufficient for independent action. It is rare that a local health officer has any management in water works. It is his important duty to show by his morbidity statistics whether or not the water is above suspicion. So, too, industrial hygiene is omitted because it also is more often, controlled by state officials. A number of newer activities, such as the campaign against cancer, or the degenerative diseases, or the prevention of mental disease, are omitted because it was deemed unwise to let this discussion get too far afield, and better to deal with actualities rather than with possibilities.

THE AIM OF COMMUNITY HEALTH WORK

It is particularly urged that the values here assigned are not final. Even among the most careful students of sanitary science there would doubtless be considerable difference of opinion. Some of these differences would disappear after free discussion. It is partly the purpose of this attempt at valuation to bring out such discussion. Minor changes might be made, but no discussion will ever demonstrate that plumbing inspection is worth more than baby nurses, or that swatting the fly is as effective as abolishing the privy vault. The purpose of the paper is not to enter a special plea for the exact values here presented, but to show the need for perspective in planning health undertakings. If relative values had been carefully considered, the ill balanced health department which was recently brought to my attention would never have grown up. In a city of 100,000, home isolation receives only such time as the health officer can spare from his executive duties, while money is available for six nuisance inspectors. There is a fumigator, but no diagnostic laboratory; three food inspectors, but no baby nurses; and several plumbing inspectors, but no welfare stations or prenatal work, and no Wassermann tests or venereal clinics.

The figures given in the schedule are intended to indicate, though ever so roughly, the real health-conserving value of certain common functions of municipal health departments. It is not intended that either money or time should be apportioned in exactly these ratios. The cost of an adequate hospital for the care of advanced cases of tuberculosis would be many times greater than a good system of dispensaries and follow up nurses. With limited funds, the dispensary and nurse comprise the most economical and effective undertaking.

If the health work of the future is to be successful we must remember first that the old, ill founded idea that health work is to be centered on the environment has been displaced by the modern one, well supported by the data of science, that it is concerned directly with men and women. We would all like to live in spotless, flyless towns. Streets should be clean, yards tidy, houses neat, every garbage can covered, the

cellar whitewashed, never a tin can on a vacant lot, every market white tiled, all bread wrapped in paper, and every laundry immaculate. This is for what we have campaigns and health weeks and for which appropriations can be obtained; but it would have little effect on the death rate. Mothers would continue to feed their babies with pickles and cookies; scarlet fever would spread; diphtheria would claim its toll; people would forget to be vaccinated; schoolboys would strain their eyes at their work; careless syphilitics would become paretics; ill treated poliomyelitis would make cripples; the man with "grip" would swallow tonics and cough medicines until he gave up work and his infant child died of tuberculous meningitis, and lifelong blindness would result from ophthalmia.

Municipal housecleaning will not cure these evils, but education, isolation and good medical care will. Community health work must have a broader outlook. It must do more than cleanse and isolate. It must make use of the best medical knowledge, not by stealing or begging it, but by paying for it, to prevent and cure disease. Many activities must be coordinated. Much has been done. There is more to do. Until there are unlimited money and unlimited talent available, let us earnestly study to do that which pays best.

PRIMROSE DERMATITIS AND ITS RELATION TO ANAPHYLAXIS *

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My interest in this lesion dates back one year or more, during which time I have been able to demonstrate that the primrose plant has been the exciting cause of at least ten cases of dermatitis. Like other American dermatologists I believe that this form of dermatitis is far from uncommon and is on the increase, probably owing to the growing popularity of the plant.

The *Primula obconica* seems to have been imported into Europe from China in 1883. Several years later it made its appearance in America, and since then several dermatologists in this country have made it and its resulting dermatitis the subject of some interesting papers. Foerster,¹ Zeisler² and Montgomery especially have given excellent reports and clinical data of cases under their observation. All of them, however, rely on one article (Nestler's³), for their analysis of the poisonous principle of the plant. Nestler was more or less of a pioneer, and though his observations were good as far as he went, his analysis was most superficial and limited. He did not say that the active poison was an oil, as some American abstractors imply and quote him as saying. He confined his description in this regard to what he termed poisonous material, which he repeats several times in his article, and then

* Read before the Section on Dermatology at the Sixty-Eighth Annual Session of the American Medical Association, New York, June, 1917.

