Original Articles.

VACCINATION EFFICIENTLY PERFORMED.*

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One hundred fifteen years ago, Dr. Edward Jenner published "An Inquiry into the Variolae Vaccinae," and showed that vaccinal inoculation protected the human organism against smallpox. Subsequent experience has substantiated his observation, and variola no longer prevails in countries where vaccination is regularly and efficiently performed.

Where this important sanitary measure is irregularly practiced, as in the United States, the disease recurs at intervals, less severe than in former times, but nevertheless, with considerable mortality and at large cost to the community; as examples, in 1900, the cost of municipal control of 171 cases of smallpox to the city of New Bedford was \$23,000; in the spring of this present year, a few cases in our city cost about \$10,000.

Smallpox has prevailed in this part of Bristol County nearly every year since 1900, limited almost entirely to people who have come from that part of Canada called Acadia, and who are without exception, unvaccinated. As their route of entrance is by rail they are not subject to the measures imposed at points of entry along the coast. Their children attend parochial schools and are not amenable to our statutory vaccinal requirement. The exceptions have been persons whose protection had long since run out.

The progress of preventing smallpox in a country like ours where vaccination is optional after the age of entrance to public schools, is rendered difficult by persons who would have others believe that the procedure is useless, harmful or fatal. Organized opposition to vaccination appears to have had its inception in Jenner's England, where compulsory vaccination may now be evaded by a declaration of conscience. An English gentleman could offer no other explanation for this opposition than the well known love of the English to protest against law. Physicians, unburdened by knowledge and unrestrained by conscience, join the ranks, to sell exemption certificates, or with a keen eye to business, as the leading Boston anti-vaccinist, who specializes in a line of "medical practice" which he cannot advertise in this state through legislative restriction.

So long as the opponents confine their arguments to theories, no harm is done. Through a

publicity service they keep informed of all illnesses and deaths which by even the wildest flight of fancy could be ascribed to vaccination. Their effective arguments against vaccination are based on the severe sore arms and loss of wage subsequent to vaccination improperly performed in factories and tenement houses in time of epidemics. We can more fully appreciate the statement of an anti-vaccinist candidate for the legislature, this fall, who said: "I expect an increased vote on account of the many vaccinations done in the mills." The real danger from this agitation is that the legislative campaign may be successful and annul our only existing law on the subject, for our legislators may be moved by arguments based on prejudice and falsehood as by truth.

The manner of combatting opposition to vaccination is to vaccinate well, and I would predict that twenty years of efficient vaccination in this state would silence all opposition.

Vaccinia is a disease communicable by inoculation, pursuing a definite course, and conferring immunity against smallpox for a varying period. Peculiar resistance may be manifested according to previous diseases or vaccinations, to innate or inherited characters, or to a number of intercurrent circumstances. In people previously unvaccinated, the eruption begins seventy-two hours after inoculation as a papule, and is fully apparent on the fifth day as a vesicle; on the seventh it has reached maturity, when it is a flat umbilicated vesicle surrounded by a rose red areola. This is the positive and unvarying picture of a successful primary vaccination, "A section of a pearl on a rose leaf." The celebrated wit, Charles James Fox, meeting Dr. Jenner in a large gathering said to him, "Tell me, Dr. Jenner, what is your vaccination like?" Exactly like a section of a pearl on a rose leaf," was the reply.

Crusting of the vesicle begins about the eleventh day and the crust is exfoliated from the twenty-first to the twenty-eighth day, leaving an indelible and characteristic scar, at first red, bleaching with time to white, sharply defined, with distinct pitting.

The "raspberry excrecence" is not infrequently seen three to seven days after inoculation. It becomes red, hard, and naevoid and may persist for months, leaving no scar, and conferring no protection. Its occurrence demands another operation.

THE TECHNIQUE OF VACCINATION.

To learn the technique of authoritative sources, a questionnaire was sent to the four medical schools in Massachusetts. The following replies were received:

Harvard, informant, Dr. M. J. Rosenau. Vaccination is taught practically and theoretically. Technique, incision; sharp needle—really a scratch. Vaccine, that licensed by the govern-

* Read at a meeting of the South Bristol District Medical Society, Fall River, November 13, 1913.

ment. Each student vaccinates one or more persons. Studies progress of the take to scar formation. Two insertions are made, each about three quarters of an inch long and about one inch apart. Students also visit the vaccine farm and see the propagation of the virus. "I spend perhaps, all told, six hours upon the subject of vaccination."

Dr. Rosenau is emphatic for incision and says that scarification is discouraged as dangerous; that it is forbidden by law in Germany.

