SERUM PHENOMENA AND THEIR RELATIONSHIP TO THE PROGNOSIS OF DIPHTHERIA.

A Thesis for the Degree of Doctor of Medicine

by

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SERUM SICKNESS.

The title "Serum Sickness", has been applied to a group of symptoms, which not infrequently follows the injection of a heterogeneous serum. The first recorded observations on serum phenomena were those of Stanley[1] in 1902; but since 1905, the year of publication of "Die Serumkrankheit"[2], the subject has figured largely in medical literature. Its pathology, still indefinite, continues to be investigated by the laboratory worker, but its symptomatology is now comparatively familiar to the clinician. The fact that the intensity of the serum manifestations may have an important bearing on the prognosis of diphtheria has not received the attention which it merits, and it is to the discussion of this aspect of serum disease that the present paper is directed. The significance of a well marked serum reaction was first commented on by Rolleston, J.D. (Practitioner, Decr. 1904)[3] The same observer has since made frequent reference to the dictum that "the more marked the antitoxin reaction, the better is the prognosis"[4]. My conclusions, based on the consideration of 1,000 cases, will be found to afford additional confirmation of Rolleston's assertion. The cases studied have been under treatment in the Grove Fever Hospital during the past eighteen months. But in des-

Rolleston's dictum.

cribing symptoms, and details capable of more general application, I have utilised my previous experience of serum disease as seen in other fever hospitals. The same type of serum was used in all the cases, and unless otherwise stated, the same treatment was employed. Pathology and symptomatology are only briefly dealt with, but in discussing questions to which these are relevant, supplementary details are introduced.

Type of Serum and dosage employed.

The serum employed was that in use at the various hospitals of the Metropolitan Asylums Board. It is unconcentrated, and contains approximately 300 units per cc. Ordinary commercial serum contains about 500 units, and the serum used in Denmark about 405 units per cc. The percentage of reactions with our serum is high, and the reactions seen are of the most typical character. They are, therefore of a suitable nature for the study of serum phenomena.

The cases seen recently have been of more than average severity, and included a large number of the "grave toxaemic type". The present tendency in the treatment of diphtheria is in the direction of ever increasing doses.

Table 1 shows how dosage has increased in the London fever hospitals during the past 10 years.

The cases in this series received an average dosage

of 25,200 units a figure which will be seen to be somewhat in excess of the usual dosage in this country. They are not, however, high when compared to institutions like the Blegdamshospital, Copenhagen,[5] where 200,000 units is often exceeded. In one case (illust. case 3), I gave with good results no less than 180,000 units. This patient -- one of a haemorrhagic type -- also received 100 cc. Anti-streptococcic serum, a procedure, which, I believe, may prove a valuable adjuvant in the treatment of certain types of cases.

All the cases were injected subcutaneously, and repeated daily dosage was the usual routine in severe cases.

Table 1.

Year	No. of Cases.	Average No. of Units given to each patient.	Percentage. Mortality.	Percentage Paralysis.
1912	6,510	14,871	6.57	9.38
1913	6,283	17,113	6.63	7.85
1914	8,101	18,240	8.47	8.76
1915	8,172	19,559	8.42)	
1916	8,479	16,607	7.19)	
1917	8,090	16,548	7.20)	Not published.
1918	8,041	19,445	8.14)	
1919	8,164	18,367	9.27)	
1920	12,285	19,788	8.61)	
1921	13,697	23,130	--)	

PATHOLOGY.

Serum sickness is usually considered to be a manifestation of the response by the injected subject to the introduction of a foreign proteid. That the Antigen is to be found in the proteins of the horse serum seems to be beyond question, but the nature of the antibodies developed in the serum of the injected subject has not yet been conclusively determined. The advance of Protein Therapy has stimulated an enormous amount of research on the effects produced by the injection of proteins, and from the results, conflicting though they sometimes appear to be, we have been able to derive some valuable information.

Toxic Protein Split Products.