1. Foerster, O. H.: *Primula Dermatitis*, THE JOURNAL A. M. A., Aug. 20, 1910, p. 642.

2. Zeisler, Joseph: *Some Uncommon and Often Unrecognized Forms of Toxic Dermatitis*, THE JOURNAL A. M. A., June 20, 1912, p. 2024.

3. Nestler's *Hautreizende Primelu*, Berlin, 1904.

goes on to mention its solvents. Nestler was under the impression that every one could be poisoned by the primrose, and after many efforts succeeded in producing a dermatitis on himself. He did recognize a varying sensibility of different individuals, however, and suggested its relation to the reaction of anaphylaxis.

In my cases of primrose dermatitis I have been struck by the lack of well-marked isolated areas of intense irritation and vesiculation with the outline of the twig and leaf such as one sees in rhus poisoning. Rather has the irritation been of a more irregular, diffuse, ill-defined, erythematous character. As a result of this apparent difference in the irritability of the two poisons, the sufferers from primrose dermatitis seldom complain of the pain, tenderness and irritation that one sees in rhus poisoning. The subjective symptoms of itching, however, appear, on the other hand, to be much more intense in primrose dermatitis. In addition to this annoying symptom the patient soon begins to show signs of irritability from lack of sleep and rest. To add to the injury a number of my cases had been diagnosed as scabies and so liberally anointed with sulphur ointment as to complicate the picture with a sulphur dermatitis.

There is nothing difficult in the diagnosis. The dermatitis, which is usually limited to the hands, lower arms and the face, strikes one as being entirely artificial. In any vague cutaneous irritation involving the above mentioned locations, one should always inquire if the sufferer handles or comes in contact with flowers. As to be expected, the removal of the source of irritation soon terminates the outbreaks, and a soothing zinc and tragacanth lotion with some such antipruritic as phenol (carbolic acid) or menthol relieves the itching and heals the lesions.

Considering the frequency of primrose dermatitis, it is rather odd that so little has been done in the search for the exciting poison. A comparison of the literature on this lesion with that dealing with rhus poison emphasizes this very clearly. The work of Syme⁴ and Ford⁵ in regard to this form of dermatitis venenata deserves praise, although the work of both has since been refuted. Syme was no doubt dealing with more than a simple glucosid, while Ford's attractive immunity and antitoxin theory built on his idea that glucosids produce specific antibodies has been attacked from several directions. I mention the foregoing experiments in order to point out the difficulties one encounters when one attempts to isolate the active principle of a plant, for we are still without this knowledge regarding rhus.

As I mentioned before, Nestler made no attempt to isolate the active poison in the primrose, while his explanations of the mode of action of what he termed poisonous material rested on the theory of anaphylaxis.

Without any knowledge of the active principle of the plants it is doubly hard to understand their mode of action giving rise to almost any hypothesis, anaphylaxis being the most frequently suggested.

The lack of information on primrose poison can only be compared with the confusion which has arisen over the mode of action of this and other poisons. The known susceptibility and immunity of certain persons to these substances so frequently observed by dermatologists are so imperfectly understood that they are apt to be confused with other reactions.

My excuse, therefore, for this preliminary paper is an effort to clarify two past misconceptions, namely:

1. An effort to further the quest for the active poison of *Primula obconica* and to correct our past ideas that this was an oil.

2. An attempt to clarify and prevent the confusion of the vague term, "cell hypersensitiveness," with that better understood and demonstrable reaction, anaphylaxis.

The question of producing an active and passive anaphylaxis, the investigation of the immunity to the primrose, and an attempt to isolate the active principle of the plant, engaged my attention in the following experiments.