Tufts, informant, Dr. W. R. P. Emerson. Taught practically at the clinic. Technique, scarify with needle; apply a drop of vaccine and allow to dry; gauze and adhesive tape dressing. Two scarifications are made. Mass. state vaccine is advised. Two insertions are made, $\frac{1}{4}$ in. in diameter, $1\frac{1}{2}$ inch apart. Patients return in one week; students see them in all stages.

Similar inquiries with an additional question on revaccination were sent to the Surgeon Generals of the War, and the Navy Department, and Public Health Service with these responses:

War Department, informant, Capt. Albert G. Love. Technique: area cleansed with green soap then alcohol; dried with cotton or gauze; abrasions made by scraping or scratching on the selected area. Abrasions, three, one inch apart. Instrument ivory point or sterile scalped. Dressing, sterile gauze, preferably, sometimes vaccine shield. Dressing changed as often as necessary to keep it clean and in good condition; if the vaccination is successful the second dressing is always sterile gauze. Source of vaccine, large manufacturers of the country. If primary vaccination fails, the process is repeated in a reasonable time and is again repeated if the second attempt fails. In practice, practically all men upon enlistment and re-enlistment are vaccinated.

Navy Department, Surgeon General C. F. Stokes. No uniform technique is prescribed. Vaccine points usually employed; source varies. All recruits are vaccinated and repeated until the medical officer is convinced that the person is protected. Crews of ships are inspected from time to time for vaccination and in the event of an epidemic all persons are vaccinated.

Public Health Service, Asst. Surgeon General J. W. Kerr. "There is a general agreement that the best method of vaccination is the simplest and in this respect scarification has a distinct advantage; the use of vaccination shields should be avoided and aseptic bandages used."

This department furnishes the information that government licenses for propagation of vaccines have been issued to nine manufacturers.

Absolute cleanliness with a minimum of injury to the skin with aseptic protection during the development of the vesicle until scar formation, are essential to a proper vaccination. Rosenau¹ writes: "The operation may be compared to the transfer of a culture in a bacteriological laboratory. Precisely similar precautions to pre-

vent contamination must be used in both cases. Vaccination must be considered as a surgical problem. No person unfamiliar with surgical cleanliness should be permitted to perform this "little" operation. "The scar should not be regarded as a deformity; to the sanitarian a typical vaccine scar is a sanitary dimple."

Dr. William Osler² refuses to vaccinate on the leg unless the patient will agree to remain in bed during the course of the vaccination.

After a discouraging experience with leg vaccination, I now refuse to vaccinate unless the deltoid site be agreed upon. Here inspection is easy, trauma is less likely to occur, and if infection follows, it runs a milder course.

I mention the shield only to condemn it. It is bulky, and invites violence. It often becomes loosened and scrapes the vesicle; it prevents radiation and produces the effects of a poultice; and among the poor it is loaned about to different children, often heavily coated with purulent secretions.

The arm having been dressed after the operation, the patient should return in seven days, or earlier, should constitutional or severe local symptoms appear. The dressing should be removed and the physician look for "a section of a pearl on a rose leaf." If present a bland ointment with sterile dressing is applied, and in this manner the lesion is cared for until it is dry. If the vesicle has not matured and a mere scratch remain, if we revaccinate the patient in a week or two we may expect to see at the site of the first attempt an awaking which aroused and runs a short course synchronously with the second inoculation, through local anaphylaxis.

When the scar is seen then may a certificate of successful vaccination be given, and not until then. A vaccinated patient should be under the observation and guidance of the vaccinator until all chance of coccogenous infection is past.

Three illustrative cases.

CASE 1. B. K., aged four; vaccinated in the last week of May, 1912; tetanic convulsions appeared June 15; brought to hospital on 16, very dirty, with foul vaccinal wound; no sign of having worn protective dressing; died on 17; death certificate signed "Tetanus following vaccination."

CASE 2. Mary B. March 17, 1913, her four-year-old son was found ill with smallpox; she was "vaccinated" (her arm was scratched with a point), and she accompanied the little son to the hospital to care for him; she developed a severe cellulitis from the point of "vaccination" involving the whole arm, and on April 5 became ill with smallpox.

CASE 3. E. B., thirty years old; four times he has been vaccinated in cotton mills during four epidemics, lost altogether eleven weeks' work, convalescing; his mother has smallpox of fourteen days' duration; the son became ill today (Aug. 25, 1913).

In the first case, B. K., it seems that the most elementary attention to cleanliness could have prevented the tragic sequence.