According to Vaughan[6] and others, the parenteral (hypodermic) introduction of foreign proteids excites the formation of specific ferments in the injected animal. These ferments are activated by a second injection of the same proteid, and have the power of splitting up the proteids into a poisonous and a non-poisonous portion. An excess of the poisonous products of protein deavage will give rise to toxic symptoms. These closely resemble the symptoms of anaphylactic shock - a resemblance often very marked in some cases of serum sickness. The chief features of the reaction produced by these products are: Increased secretion of glands, increase in the antibodies and proteo-

lytic ferments[7] of the blood; and increased permeability of the capillaries of the liver and skin. This increased permeability results in an increased lymph flow, which carries into the blood a variety of the products of cell metabolism. (Clark)[8]. The effect on the skin capillaries is intimately connected with the production of Urticaria, and the endermic injection of protein poisons has been shown to give rise to wheals. The theory that histamine[9] which produces similar effects, might be the active principle of these toxic bodies, has been disproved.

Histamine.

It has been suggested that serum sickness is a form of Auto-anaphylaxis, in which a portion of the injected serum remains unaltered in the subject, ready, after sensitization has taken place, to play the part of a reacting dose. This seems feasible, but in the period of reaction, one would expect to find similar antibodies in the blood in both serum sickness and anaphylaxis. Experimental evidence does not support this. Indeed it has been stated that the anaphylactic state depends on the presence of antibodies in the tissues, and their absence from the blood. Friedmann[10] is of opinion that Anaphylactic antibodies are of the nature of haemolysins, and Kritchevsky's[11] recent work on the rabbit, supports this view. Volta,[12] however, considers that conclusions based on compliment fixation experiments cannot be upheld in the case

of serum sickness. His experiments show that the injection of horse serum provokes, in man, the production of specific "Haemo-agglutinins", which have a very definite agglutinating action on the red cells of the blood of the horse. The reaction is analogous to that which occurs when bacilli are acted on by their specific serum. The reaction requires an incubation period of 6 days, and attains its maximum intensity about the 12th day. It could still be obtained after 4 months. The intensity of the reaction was found to be proportionate to the clinical manifestations, being most marked in cases where the symptoms, notably the rash and joint pains, were most severe. The fact that Volta's work is in such close accord with our previous clinical observations, carries considerable weight, and if confirmed it will mark a decided advance in our knowledge of the etiology of serum disease. Some workers in this country have endeavoured to associate serum disease with the presence of precipitins in the blood, but Wyard,[13] from observations based on the study of 51 cases has found it impossible to establish any connection. He concludes that men, whose blood contains these antibodies, are not in any way more susceptible to serum disease than those in whose blood they are absent. Busacchi[31] has studied the question of diphtheria toxin as a possible factor. Though obviously not the cause, toxin

has, as I hope to show later, an important modifying influence on the development of serum phenomena. On the highly controversial question, as to the precise relationship between anaphylaxis and serum sickness, I do not propose to comment further than to state, that, whatever may be the etiological association, clinically, at any rate, demarcation is possible. I refer, of course, only to the "normal reaction", seen in subjects who have not been sensitized by a previous injection of serum. In a sensitized patient, the differentiation between what constitutes merely serum sickness, and what might be termed anaphylaxis, is often only arbitrary.

THE SERUM PHENOMENA.

The most characteristic feature of the reaction is the appearance of a rash, but a prodromal stage can sometimes be distinguished. Perspiration, even within a few hours of injection, and oliguria, are the earliest signs. Drowsiness, at all events on the day preceding the eruption, is common, but the eruption itself is usually the first definite manifestation. It comes out on the 7th or 8th day, but may be delayed for a further period of from one to four days. It rarely develops later than the 14th day following injection. In one exceptional case, recently under treatment in the Grove Hospital, a rash was first noted on the 33rd day, but as it was of the circinate variety, it may have been only secondary to an earlier rash, which escaped notice on account of its transient character. The area surrounding the site of injection is usually first affected, and this holds good whether the serum has been given subcutaneously, or intramuscularly. A preliminary erythema, sometimes punctate, is the initial, and in severe cases may be the only phase of the eruption. (Cases 1, 2, 6,). It must be distinguished from the redness, often seen shortly after injection, which may be caused by the insertion of the needle. This preliminary erythema is rapidly succeeded by the characteristic

rash.

Varieties of rash. Urticaria is the common type, but Erythema Multiforme, Scarlatiniform, or maculo-papular types may be met with. A circinate appearance is more usually associated with a secondary rash. Scarlatiniform appearances may occasion some difficulty in differential diagnosis, especially if as sometimes happens, the rash is

Duration

accompanied by pyrexia. When present this pyrexia may last for as long as 10 days (case 3). The rash may persist for 3 or 4 days and may exhibit a protean propensity, changing in character almost as observed, or it may fade and re-appear at intervals during a similar period. If very intense, it may be followed by slight desquamation.

Irritation

The urticarial variety often gives rise to considerable and sometimes almost intolerable irritation. Adults complain most of the discomfort, particularly at night; but the numerous scratches seen on the abdomen and buttocks of children, who have had a marked eruption, show that they too may suffer.

Other Symptoms.

Vomiting may occur, but it is more common, and more severe in "accelerated" reactions. Oedema, marked by puffiness under the eyelids and swelling of the extremities is not seldom seen, (case 9) but Orchitis, recently reported by French observers,[14] must be extremely rare. It was not noted in the present series. Joint pains may add to

the discomfort of the patient, but these are more often among the later sequelae, which develop in a certain percentage of cases.

Differentiation of the serum urticaria.

Volta claims that his Haemo-agglutination test may be utilised in differentiating a serum urticaria from an urticaria of other origin.[12] As the number of cases in which the question of diagnosis might arise, are few, and the technique of the test elaborate, the physician will continue to make the distinction on clinical grounds alone.

LATER SEQUELAE.

In certain cases serum phenomena do not terminate at the stages just described. After a varying number of days, exceptionally as long as 12, a supplementary rash may appear, but very frequently, especially in patients who have received large daily injections of serum, the primary rash merges almost imperceptibly into the second. The 12th day following injection is the one on which the secondary rash is most likely to be observed, and if not circinate from the beginning, it will in all probability assume this appearance later. Its duration is similar to that of the earlier urticaria. After the fading of the rash slight staining may be left. The staining may resemble that seen in Measles, but is sometimes haemorrhagic, (case 5). Pyrexia is common, as is also conjunctival injection, and adenitis. The adenitis may be cervical, axillary, or inguinal. Protein injections in experimental animals may cause considerable hepatic enlargement.[15] This, however, is more particularly applicable, when the method of administration has been intravenous. This does not occur* as one of the sequelae of subcutaneous injection, and I have not, so far heard of it as a result of intravenous. Liver enlargement is frequently associated with fatal cases of diphtheria,[16] but in these, the usual serum

* Since writing the above, a colleague has informed me of a

sequelae are absent (case 4) or only very slightly marked. (Table 4).

Joint Pains.

The joints which may be affected are the wrists, elbows, shoulders, ankles or knees. Muscular pains in the limbs may also be complained of. As in rheumatic fever, the tendency is for these pains to flit from joint to joint, but in many cases, only a single joint is involved. As Rolleston has pointed out, the rash and joint pains usually co-exist, but either may be the only symptom present. The pains usually last from 2 to 3 days. Concomitant symptoms are slight headache, anorexia and depression. Sometimes a few specks of exudate may be seen on the tonsils, a condition to which Rolleston has given the name of Angina redux.[17] In patients who have previously exhibited signs of laryngeal obstruction a return of the croupy symptoms may cause some anxiety, but operative interference is unlikely to be called for.

Angina redux.

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case now in hospital, in which the liver reached to the umbilicus. The enlargement was associated with an unusually severe attack of serum sickness, and only lasted for 24 hours. The diphtheria did not appear to be of a type severe enough to give rise to hepatic enlargement --- at any rate, not to this extent.

ABNORMAL REACTIONS.

An abnormal reaction may follow a first injection of horse serum. The symptoms are those of anaphylaxis. The reaction sets in almost at once, and is characterised by dyspnoea, cyanosis, respiatory failure and collapse. The victims are chiefly asthmatics, about 4% of such individuals being susceptible. Only about one case in 50,000 dies after primary injection, but as small a dose as 1 minim has been recorded as having brought about a fatal issue.[18] The type, however, with which we are familiar in fever hospitals is that met with in patients, who have previously received serum treatment. It is possible that, once established, the sensitized state may last indefinitely. This type is sub-divided into three groups.

In group (a), the reaction appears in not less than 7 days after injection. The symptoms are those of the normal reaction, but they are of greater severity.

In group (b), the reaction appears after any time from 12 hours to 6 days. As a rule its course is similar to the aforegoing, but it may be anaphylactic in character. The "accelerated reaction" is the name applied to this group.

In group (c), the reaction -- "immediate" -- may develop within an hour of injection, but it may occur up to 5 or 6 hours. Its features are: a severe rash, accom-

panied by vomiting, cyanosis, dyspnoea, faintness and collapse. The temperature is at first normal or sub-normal, but later it may be raised.

FREQUENCY OF SERUM PHENOMENA.

The frequency of serum phenomena has a very intimate bearing on the question of prognosis, and for this reason it must be considered in some detail. In any computation of frequency the rash, which is the most constant and most reliable sign, must be taken as the index. In the accompanying table (2), it will be seen that the figures of various authorities show a very wide divergance. Even after due allowance is made for the differences in serum, and the liability of evanescent rashes to upset calculations, there remains a very considerable disparity. (I believe I am correct in assuming that unconcentrated serum was used by the observers referred to). It is a significant fact that Ker,[28] who advocates a much lower dosage than that in use in the London Fever Hospitals, records the lowest figures, while Rolleston, in whose cases the doses ranged as high as 78,000 units, records the highest. The discrepancy is, therefore, very largely explained by the amount of serum used. What are the factors which determine the appearance of a reaction in any particular case? These are:

Factors influencing frequency.

(1) Dosage.
(2) Type of serum used.
(3) Individual idosyncrasy.
(4) Severity of the disease.

The first has already been discussed. With regard

to the second, it is claimed that the use of concentration methods in the preparation of serum, has resulted in a noteworthy reduction in the incidence of serum sickness. This may be correct, but on account of its expense this type of serum is not used, on any considerable scale in this country. We frequently admit patients to hospital, who have been injected with concentrated serum by their medical attendants, but as the doses are almost invariably too small, re-injection is the rule. For this reason we have few opportunities of observing its effect. In this connection it may be noted that Walbaum has discovered that in subcutaneous injection, sera with normal protein content are best absorbed, the more concentrated showing a less efficient absorption.[19] A remark of Madsen's[20] is of interest. "There is a tendency at the present time to concentrate and "purify" the antitoxic sera, especially by means of the recently introduced precipitation methods, but it may be advisable to point out that it is very necessary to test whether under the concentration process, they have preserved their power to be absorbed, unaltered."

It has long been known that the sera of different horses may show a decided variance in toxic qualities. Individual idosyncrasy is of some note, and apparently this may be familial. Included in my series are the cases of a mother and three daughters. All received serum, and the quantity

and brand used were different in each case. They were not admitted to hospital simultaneously, and they had attacks of diphtheria of varying severity. Although the brands used, produced the usual quota of reactions in other patients, no member of this family was in any way affected.

In examining a large number of cases, it is reasonable to suppose that these factors will tend to offset each other.

From a cursory glance at the appended tables (3, 4, 5), one will have little hesitation in inferring that the severity of the attack exercises an important influence on the frequency of the serum reaction, and that this relationship may be made use of from the standpoint of prognosis.

TABLE 2.

Frequency of Rashes.

Observer.	Percentage.
[21]Sturtevant.	5-30
[22]Ker. (Series 1)	18
(Series 2)	25.5
[23]Goodall.	40.1
[24]Brownlee.	47
[25]Rolleston (1907).	66.7

TABLE III.

No. of cases. 1,000.	Average dosage per case 25,200	
No showing serum phenomena.	765.	Percentage 76.5
No showing no reaction.	235.	23.5

III(A). Showing how dosage affects the frequency of phenomena.

Classification.

1. Mild cases.	Dosage 3-12,000 units.
2. Moderately severe.	13-24,000
3. Severe	25-48,000
4. Very severe	49,000 and upwards.

	No. of cases.	No. showing phenomena.	Percentage.
Class 1.	307	225	73.2
Class 2.	321	250	77.8
Class 3.	268	218	81.3
Class 4.	104	72	69.2
	1,000	765	76.5

In compiling this table, only cases of definite (clinically) faucial diphtheria were considered. Cases which terminated fatally, before the day on which a rash might reasonably be expected, and patients who suffered from any concurrent disease

within 14 days of injection, were not included. Patients, who had been sensitized by a previous injection, were also omitted. 2 Cases, in which joint pains were complained of, but in which no rash was seen, are counted as negative.

INFLUENCE OF DOSAGE ON FREQUENCY.

I have already referred to the suggestive fact that authorities who favour small doses record comparatively small percentages of reactions. The first three classes in Table III. seem to be in accord with the conception which one would be inclined to form. It is interesting, though possibly not of great import, to note that the frequency seems to increase by approximately equal increments. If this ratio of augmentation were maintained throughout the series, the figures for Class 4, would be about 85%; instead of which we get 69.2. Are we to infer from this that very large doses give fewer reactions than very small ones? The explanation of the apparent anamoly is to be sought for, not in the amount of serum given, but in the severity of the disease. The large dose is an index of the severity of the disease, and presumably when we reach Class 4, we have reached a point where even a largely augmented dosage is insufficient to keep the percentage at its former figure, let alone raise it. So great an authority as Bie[26] has stated that the enormous dosage at the Blegdams-Hospital has apparently produced no appreciable increase either in the frequency or in the severity of the reaction. At the Copenhagen Hospital, the practice is to give large doses

intravenously, and their excellent results testify to the efficacy of this treatment. Speaking only of cases of the grave toxaemic type, few will doubt Bie's assertion, but one is not inclined to go so far in respect of the less severe forms. It must be remembered that Bie is now using a serum for intravenous work which contains no less than 12,000 A.U. per cc. I have frequently observed that with an intensive dosage, given subcutaneously, though not all in a single injection, one rarely fails to find some signs of a reaction, after the ninth day. Even in many of the worst cases, a rash, though delayed and usually modified, will make its appearance if large daily injections have been the line of treatment. The non-appearance of the eruption is a portent, which presages a serious, and often fatal termination to the case. In milder forms, it is naturally not of much significance as an idex of prognosis.

Goodall is of opinion that serum phenomena are now less severe than formerly. They do not seem to be less frequent.

MORTALITY. In making a computation of the incidence of the reaction in fatal cases, a series of 100 was taken, the basis of selection being the question of whether or not the patient survived long enough for phenomena to develop. Only six were 8-day cases, and fatalities which might have been influenced by concurrent diseases, tracheotomy etc., were not considered. As the series of 1,000 cas cases was not large enough to include 100 deaths, the deaths in the series have been supplemented from the records of the hospital. To find 100 cases conforming to these conditions, it was necessary to include almost the entire number for the years 1920, 1921, 1922.

TABLE IV.

100 Fatal Cases. Average number of units per per patient A.T. 66,330

(a) Number of 8-day cases 6
" " 9-11 " " 28
Beyond 11th day " 66
100

showing ction.	(b) Secondary rashes	Rash followed by pains.	Good rash	Slight rash	Rash limited to injection site.	Total
	0	3	5	10	8	26
showing no reaction	...	...	...	...		74
al	...	...	...	...		100

PROGNOSIS. What inferences may be drawn from this highly instructive calculation? Obviously the rash is only seen in about a fourth of those cases which are to have a fatal ending, and apparently a well marked reaction can only be expected in 8% of cases. No secondary rash was seen. As already stated (page 25) these serum phenomena were those recorded in a large hospital over a period of three years. It may therefore be assumed that the appearance of a secondary rash must be excessively rare in a fatal case. A secondary rash, then, may be taken as a harbinger of recovery.

Joint pains only figured three times in the same period. Their appearance would seem to be a very encouraging omen.

When we look at the difference in incidence between the mortality table and Table 3, it becomes evident that a reaction of any kind is greatly in favour of the patient. Even a few spots round the site of injection may give grounds for hope (Case 1, 6), and a well marked rash constitutes a good prognosis as regards mortality.

Does the appearance of a reaction have any relationship to the time a patient may be expected to survive? It has. In the 100 cases the average number of days survived by the 26 reacting cases, was 23.7. In the 76 remaining cases the number of days survived was only 15.9. So we may

gather from this that, if a rash is seen, the patient's chances are good; and even if death results, it is likely to be deferred. Case 3 shows that even in a patient with marked hepatic enlargement, and haemorrhagic manifestations, a good rash is an indication that recovery is by no means out of the question.

TABLE V.

Cases of paralysis in the series. Total number 215.

	Reaction	No reaction	Percentage of reactions.
Mild and moderately severe	122	37	72.7
Severe	16	40	28.5
Totals 215.	138	77	64.1

From the study of this table it is evident that reactions appear in the milder forms of paralysis, only a little less frequently than they do in the average case. In the severe type, however, the percentage of reactions is very markedly reduced, and it will be noticed that the percentage very closely approximates that recorded in fatal cases. It is not illogical to assume that a similar inhibitory process is concerned both in the fatal and graver paralytic cases. Here again it may be stated that, as the

percentage of severe cases which show the reaction is so decidedly reduced, a good serum reaction is of good prognostic import. In the list of illustrative cases, many examples will be found to show that in a case which has been severe at the beginning, a good rash will suggest a strong possibility of recovery without any grave paralytic sequelae. The converse is, of course, equally applicable.

THE INHIBITORY INFLUENCE OF TOXIN ON THE REACTION.

We have seen how increased dosage raised the incidence of serum manifestations to a point at which other factors began to exert an antagonistic influence; and how the percentage of reactions was successively lowered from 81.3 to 69.2 in very severe, to 28.5 in the graver varieties of paralysis, and finally to 26 in fatal cases. Even granted that different estimations would show a certain discordance, it can hardly be doubted that the disparity is too great to be accounted for on the basis of erroneous comparisons. As the inhibitory influences reached their maximum in the groups, where one would expect the severest toxaemia, the antagonistic force must almost assuredly be the toxin of diphtheria. The influence may be exerted directly on the antibodies in the circulation which are associated with serum disease, or indirectly by limiting the response by the tissues to the introduction of foreign proteids. Rolleston,[4] instances the parallel of small-pox, where the absence of the usual inflammatory reaction in the skin surrounding the pastules is a well known and ominous indication of certain malignant forms. He suggests the possible explanation that the toxins exercise a "profound vaso-motor depression." Most authorities are agreed that diphtheria

toxin, after having invaded the blood quickly disappears from it again. It is in the tissues that it chiefly exerts its baleful influence. The most probable explanation of the inhibitory process seems to be that toxin having become bound up in the tissue elements, renders them too inert to exercise their normal resistance to foreign proteids.

The prognosis of serum sickness itself, remains to be considered. It is of course favourable, and apart from the somewhat rare cases of anaphylasis, it is doubtful if its influence is deleterious. The super-adding of one disease on another is hardly likely to be beneficial, but on the other hand, the association of a happy result in a severe case, with the presence of a good reaction, seems to indicate that it might possibly have a mild influence for good. In the Harben lectures for 1922, we find Madsen[29] stating, "We have frequently had the opportunity of observing that an inflammation occurring in an antitoxin producing animal may be accompanied by a considerable rise in the anti-toxin formation." He of course referred chiefly to the horse, but De Laverigne and Zoeller[30] have demonstrated that man possesses a greater capacity for antitoxin production than was formerly supposed. Any suggestion however that the mild in-

flammatory process, which accompanies the serum reaction could have the power of stimulating antitoxin formation, would require to be supported by very conclusive evidence.

TABLE VI.

Secondary Phenomena.

No. of cases considered 1,000.

Rash only	Rash and joint pains.	Pains only	Rashes total	Phenomena. total.
84	51	52	135	187.

Percentages. Total Rashes 13.5 Total Pains 10.3

VI. A. Total number 215. Paralysis cases.

	Mild and Moderately severe	Severe Paralysis.
2 ry.Phenom.	24	1
Percentage	11.1	0.46

THE SECONDARY PHENOMENA AS A PROGNOSTIC INDEX.

The secondary phenomena, are, as we see by this Table, relatively infrequent. In 1905, Rolleston compiled some tables, dealing with a series of 568 of his cases. His percentages for rashes and joint pains were 19.08, and 10.24 respectively; seemingly the earlier phenomena are now slightly commoner, while the later do not seem to have varied much. The secondary rash is not always easy to differentiate, as in many cases the tendency is for the earlier eruption to merge into the later. When a rash is of the same type throughout both stages, classification becomes a matter of some difficulty.