EXPERIMENTS

In order to show that primrose dermatitis does not depend on the general irritability of the skin, a reaction such as one often sees in some patients after the application of almost any degree of traumatic or chemical irritant, I applied a leaf of the plant to the arm of a patient who was in the midst of an attack of urticaria and who not infrequently suffered from an idiopathic eczema. Twelve hours later there was no sign of dermatitis or irritation, and the outline of the leaf on the skin was barely noticeable.

For control skin tests I then made an extract of leaves by grinding them up with sterile bird sand in sterile physiologic sodium chlorid solution. For controls I made a similar extract of lily stems and the blooms of narcissus, two flowers that not infrequently produce dermatitis in susceptible handlers. As an additional control I used sterile bird sand and physiologic sodium chlorid solution. These were separately filtered and superficially inoculated into the arms of several susceptible and normal persons. In no case did I get a reaction in the controls, while the primrose extract produced a severe dermatitis in the susceptible patient which spread quite beyond the area of inoculation.

I then attempted to produce active and passive anaphylaxis in two guinea-pigs by an intraperitoneal injection of a sensitizing salt solution extract of the primrose; in two other pigs the sensitizing injection was composed of serum obtained from one of my susceptible patients. Five days later I reversed the injections, this time giving the serum to the primrose animals and the primrose to the serum animals. In one other animal both the sensitizing and anaphylactic intraperitoneal injections, five days' interval, were of primrose extract. In this work only one of the animals died or showed signs of shock the same day the second injection was given. On repetition of the test on another pig, however, the animal lived three days and died not of shock but from what I believe to have been actual plant poison, an indurated abdominal lesion being present similar to that which Ford found in his animals after injecting rhus extract.

In my efforts to learn the part played by the plant protein in the dermatitis, I prepared an extract of the leaves by grinding them up in sterile bird sand and a 10 per cent. salt solution. This was filtered through paper until the solution was clear and was then made very faintly acid by the addition of a few drops of diluted nitric acid, after which it was placed on ice for twelve hours. At the end of this time the solution was heated just to the boiling point, which caused a rather heavy murky precipitate to form. The mixture was then centrifuged for four minutes and the clear supernatant liquid was pipetted off, leaving the precipitate which gave the Millon test for protein. I inoculated a concentrated extract of this precipitate into two scarified areas on the arms of two of my susceptible patients, who were kept under observation for ten days. During this time neither patient experienced the slightest subjective or objective symptom of a skin reaction.

On another lot of leaves I made an effort to isolate an alkaloid. Two extracts were prepared, one being an acidulated water mixture, the other a mixture of ether, chloroform and alcohol. These were allowed to digest twelve hours, after which they were evaporated to dryness over a sand bath.

4. Syme: Johns Hopkins Thesis, 1906.

5. Ford: Jour. Infect. Dis., 1907, 4, 541.

The residue of both mixtures was tested with Meyer's reagent or potassium mercuric iodid, and showed no evidence of an alkaloid.

I next prepared a decoction of leaves in distilled water which was digested twelve hours. The mixture was then digested six hours with litharge, the precipitate washed to free it from any tannin or coloring matter, then filtered, and the filtrate evaporated without heat. The result of this process was a dry, brownish, deliquescent, coarse powder which under the microscope contained many needle-shaped crystals. A small particle of this powder which was dissolved in sterile water and applied to the right arm of a susceptible patient produced intense edema, irritation, itching, burning and inflammation that extended beyond the area inoculated. This reaction appeared in thirty minutes, increasing in intensity for eight hours, and was well marked thirty-six hours later. This patient did not suffer from dermatographia, and the solution did not cause a reaction in normal individuals. I was justified in considering this substance as a crude glucosid.