The same can be said of M. B. The coccogenous infection killed the vaccine bodies, and variculous infection followed.

E. B. has my heartiest sympathy, in that risking his life, in four vaccinations in a dusty mill, all unsuccessful, with eleven weeks of suffering and loss of wage, he did not acquire immunity; I rejoice that he survived and congratulate him on finally achieving smallpox, which will put him beyond the reach of factory vaccinators in the future. You of Fall River appreciate how poorly factory vaccination is done, and the invalidism that follows. The bad results are interpreted by the laity as evidences of the true vaccinal course, and as the operator does not see the patient a second time, the unhappy victim goes on his way to expose himself perhaps recklessly to infection. If he have variola, his experience is capitalized by the opponents of vaccination.

In Dr. Jenner's time it was believed that the immunity conferred by vaccination lasted through life; subsequent observation has shown this to be within wide ranges.

Theobald Smith³ has recently explained the variation in this way: "It is now well known that vaccination protects only for a limited period. The body forced to produce a variety of antibodies under pressure is not likely to continue such manufacture indefinitely after the stimulus is removed. Nature is not lavish in producing unused commodities. Animals naturally immune do not carry an appreciable quantity of immune bodies about. Their protection is guaranteed by more economical processes of life of which we know as yet very little. The length of time elapsing between vaccination and exposure, therefore, is of great significance in the success or failure of protection. . . . There is the principle of active immunization itself which must be carefully kept before us. When we discuss vaccination as a preventive, we mostly fail to take into account that we are asking something of the individual to be vaccinated, rather than giving him something. We are asking his tissues to go through the preliminary process of training to meet some future emergency. Vaccination is a process of education for being better prepared to meet an invasion at once, before it has grown to any dimensions. We have no reason to suppose that the characteristics of the body will be materially and permanently altered by such a training. If the body is below par in the supplying of immune bodies, it is likely to remain so, despite the vaccination. Of two individuals treated preventively alike, one may be able to cope successfully with a large or more virulent dose than the other. The plane of immunity of both is raised by vaccination, but unequally so, and in proportion to their natural endowments."

REVACCINATION.

Kitasato⁴, 931 revaccinations.

After 1 year	14	per	cent.	successful
" 2 years	33	"	"	"
" 3 "	47	"	"	"
" 4 "	57	"	"	"
" 5 "	51	"	"	"
" 6 "	64	"	"	"
" 7 "	73	"	"	"
" 8 "	80	"	"	"
" 9 "	85	"	"	"
" 10 "	89	"	"	"

Lescohier⁵ in a series of 251 revaccinations obtained practically the same results. Millard⁶ states that the government report of the German Confederacy shows from 91 to 93% successful revaccinations after ten years. It is manifest that protection is exhausted in one half of all people five years after inoculation and in the rest at the latest about the tenth year. The power to modify the disease continues into later life.

Vaccination is clearly indicated at five or at the latest, ten year intervals. The results of periodic vaccinations support this statement. A recent writer estimated that the unvaccinated in England was rapidly increasing, due to parents availing themselves of the "conscience clause" and that a few years would prepare the country for a wide spread epidemic. Since our state law requires vaccination only as a requirement on entering school, and except on possible exposure, no revaccination is done, it is evident that our cities are practically unprotected. True, our immigrants before mentioned have borne the burden, so far being virgin soil for that seed. The devaccinated have some immunity and have shown the resistance.

The local response to revaccination varies in proportion to the amount of ferment remaining from the reaction induced by the primary inoculation. We may observe the typical primary picture, showing complete loss of immunity; or a rapid course of a few days; or a small papule or transient erythema may be the only sign, and leaving no scar.

Dr. Jenner and his immediate successors made one puncture or incision. In seeking to prolong immunity when smallpox among the vaccinated occurred multiple incisions were employed, and have been generally employed throughout Europe ever since. Bonn⁷, Immermann⁷, Pfeiffer⁷, Seaton⁸, Simon⁸, Roger⁹ and Cory¹⁰ agree that a constant relation exists between the number of scars and the degree of immunity afforded.

The figures of Marson are familiar:

	Cases.	Deaths.	Mort. %
Unvaccinated	2654	996	37.2
Stated to be vaccinated but			
with no scar	290	74	25.5
One scar	1357	125	9.2
Two scars	888	53	5.9
Three scars	274	10	3.6
Four or more scars	268	3	1.1

Rosenau in his recent text book says: "The number of incisions has an important bearing on the probability of the take as well as protection; it is not wise to depend on one; the relation to the number of vesicles and the amount of reaction to the degree and length of immunity has not been worked out."

American vaccinators generally have been content with one puncture and regard additional punctures as assurances of a successful take.

Size of Scar to Immunity: Russell, Marson and Gayton are quoted by Hanna¹¹ as believing that the quality and size of the scar area have an important bearing on the amount and extent of the eruption and consequently on the severity of the disease. Corlett¹² believes the protection to be proportional to the size of the scar.

Hanna in a study of the scar area in 943 revaccinated persons who developed smallpox in Liverpool drew the same conclusions.

These phases seemed to me to be of unusual interest and well worth further investigation. Marson's figures, and the continued European practice of multiple incisions with the low incidence of smallpox would warrant further study. For this purpose these questions were submitted to two biologists and two clinicians:

Is greater vaccinal immunity conferred by multiple incisions?

Is the degree of resulting immunity to be estimated by the diameter of the scar?

Dr. Simon Flexner replied that he was unable to answer the questions.

Dr. Alvah H. Doty answered: "I am entirely satisfied that multiple punctures are unnecessary and that all the immunity that vaccination affords can be obtained by a single scarification properly performed with tested virus. This practice has been followed by the Department of Health of New York with the most satisfactory results and is accepted throughout the U. S. and is becoming generally accepted throughout Europe.

"I do not believe that the degree of immunity can be estimated by the diameter of the scar or scars provided the latter are of reasonable size and typical. . . I believe it is unnecessary and a mistake to make the scarification too large. The success of the operation depending rather on the character of the virus and having it well rubbed in without the too free escape of blood."

Dr. Theobald Smith: "I would say that immunity is strengthened in proportion to the number of vaccinal punctures. This fact has been determined by observation. I am not sure that we can explain it on the basis of our present knowledge of immunity.

"As regards the size of the scar, a number of factors may enter. The pustule may have been disturbed; the scab may have been torn off and the ulcer increased in size. It is also possible that when two vesicles are close together they may fuse and thereby increase the size of the scar. The final scar may be increased by injury

due to secondary infection of the vesicle. In any of these cases, it would be difficult to say how far the immunity had been influenced."

Dr. John H. McCollom: "It seems to me that a longer immunity is conferred by making three scarifications. . . I can give you no definite figures on the matter, but after a very careful study of the whole subject, I am thoroughly convinced that there should always be three insertions of virus when a person is vaccinated. The experience of the German Empire is confirmatory. It is the custom there in many of the cities to vaccinate a person on each arm and to make three incisions. I never yet have seen a person with six scarifications, no matter how long a time had elapsed since vaccination was performed, have smallpox.

"In regard to your second question so far as the appearance of the scar is concerned, that is a question that cannot be definitely answered. Three reasonably good scars is a fairly sure indication of protection, but the mistake must not be made of thinking that because a person has a large scar, it is an indication of successful vaccination." Here follows the description of the scar resulting from a negative take and the letter concludes thus: "Physicians and the public must be carefully taught that vaccination is not such a simple matter; that it requires an expert to state definitely whether vaccination has been successful or not."

Vaccine: The State Board of Health has propagated and issued vaccine to the physicians of the state since 1904; in the years 1904-1912, 449,378 tubes were dispensed, and from Dec. 1, 1912 to Oct. 14, 1913, 102,942 tubes; a few complaints have been made, which on investigation have always been found to be based on errors of technique rather than to defects in the vaccine.

For more than a year I have used this vaccine exclusively on all patients and on myself. I have been able to get a take in every primary vaccination on the first trial with slight constitutional reaction.

CONCLUSIONS.

Vaccination is a surgical procedure; hence demands surgical asepsis.

The patient must be under the supervision of the physician until scar formation, when a certificate may be given.

He should be told that his immunity is for a limited time; if liable to exposure to be revaccinated.

As those countries are most free from smallpox where vaccination is regularly imposed, a revaccination of all persons in a state should be required at stated intervals.

Vaccination should be done with a minimum of trauma.

The experience of most observers warrants two or more incisions.

Vaccination efficiently performed protects against smallpox.

Vaccination efficiently performed silences opposition.

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CORRELATIONS OF CEREBRO-SPINAL FLUID EXAMINATIONS WITH PSYCHIATRIC DIAGNOSES. A STUDY OF 140 CASES.*

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THE scarcity of actual correlations between findings in the cerebrospinal fluid and psychiatric diagnoses in any considerable series of cases makes of value a review of the results in a large hospital for the insane. The object of the present study has been to discover of how much value examinations of the cerebrospinal fluid have been in changing, confirming or making more accurate the psychiatric diagnoses. The focal points of interest in this connection are, of course, the diagnosis of paresis and of cerebral syphilis. It may be said in a general way that this review has shown that paresis is not actually as frequent as would appear from purely clinical examination, and that the cases which are most likely to be mistaken for it are Korsakow's psychosis, cerebral arteriosclerosis and cerebral syphilis.