The secondary rash, as a prognostic factor is much more reliable than the Urticaria. Its appearance, apart from the fact that the patient will by then have reached the 10th or 12th day, is an exceptionally favourable sign. The rarity of the rash in cases , destined to suffer from severe paralysis, is a striking feature, and even in the milder forms of paralysis, it is far from common. It will be remembered that the primary rash, while it suggested that the probabilities were against severe paralysis ensuing, gave no grounds for expecting immunity from any form of paralysis.

CONCLUSIONS.

Increased dosage increases the incidence of serum manifestations, but diphtheria toxin exercises an inhibitory influence both on the frequency and the intensity of serum reactions. In very severe cases the rash is late in development, scanty, or entirely absent. The presence of a rash, even of the most limited nature is favourable to the patient. A good rash suggests a good prognosis. A case with a well marked reaction is not likely to end fatally, and the appearance of a rash affords some assurance that severe paralysis is unlikely. A primary rash is valueless in forming an estimate as to the likelihood of paralyses generally, its value being restricted to the severer forms. A secondary rash enables one to forecast with confidence, that a patient will neither die nor suffer from a paralysis of any of the graver types.

ILLUSTRATIVE CASES.

These cases, twelve in number, are chosen because they illustrate phases of the prognostic significance of the serum manifestations. Some of them are good examples of a severe type of diphtheria, but others, apart from the serum phenomena, will not be found to be of any special clinical interest.

Nine of the cases figured in the series of 1,000 cases, and two have been included because they are instances of how serum sickness affects the sensitized subject. The remaining case, No. 3, though still in hospital, has been included on account of its special interest. All ~~nine~~ were of a severe type.

Case 1. Initial prognosis grave, scanty rash - prognosis slightly more favourable. Severe paralysis. Recovery. Serum 105,000 Anti Strep 25.cc.

2. Initial prognosis appeared hopeless. Modified rash on 9th day, gave grounds for hope. Severe paralysis. Recovery. Serum 114,000. A.T. Anti strep. 50 cc.

3. Initial prognosis as in Case 2. Well marked rash on 7th day, and recurring (Secondary). Prognosis favourable despite grave signs. Paralysis not of a severe type. Convalescent. A.T. 180,000. Anti Strept. serum 100 cc.

4. Initial prognosis bad, no serum reaction, very severe paralysis. Died.

Case 5. Initial prognosis bad. Late case. Very marked reaction. Prognosis good. No paralyses. Recovery. A.T. 117,000
Anti Strept Serum 23. cc.

6. Initial prognosis as in case 2. Modified rash. Chances improving. Severe paralyses. Recovery. A.T. 90,000.

7. Severe diphtheria in sensitized patient. Early and marked reactions.

8. Ditto.

9. Initial prognosis bad. Marked reaction. Prognosis favourable. No paralyses. Recovery. A.T. 84,000
Anti Strept Serum 25 cc.

10. Initial prognosis hopeless. No real reaction. Prognosis uninfluenced, Cardiac paralysis. Died. A.T. 124,000
Anti Strept Serum 150 cc.

11. Initial prognosis not good. No reaction. Outlook unpromising. Moderately severe paralyses. Convalescent 130th day. A.T. 66,000.

12. Initial prognosis not good. Marked reaction. Outlook promising. No paralyses. Recovery. A.T. 42,000.

N.B. In the Illustrative Cases, a fractional index is used to denote day of month and day of disease, the first number being day of month and the second day of disease.

Faucial Diphtheria. (Toxaemic).

B.F.H. Female, Set 2. 3rd day case.

5/10/22. Nausea, vomiting, sore throat, left cerv. adenitis.

8/10/22 (on admission). Fauces injected. Exudate covering tonsils, pillars of fauces, uvula, and soft palate. Cervical adenitis marked on both sides. Pulse and colour fair. A.T. 21,000 units.

(evening) Persistent vomiting. Pulse rapid. Ht. sounds muffled. Colour poor. ℞ Brandy 2 drachms T.D.S. Sinapism applied to epigastrium.

9/5 Exudate still considerable. Vomiting ceased. Colour somewhat improved. Ht. sounds as noted. A.T. 21,000.

10/6 Fauces as before. Vomiting again at intervals. Adenitis less on rt. side. Drowsiness. Waxy-green toxaemic appearance. Chest - bronchitis. -rales and ronchi heard all over. No consolidation. Ht. as noted. A.T. 18,000. Iodex to chest.

11/7 Exudate deliquescing. