

DURATION AND DEGREE OF IMMUNITY AGAINST SMALLPOX CONFERRED BY INFANTILE VACCINATION

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THE question of duration and degree of immunity against smallpox conferred by primary or infantile vaccination is certainly of very great interest, from both the theoretical and practical points of view. The importance and advantages of infantile vaccination are almost universally recognized and admitted. In most countries vaccination of infants is enforced to a greater or smaller extent by legislation or otherwise. Though this measure in protecting one against smallpox is rather extensively adopted, it is to be noted that infantile vaccination does not protect an individual permanently. The immunity conferred is only for a limited period. Experiments and experience have shown that the protection it affords, though absolute for some years, gradually wears off almost completely. It is therefore in view of this fact that though in vaccination we have had a most effective weapon against smallpox for the last 150 years or so, since Jenner discovered it in 1796, this epidemic disease still prevails throughout in some form or other. It must be admitted, however, that though primary vaccination alone does not afford full protection, it has even then a considerable effect against the epidemics of this disease. The great fall of smallpox morbidity throughout the world, as compared to the pre-vaccination days, is certainly to be attributed to the vaccination in general. To conquer smallpox effectively and protect an individual permanently against it, both primary or infantile vaccination and re-vaccinations at a proper period or interval are absolutely necessary. This point is fully realized by some countries in which both these are compulsorily enforced. But the periods fixed for the latter vary considerably. There appears to be a complete lack of uniformity about it, though it is generally believed that primary vaccination protects one for seven years.

Practices in various countries

In Germany, vaccination of infants is compulsory and re-vaccination is enforced as a rule on entering school and at the time of conscription,

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operation. In operable cases, or cases treated by radium, hypogastric neurectomy is a safeguard against future pain should there be a recurrence. The surgery of the sympathetic system is at present only that of mutilation or extirpation; perhaps, as knowledge increases, it too will advance to something constructive, and become more physiological and less strictly anatomical in its principles.

but as a whole it is obligatory at the 12th year. In France, infantile vaccination during the first year of life and re-vaccination during the 11th and 21st years are compulsory. The same legislation as in France is in force in the Union of Soviet Republics. In Italy, vaccination in the second six months following birth and re-vaccination during the 10th year is compulsory. In Portugal, both vaccination and re-vaccination are compulsory and the period of immunity definitely specified by the law is seven years. In Japan, re-vaccinations are obligatory every five years. There is similar legislation in all countries where infantile vaccinations and re-vaccinations are enforced by law. In England, however, the vaccination law is so drafted with a 'conscientious objector's' clause, which practically nullifies the obligation to be vaccinated, resulting in a large number of people, reckoned to be at present nearly 50 per cent of children born, remaining completely unprotected against smallpox. In India, the Vaccination Act was promulgated by the Government of India in 1880. This was amended in 1909, but still it does not enforce compulsory vaccination for the whole of India. There are however several cities and towns where infantile vaccination is made compulsory. But nowhere in India is regular re-vaccination at any period made compulsory by law. It will be therefore seen that there is extensive divergence of views held throughout the world on this important point.

Even scientific observers and experts on the subject seem to hold equally divergent views. Winsch contends that re-vaccination at 12 years is generally as positive as infantile vaccination. Gins, of Berlin, on the other hand states that under similar conditions he found only 20 per cent to show typical primary vaccination results and four-fifths of re-vaccinees to be sufficiently protected against smallpox. Kitisato, in Japan, found that nearly 13 per cent can be successfully re-vaccinated at the end of one year and nearly 64 per cent at the end of six years. Weil reported about 72 per cent successful re-vaccinations at seven years' interval. Both these probably have included in their successful re-vaccination also the accelerated reactions. Sergeant and Trener in 1932 analysed about 300 cases of re-vaccination. Most of these were aged two and three years, some 250 of them with scars of previous vaccinations. They found that their results were similar, whether the age periods taken were one year, 10 years or under, and over 30 years, successful takes being recorded in about two-thirds of the cases. Therefore it has been concluded that immunity is lost in about two-thirds of cases within three years. Under these circumstances it might be quite reasonable to inquire into the possible causes of these divergent views and findings by various observers. One would feel inclined to attribute this

possibly to the fact that various factors as regards vaccination and re-vaccination have been considered or accounted for from different points of view.