The method† adopted in this hospital is to have a Wassermann test made on the serum of each new patient unless this has been recently done in another institution. If the result is positive, and also in negative cases in which the symptoms or signs are suggestive, the cerebro-

spinal fluid is examined for the Wassermann reaction, cytology and globulin content. Similar tests are being carried out also on old patients as rapidly as possible. The Wassermann reactions are done at the laboratory of serum diagnosis of the Harvard Medical School. The remainder of the examination, except the differential count, may be done by a non-medical laboratory assistant, who is familiar with blood counting and elementary chemistry.¹

Statistics. The period chosen for study was the year ending Jan. 1, 1914. During this time 626 Wassermann reactions have been done on the sera of 618 patients, 445 of whom were admitted in 1913, and 173 before that time. The 1913 admissions form an unselected group from which may be estimated the frequency of syphilis in patients admitted to this hospital. The results are:

Wassermann reaction in the serum positive in 80 cases (18%).

Wassermann reaction in the serum negative in 362 cases (81.3%).

Wassermann reaction in the serum doubtful in 3 cases (0.7%).

This percentage of positive sera is lower than that of Paine,² who in his study of 200 consecutive admissions to the Danvers State Hospital found 24.5% positive.

During the year ending Jan. 1, 1914, 142 cerebro-spinal fluids from 140 patients have been examined for the Wassermann reaction. Of the 76 specimens from 1913 admissions, 33 (43.4%) gave a positive, 43 (56.6%) a negative result.

CLASSIFICATION.

We have used as a basis of our grouping of the fluids for study, the diagnosis given by the physician on the card accompanying the specimen to the laboratory, combined with the serological and cytological findings in the fluid. It must be emphasized in the beginning that in many instances this clinical diagnosis represents not the final, but the provisional diagnosis after the routine physical and mental examination, and is made with the reservation that it may be changed by the serological and cytological evidence.

* Worcester State Hospital Contribution No. 20 (1914. 1).

† METHOD.—The following is the method adopted for the Wassermann reaction: "Three antigens differing in fixing power are used for each specimen. Two are from human hearts and are reinforced with cholesterol; the third is the alcoholic extract from a fetal syphilitic liver. The complement, which is ten per cent. guinea-pigs' serum, is titrated daily to determine the unit; two units are used in the test. The amboceptor is titrated against .5 cc. of 10 per cent. guinea-pigs' complement in order to determine the amboceptor unit. Two units are used in the test. The amboceptor value is re-determined before each test. Washed sheep's corpuscles, are made up with normal salt solution to 5 per cent. suspension. Five-tenths of a cubic centimeter is used."

"The following controls are used for each test: a strongly positive syphilitic serum; a weakly positive serum; a negative serum, and tubes containing double the amount of each antigen."

"All doubtful cases are repeated at the next test, and if there is sufficient serum, varying amounts of antigen and serum are used, so that the resulting test rarely gives a doubtful result."

The Noguchi test for globulin was used, and was performed as

follows: to 0.2 cc. of cerebro-spinal fluid, 0.5 cc. of a 10 per cent. solution of butyric acid in normal salt solution is added, and the mixture heated to boiling. One-half a cc. of normal sodium hydroxide solution is added, and the tube boiled slightly. A flocculent precipitate within 15 minutes indicates a positive result.

For the cell count in the fresh fluid, 0.1 cc. of 3 per cent. acetic acid and 1 cc. of cerebro-spinal fluid (well shaken) are mixed in a white blood counter, and ten fields are counted.

The sediment is prepared for differential counting by the Alzheimer method, i.e. by adding to 3 or 4 cc. of cerebro-spinal fluid twice its volume of 95 per cent. alcohol, centrifuging for one hour at high speed, and hardening the precipitate in absolute alcohol, followed by absolute alcohol and ether. The coagulum is removed from the centrifuge tube with a pointed glass rod; embedded in celloidin; cut in sections 7 m. thick, and stained with pyronin-methyl-green. In fluids showing a high or moderate pleocytosis 200 cells were counted. When cells were present in normal or slightly increased numbers, several sections (5 to 8) were gone over carefully and the actual number of each variety of cell present was stated.