Another lot of leaves were extracted with alcohol, let stand three hours and the alcohol distilled off. The residue was extracted with acetone for three hours, after which the mixture was allowed to evaporate spontaneously. The result of this was an oleoresinous mixture which caused an intense irritation when applied to the left arm of the same patient, but which was unlike the glucosid mixture in that it acted slower, was quiescent several hours and not until twelve hours later did the subjective and objective symptoms equal these on the other arm. This oleoresinous compound did not irritate the skin of normal patients, and part of it was frozen in ice and salt to see if it contained a stearopten, such as menthol in peppermint. No such crystal formed. The oleoresin was now digested in alcohol and acetone solution for three days, after which it was filtered and the filtrate evaporated to dryness over a sand bath. After the filtrate had been evaporated to a dark brown powder eliminating any oil, a particle of the powder was dissolved in diluted alcohol and applied to the arm of a susceptible patient. This called forth a severe dermatitis which spread beyond the point of irritation. The active poison of the oleoresin was most probably an acid.

COMMENT

We, therefore, most probably have two active poisons in *Primula obconica*, one obtained by precipitating an extract with litharge and of a glucosid nature, the other a slower acting poison which appears to be an acid constituent of the resin, both, however, independent of any oil.

Many of the cases of dermatitis venenata reported in recent years have been ascribed to anaphylaxis until almost every unusually severe skin and systemic reaction that occurs during the administration or application of a drug is cited as an instance of this disturbance. The frequently seen skin reactions to quinin,⁶ iodine,⁷ iodoform,⁸ mercury and salvarsan have been cited by some as examples of the reaction. One is irresistibly struck by the clinical similarity of these reactions to the mucous membrane and skin hypersensitiveness seen in hay-fever and tuberculosis, both of which are supposed to be examples of anaphylaxis. In the cases of susceptibility of certain individuals to primrose poison we are also dealing with cases of hypersensitiveness which certainly more closely coincide with our conceptions of true anaphylaxis than many of the reactions cited above. The plant at least contains a proteinlike substance which in this respect, unlike iodine, mercury, salvarsan and other chemicals, fulfils one of the rudimentary requirements for a true specific anaphylaxis.

I have shown, however, that the skin irritability is not due to protein sensitization; therefore the reaction which may superficially resemble an anaphylactic reaction in reality has no direct relation to it.

In other words, we have gone far astray in our efforts to explain drug hypersensitiveness, and in our haste have distorted the theory of the reaction of anaphylaxis in order to try to make it explain a totally different phenomenon. Some such confusion resulted before the terms contagion and infection were better understood and more clearly defined.

It seems timely, therefore, to sound a word of warning against this misnomenclature and to recall to mind that while anaphylaxis is not entirely understood there are certain fundamental requisites necessary in order to produce a true reaction.

Richet⁹ was one of the first to suggest that anaphylaxis depended on the previous injection into or the presence in the body of some sensitizing substance or antigen. Another demonstrated fact is that such an exciting antigenic substance must necessarily be of a protein nature. The suggestion that pure lipoids, unmixed with proteins, cause antibodies has been refuted by Miller,¹⁰ Richet, Thiels,¹¹ and others. Zeiler¹² questions the validity of experiments that tend to show that certain chemicals combine with the proteins of the blood or tissues to form a foreign protein and cause hypersensitiveness. Zinsser¹³ says that to date not a single exception to this has been found, nor is any to be expected. The sole contestor of this being Ford,¹⁴ who could not have produced antibodies to his glucosid for the reason that he was not working with a pure glucosid but a compound substance. Von Adelung¹⁵ was unable to duplicate Ford's results, while Stevens and Warren¹⁶ and MacNair¹⁷ claim that the substance he was dealing with was not a true glucosid or a compound of rhamnose, gallic acid and fisetin, but an unknown compound. The recent report by Novy and DeKruif,¹⁸ which tends to show that anaphylactic shock can be produced in an agar sensitized animal by a second injection of agar or even distilled water, is another effort to prove the nonspecificity of the reaction. A somewhat similar line of reasoning regarding Witte's peptone was advanced by Biedel and Kraus.¹⁹ Different lots of this substance, however, were afterward found to contain toxic and nontoxic qualities which Brieger²⁰ says accounts for the conflicting anaphylactic results. The origin of both Witte's peptone and agar, of course, throw more doubt on such reports. Novy and DeKruif in comparing agar with Witte's peptone apparently do not recognize this.

Zinsser states that the analogy between cases of drug hypersensitiveness and the phenomenon we classify as anaphylaxis is a striking one, but he agrees with Friedman²¹ that they depend on quite different processes. For instance, in drug hypersensitiveness, increased and continued administration or application

6. Boerner, Fred: A Skin Reaction to Quinin, THE JOURNAL A. M. A., March 24, 1917, p. 907.
7. Friedberger: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1912, 12, 241.
8. Block: Ztschr. f. exper. Path. u. Therap., 1911, 9, 509.

9. Richet: Compt. rend. Soc. de biol., 1898.
10. Miller: Jour. Path. and Bacteriol., 1913, 17, 249.
11. Thiels: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1913, 16, 160.
12. Zeiler: München. med. Wehnschr., 1912, 59, 401.
13. Zinsser: Infection and Resistance, p. 307.
14. Ford: Jour. Infect. Dis., 1907, 4, 551.
15. Von Adelung, Edward: An Experimental Study of Poison Oak, Arch. Int. Med., February, 1913, p. 148.
16. Warren: Jour. Am. Pharm. Assn., 1907, 80, 518.
17. MacNair: Jour. Infect. Dis., 1917, 20, 485.
18. Novy, F. G., and DeKruif, P. H.: Anaphylatoxin and Anaphylaxis, THE JOURNAL A. M. A., May 26, 1917, p. 1524.
19. Biedel and Kraus: Wien. klin. Wehnschr., 1909, No. 11.
20. Brieger: "Die Ptomaine," 1, p. 14, and Hammersten, Physiological Chemistry.
21. Friedman, quoted by Zinsser: Infection and Resistance, p. 408.

of the drug increases the reaction, while in true anaphylaxis the reaction, if not leading to sudden death, decreases and finally ceases with continued administration of the antigen. Also in drug sensitization we are dealing with a primary poison against which in the reacting animal a neutralizing substance is formed, a condition quite different from that seen in hypersusceptibility against primarily harmless proteins. Zinsser further states that in true anaphylaxis not only are specific antibodies present in the blood, but the production of passive anaphylaxis in animals shows that this antibody, if originating and residing in the fixed cells of the body, must necessarily also circulate in the blood stream.

In primrose dermatitis, although an example of hypersensitiveness to drugs and chemicals, the requisites of anaphylaxis are not fulfilled; and while superficially similar, the confounding of the two quite different processes is incorrect. As I have shown in primrose dermatitis, it is not possible to sensitize an animal either actively or passively with the poison of the plant, that no specific amboceptors are present in the blood of susceptible patients, that the protein of the plant has nothing to do with the reaction, and that this being the case it is as impossible to produce an antitoxin to the poison of the plant as it is to produce a condition of artificial specific sensitization.

The cases of skin "anaphylaxis" above cited seem to be examples of cellular or epithelial irritability, and being so are considered symptomatic expressions of local cell hypersensitiveness established spontaneously and not dependent on toxins or any immunologic process. The antibodies, if concerned in the reaction, are present only in the sensitive cells, the protoplasm of which, Block showed, has an increased affinity for that particular poison.

I did not attempt to produce a protein from the bloom of the plant, as it has been proved that the active poison is secreted from glandular hairs of the leaves, and that poison has no relation to a protein for two reasons: 1. A protein made from the leaves and stem causes no skin reaction in hypersensitive patients. 2. The poison is soluble and can be extracted by absolute alcohol, which does not dissolve proteins.

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ABSTRACT OF DISCUSSION

DR. PHILIP KILROY, Springfield, Mass.: While this paper needs no discussion, it should not be let pass without an expression of gratitude to the author. It is a demonstrative paper which should get rid of the tendency to give mystical explanations of very commonplace facts. The tendency to look for a mystical anaphylactic reaction has gone so far that I expect soon to be told that the sore caused by a burn is the anaphylaxis of some previous burn. Those of us who have been stung by a nettle or a wasp know that the result is only the irritation of the skin by an irritating substance. That the result is greater in one person than in another requires no explanation other than that assigned by Dr. Simpson. Some people will get a violent dermatitis from a sun exposure that will not even tan the skin of others.

DR. WALTER J. HEIMANN, New York: I regret that Dr. Simpson did not carry his work to what seems to me to be completion. His work has been confined to leaves and stems, while I think he should have done something on pollen, and perhaps on petals. I believe as he pursues his investigation he will take up these features. In using the word "hypersusceptible" I think Dr. Simpson has weakened his own case. Hypersusceptibility we have assumed to be due to previous exposure to an alien protein. What Dr. Simpson means, I believe, is an ordinary susceptibility.

In any kind of chemical dermatitis the majority of people do not react to the pathologic agent. Those who react are considered susceptible, and the others are not considered susceptible. Those who react very strongly might be considered hypersusceptible. In spite of Dr. Simpson's endeavor to be clear, his use of the word is unhappy, as it refers to allergic phenomena, which in his experiments are not present.

DR. C. AUGUSTUS SIMPSON, Washington, D. C.: I undertook this work in order to clear up the confusion which has resulted from the reports of iodine and quinine eruptions, which are cited as examples of anaphylaxis. If we understand that true anaphylaxis depends on a presensitization of the individual with a protein, then it is obviously impossible for a chemical, alkaloid or a glucoside to perform this function.

In regard to the question asked by Dr. Heimann, I will say that I did not work with the pollen of the flower for two reasons: First, the poison that causes the dermatitis does not reside in the flower or pollen, but is a product of the glandular hairs of the leaves; second, the poison can be extracted from the leaves by digesting them in absolute alcohol, which does not dissolve or extract proteins. In view of the work of Wells and Osborne on plant proteins, I have no doubt that a true protein could be extracted which would naturally produce a true anaphylactic reaction in animals. This, however, is not the object of this paper. I have tried to show that the well-known specific susceptibility to the primrose (dermatitis) has no relation to anaphylaxis.

THE PREVENTION OF ENDEMIC TYPHUS IN CALIFORNIA

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During early civilization, typhus fever was the predominant disease, whereas typhoid was of secondary prevalence. With the advancement of civilization, however, and the adoption of personal hygiene, typhus has receded. On the other hand, with the increasing density of population and the resulting contamination of food and water supplies, typhoid has become pandemic. Except under war conditions, epidemics of typhus are now rare, although the disease is endemic on the Great Plateau of Mexico, in parts of Ireland, France and Russia, in Algeria, Egypt, Hungary and certain provinces of the Balkan States. The recent Serbian epidemic, still fresh in our memories, is an instance of war-borne typhus.

TYPHUS IN EASTERN UNITED STATES

The three chief visitations of this disease to the United States occurred in New York in 1881 and 1882, and again in 1892 and 1893, and in Philadelphia in 1883. Sporadic cases have not been uncommon in our seaports. Furthermore, it has recently been shown that the syndrome known as Brill's disease is in reality typhus fever. In 1909, Dr. Nathan E. Brill reported 200 cases of an acute infectious disease of unknown origin observed by him in the wards of the Mount Sinai Hospital. He had previously reported seventeen cases of the same disease. The important phases of the disease are thus summarized by Brill:¹

An acute infectious disease of unknown origin and of unknown pathology characterized by a short incubation period

1. Brill, Nathan E.: An Acute Infectious Disease of Unknown Origin: A Clinical Study Based on 221 Cases, *Am. Jour. Med. Sc.*, April, 1910.