It is universally admitted that apart from the important factor of individual susceptibility, various others are also to be considered, specially:—(a) Technique and extent of vaccination incisions and vesiculations obtained. (b) The quality and potency of lymph used. It is common knowledge that most of these factors vary to a great extent in various countries. It is a recognized fact that the results and the immunity both in regard to degree and duration is proportional not only to the number and size of incisions made, to the extent and quality of vesicles obtained, but also to the quality and potency of lymphs used. The International Committee on Small-pox and Vaccination of the Health Organization of the League of Nations in their report of August 1928 state:—'The best lymphs may have the most different results, according to the manner in which they are used. Next to individual susceptibility, one of the most important factors is the vaccination technique'. It might be therefore interesting briefly to discuss some of these factors.

It appears that the findings of various observers are based on the results of the primary vaccinations on infants being judged from the scars seen at the time of re-vaccinations, and the results of these re-vaccinations from vesiculations or reactions. Though it is true that there is a definite relationship between the immunity and the vaccination scars, and these do give a fairly good indication of results of past vaccination, it might also be noted that it is a rather uncertain factor, or at least not an accurate indication. The area of scars measured in a growing child is not always a satisfactory test because it is seen that they increase in size as the child grows. In this connection the following observation might be interesting to note:—

Average vesicular area of four insertions as measured on the eighth day of vaccination = 0.505 square inch or about 315.6 square millimetres.

Scar area of these on the 22nd day after the scabs had fallen off = 0.4421 square inch or about 263.1 square millimetres.

The same scar area at the end of three months = 0.483 square inch or about 301.8 square millimetres.

The same scar area at the end of six months = 0.523 square inch or about 326.8 square millimetres.

It will be seen therefore that a more satisfactory factor for accurately judging the relative results of vaccination, particularly infantile vaccination, would be to evaluate them from their typical 'takes' or typical vesicles, and their total area.

Technique, and nature and number of incisions.—As regards the method or technique of

vaccination, it varies considerably not only in various countries but even amongst individual vaccinators and observers. Not only cutaneous but also intracutaneous and subcutaneous methods are used. Everyone seems to adopt his own method, considering that to be the best one. Linear incisions with the ordinary scalpel or other cutting-edge vaccinating lancet is the one generally adopted in Europe. France, Spain, Italy and other countries use for the purpose a sort of nib-like cutting instrument. Force in America uses his drill method, which consists of in applying vaccine lymph to a 2-millimetre circle of derma, exposed by removing the epidermis by means of the rotary motion of a small drill held perpendicularly to the tightly-drawn skin. On the other hand Leake of the United States Public Health Services has adopted 'acupuncture' or the multiple puncture method with remarkable success. Both these methods are officially approved and recommended under the New York Regulations. Dudley also used the 'acupuncture' method at the Greenwich hospital with excellent results.

Further, it may be noted that, besides technique, both the number and the size of incisions or marks also vary throughout to a great extent. In Canada, the one-mark puncture method is officially recommended and adopted. In England, the Ministry of Health, though it prescribed no special technique or method, till recently insisted that in primary vaccination a total vesiculation area of not less than half a square inch should be aimed at. This standard of a half square inch area of vesiculation which was determined long ago by the Royal Commission on Vaccination, as a necessary requirement of primary vaccination to secure maximum protection, remains unchallenged and its effectiveness is admitted on all sides. But of late, on the recommendations of the Vaccination Committee of 1928, England has adopted the American and Canadian practice of one-mark incision or vaccination. This appears to be a sort of compromise arrived at between vaccinationists and anti-vaccinationists. It is also said to be a device to popularize vaccination by making it as little painful or incommoding as possible, and thus to induce people to resort to voluntary re-vaccinations more readily. Whatever may be the value of this measure it must be admitted that the value of the duration of immunity secured by infantile or primary vaccination is being sacrificed.

Quality and potency of lymph used.—The lymph used is also an equally varying factor. It is known that not only do the process of manufacture and the quality of lymph vary considerably but also the kind. Though calves are the usual vaccinifers, other animals like buffaloes, asses, sheep, etc., are also employed. Neuro-vaccine prepared from the brains of

rabbits is employed in some countries, particularly in Spain. Testicular vaccine may also be used. Vaccine lymphs in several countries are commercialized products. There is no standard of dilution, which may vary from 1 in 3 to 1 in 10. It is evident therefore that not only the quality but also the doses of vaccine virus used for the purpose may vary. It is true that all such lymphs used are expected to pass the prescribed International Standard Test. It is also seen by experiments that lymphs with much greater dilution than 1 in 10 can produce vesiculation, but this does not prove the uniform quality of lymph used in all cases by all observers. On the other hand it has not been possible so far to determine the dose or the optimum quantity of vaccine virus required to secure the desired immunity. It is the ultramicroscopic properties of this vaccine virus that makes the position of vaccination so unique and to a great extent so empirical.

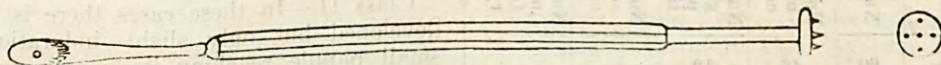
Author's observation

Taking therefore into consideration all the factors discussed above, a careful investigation on the subject was carried out. It covered observations on 1,102 cases of infantile vaccinations and their re-vaccinations at varying periods. But, before stating the results of my findings, it might be of interest to note the factors and exact conditions under which it was carried out. All primary vaccinations were on infants below 12 months of age. The technique used for all vaccinations and re-vaccinations was quite uniform. In all cases (both infantile and re-vaccinations) the number and size of incisions made were absolutely the same:—four incisions in either case and of the same kind and size. All cases selected for re-vaccinations had four good scars and a record of four good vesicles seen on the eighth day of their primary vaccination. All cases were vaccinated with the rotatory vaccinating lancet which was devised and is manufactured at this institute. This lancet is used by all public vaccinators in Bombay Presidency. It is shown in the illustration below:—

is gently pressed and rotated. This results in breaking the skin very superficially in a circular incision 4 millimetres in diameter. The central needle point does not as a rule break the skin. Its main function is to fix the lancet and it, being slightly longer than the peripheral ones, serves to press the skin down and thus stretching it helps to cut it more easily by the latter. It will be seen therefore that in all my cases uniform technique and method was adopted, all incisions being of an absolutely uniform size, unlike perhaps the linear and other ones, the sizes of which are evidently judged only roughly. Further it may be also interesting to note that all my circular incisions of 4 millimetres diameter result in uniform shapes and sizes of circular vesicles between 10 and 11 millimetres in diameter.

Total vesiculation area covered by four such insertions or incisions is on an average just about half a square inch.

As to the lymphs used in all my cases, they were all manufactured in this institute and were of uniform standard of quality, potency and purity. All lymphs prepared in this institute are dermal. Heifers below two years old are the vaccinifers. A solution in distilled water of 50 per cent re-distilled glycerine of a specific gravity of 1.260 is the diluent. Dilution is in proportion of 1 in 5 by weight. Purification of lymphs is by the chloroform vapour method. They are not filtered. All lymphs are tested bacteriologically for their purity. They are also tested for potency according to the recognized international standard tests and also by special tests used in this institute. The lymphs issued from this institute are reported to give nearly a 100 per cent success rate. From the result statements submitted by public vaccinators throughout the whole Bombay Presidency, including Sind, from 763,610 primary vaccinations done by them during the last year, a case success rate of 99.96 per cent and insertion success rate of 99.46 per cent are reported. Also all my vaccinations and re-vaccinations were carried out by the same two vaccinators of this institute. All results of vaccinations



Rotatory vaccinating lancet (actual size), Belgaum Vaccine Institute pattern.

The circular disc end is provided with five tiny conical-shaped needle points; four of these are on the periphery of the disc and one very slightly longer than the others in the centre. The tiny scoop on the other end of the lancet is used for the purpose of placing a drop of lymph on the area to be vaccinated. Through the drop of lymph thus applied on the skin, the disc end of the lancet, held perpendicularly,

were personally seen by the writer and carefully recorded. Primary vaccination results were seen on the eighth day and those of re-vaccinations generally on the sixth day and earlier. There is not much to be said or noted about the primary or infantile vaccination reactions, but the same cannot be said as regards re-vaccinations. The types of reactions of the latter may and do considerably vary from the

former. In the correct interpretation and significance of these, conclusions are to be drawn. The importance of accurate records of re-vaccination reactions therefore is obvious. More or less in accordance with the views expressed on this point by the International Committee on Smallpox and Vaccination of the League of Nations, the results of my cases have been classified as follows:—

Class I.—Definitely unsuccessful.

Class II.—Very slight reaction. Allergic or early, showing just a small papule with very slight or no areola.

Class III.—Accelerated vesicular reaction. Developing earlier than in the primary vaccination type reaction.

Class IV.—Definitely successful. Showing a typical reaction of primary vaccination type as seen on the eighth day after vaccination.

The statement below shows the results, tabulated, for half-yearly periods, of 1,100 cases of children vaccinated when they were infants and the same re-vaccinated at varying intervals, in both cases at this institute and under absolutely identical conditions. From the statement are excluded two cases in view of their exceptional results. They seem to demonstrate forcibly the individual susceptibility factor in vaccination. One child being re-vaccinated within about 10 months was found to show an extraordinarily good reaction of a definite primary type. This child was vaccinated on 7th September, 1932, when five months old and was re-vaccinated on 2nd August, 1933. Results on both occasions were seen to be practically identical. The other child being re-vaccinated within five months was found to

TABLE I

Showing results of re-vaccination at different intervals in children vaccinated in infancy

Interval between infantile vaccination and re-vaccination	Number in group	CLASS I	CLASS II	CLASS III	CLASS IV
		Number definitely unsuccessful	Number of allergic or early papular reactions	Number of accelerated vesicular reactions	Number definitely successful — Primary type
1-6 months	60	48	12
7-12 "	98	76	22
13-18 "	101	67	30	4	..
19-24 "	67	38	23	5	1
25-30 "	124	60	39	12	13
31-36 "	91	30	36	14	11
37-42 "	93	26	32	17	18
43-48 "	55	16	22	6	11
49-54 "	95	22	32	14	27
55-60 "	65	18	24	12	11
61-66 "	63	7	18	9	29
67-72 "	62	15	17	10	20
73-78 "	60	10	15	10	25
79-84 "	66	10	15	10	31

show also an exceptionally good reaction of the accelerated type with good vesicles and areola.

From the above figures it will be seen that, though the results obtained give on the whole a fairly definite indication of progressive march one way or the other, at some age periods this is not quite as regular as one would expect. If, however, these same results are grouped together in one-yearly periods, they furnish more intelligible data and enable one to draw some definite conclusions.

TABLE II

Showing results of re-vaccinations at different intervals in children vaccinated in infancy, grouped in one-year time periods and shown as percentages

Interval between infantile vaccination and re-vaccination	Number in group	CLASS I	CLASS II	CLASS III	CLASS IV
		Definitely unsuccessful, per cent	Allergic or early papular reactions, per cent	Accelerated vesicular reactions, per cent	Definitely successful — Primary type, per cent
1 year	158	78.30	21.70	0.625	0.625
2 years	168	62.10	31.50	5.85	0.55
3 "	215	41.25	34.95	12.55	11.25
4 "	148	28.75	36.15	15.50	19.60
5 "	160	25.45	34.55	16.10	23.90
6 "	125	17.65	28.05	15.20	39.10
7 "	126	15.95	23.95	15.95	44.15

Class I.—The figures above in this class will show that even within one year only about 78 per cent show definitely unsuccessful results; in seven years this figure gradually dropped to about 16 per cent. This drop, it will be seen, is steady and marked during the first three years, after which it becomes less definite. The possible explanation of this lies in the fact that infantile vaccination is performed in a body of small weight, about 15 to 20 lbs., which is undergoing rapid developmental changes and so the adjustment of immunizing powers which has taken place in the infant fails to meet the demands of the rapidly-growing body and tissues.

Class II.—In these cases there is no vesicle developed but only slight induration and a small papule reaching its maximum reaction between the second and fourth day of re-vaccination. It is only an allergic or papular reaction; it is not a definite indication of loss of immunity. Some observers, like Muller, even go to the extent of suggesting the reaction to be the true evidence of immunity. Anyway, it may be taken as a beginning or the first step of the backward journey on the ladder of vaccination immunity. Except on the first and sixth years the percentage figures of these cases are fairly constant.

Class III.—In this class there was a definite vesicle and some areola but the development of the reaction nearing the primary type was accelerated. It was seen at its height generally between the fifth and sixth day. A small number was found in the second year; this was more than doubled during the third, reached 16 per cent in the fourth year, and remained practically steady at the subsequent age periods. This accelerated reaction is considered by some also as a definite evidence of immunity. This is true to some extent, but I would consider it as a residual immunity in about its last waning stage and affording a poor protection against smallpox.

Class IV.—Apart from one exceptional case, referred to above, it will be noted that a definite though small number of primary type reaction begins to appear even within two years; in the third year it had reached 11 per cent, and kept on steadily and progressively rising every year. At seven years, almost half of the children that had been vaccinated in their infancy were found with no immunity left and so were definitely unprotected against smallpox.

In this connection it is admitted that opinions may differ as regards the interpretation of the above results. Generally, papular and accelerated vesicular reactions are considered by some as immunity reactions. This being so, all the cases under the above classes I, II and III would be put down together as 'immunes', and class IV as 'non-immunes'. If this classification is accepted my results would stand as follows :—

TABLE III

Showing rate of loss of immunity conferred by infantile vaccinations, percentages at different time intervals

Intervals	Immunes, per cent	Non-immunes, per cent
1 year	100-00	0-55
2 years	99-45	11-25
3 "	88-75	19-60
4 "	80-40	23-90
5 "	76-10	39-10
6 "	60-90	44-15
7 "	55-85	

Though the above classification may be academically correct, I consider it inadvisable to accept it as a safe guide from the practical point of view. There can be no two opinions as regards the significance and the interpretation of results under class I and class IV. These are definite, but between these two extremes are to be found class II and class III. The former is a very slight deviation of class I, and it may be taken as an indication of good immunity, but the latter, though to some extent an indication of immunity reaction, is certainly one on which it would be inadvisable to

rely as a sufficiently effective protection against smallpox. For practical purposes, therefore, I would classify the above results under two categories—class I and class II may be taken together as being within the effective safety margin of protection, and class III and class IV taken together as outside this safety margin. So that there will be one group of cases taken as adequately protected against smallpox and may be considered as 'safe', and the other unprotected or not sufficiently protected and for all purposes to be considered 'unsafe'. This is shown in the table below :—

TABLE IV

Showing rate of loss of immunity conferred by infantile vaccinations, percentages at different time intervals; regrouped to conform with author's views

Intervals	'Safe' (classes I and II), per cent	'Unsafe' (classes III and IV), per cent
1 year	100-00	0-55
2 years	93-60	6-40
3 "	76-20	23-80
4 "	64-90	35-10
5 "	60-00	40-00
6 "	45-70	54-30
7 "	39-90	60-10

From the above figures it will be evident that more than one-third of the children between the ages of four and five years vaccinated in their infancy are in danger of contracting smallpox; similarly more than half of those at six years and nearly two-thirds at seven years. Practical application of these figures for judging the degree and duration of immunity conferred by infantile vaccination against smallpox is obvious.

Conclusion

It is an admitted fact that vaccination protects not only against smallpox but against itself. It is also known that the degree and duration of immunity conferred by it to be greater against smallpox than against vaccination itself, but, in spite of this fact, for practical purposes it would be advisable to judge the immunity from the re-vaccination results. Considering therefore this question from this angle of view and judging it from the above facts and figures it will be abundantly clear that the degree and duration of immunity conferred by infantile vaccination is certainly much poorer and shorter than is generally believed.

Gins states that about one-fifth of children vaccinated in infancy completely lose their immunity when 12 years old. Sergeant on the other hand found that two-thirds of cases lose their immunity within three years. From my investigation I come to the conclusion that in

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SOME OBSERVATIONS ON THE LACTOSE-FERMENTING ORGANISMS ENCOUNTERED IN THE BACTERIOLOGICAL ANALYSIS OF WATER IN THE TROPICS

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A CAREFUL study of *The Bacteriology of Surface Waters in the Tropics* by Clemesha (1912) shows that he mentions 29 of the 42 different species of lactose-fermenting organisms which are tabulated numerically and shown in table XII (a) (after MacConkey, 1909) at the end of that book.

The identification of the organisms contained in MacConkey's table is determined principally by their behaviour in five different sugar media, by the indol and Voges-Proskauer tests and by the presence or absence of motility. With the use of these eight tests it is possible to identify each species separately. Taylor, Martin, Naidu and Naidu (1927) gave an 'Identification table for lactose-fermenting organisms which are citrate non-utilizers or variable' (table XVII). In this table the two sugars, adonite and inulin, and the Voges-Proskauer tests as shown in MacConkey's table are omitted, so that the identification of organisms is determined by means of five tests. The same paper also contains a table showing the 'reactions of organisms isolated from different sources to the citrate, methyl-red and Voges-Proskauer tests'. The Clemesha class to which they belong is also shown (table XVI). [These two tables will, for purposes of convenience, be referred to as table XVI and table XVII.]

Table XVI contains 31 different species of organisms, eight of which, nos. 7, 36, 66, 70, 71, 97, 102 and 109, are not included in the 29 organisms isolated by Clemesha. There are therefore 23 species of organisms isolated by Clemesha and by Taylor and his co-workers. Six species of lactose-fermenting organisms additional to these 23 species have been isolated

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the Bombay Presidency about one-fifth of the children vaccinated in their infancy completely lose their immunity within four years and about one-half in seven years. Therefore the desirability and importance of re-vaccination at an earlier interval or age period than is generally adopted in some places is obvious. Also, apart from the advisability of it being done even within one year in the presence of epidemics of smallpox, I consider it most desirable that besides infantile vaccination re-vaccination of all children as they attain the age of four or five years should be enforced by legislation or otherwise.

by Clemesha alone, and, as already stated, 8 species by Taylor and his associates, making altogether 14 species which have been isolated by one author only. These 14 species, together with 23 species mentioned above, i.e., 37 of the 42 species contained in MacConkey's table, have been isolated from different sources in the tropics.

The six lactose fermenters isolated by Clemesha alone are nos. 3, 6, 9, 33, 37 and 103, and the 23 organisms isolated by Clemesha and also by Taylor and his associates are nos. 1, 2, 4, 5, 8, 34, 35, 65, 67, 68, 69, 72, 73, 74, 75, 98, 100, 101, 104, 105, 106, 107 and 108.

Clemesha has classified 24 of these 29 organisms into three classes, according to their power of resistance to sunlight. He has left five unclassified, viz, nos. 8, 37, 69, 104 and 105.

Of the 23 species isolated by Clemesha and Taylor, 19 have been classified by Clemesha, those unclassified being nos. 8, 69, 104 and 105. The five organisms which have been classified by Clemesha additional to these 19 referred to above are nos. 3, 6, 9, 33 and 103. An analysis of table XVII shows:—

1. Eighteen species of lactose-fermenting organisms.

2. That of these 18, twelve—nos. 1, 2, 4, 5, 8, 34, 35, 72, 74, 100, 106 and 107—are included among the 23 organisms which have been isolated by the authors of both publications.

3. That, of these twelve, eleven have been classified by Clemesha, no. 8 being omitted.

4. That three organisms—nos. 69, 104 and 105—included in the group of 23 species referred to, and unclassified by Clemesha, are excluded.

5. That eight species, nos. 65, 67, 67, 73, 75, 98, 101 and 108, classified by Clemesha are also excluded.

6. That six of the eight organisms, nos. 7, 36, 66, 71, 97 and 109, already referred to are included, nos. 70 and 102 being omitted.

7. That all the organisms contained in this table give a negative Voges-Proskauer reaction with the exception of B. 97.

The water bacteriologist on completion of certain tests must refer to a table to enable him to identify the organisms isolated and has the choice amongst others of MacConkey's table or table XVII. The use of the former is advantageous in that it has a very much wider selection of organisms but the necessity of having to perform eight different tests is a disadvantage. The use of table XVII is very convenient since only five tests are necessary. The number of species of organisms contained in this table is, however, limited to eighteen and it will be noticed that, in spite of the reduction in the number of organisms, instances occur where two or even three species are grouped together and not identified singly.

For purposes of record and study of results of water examinations, it is desirable that the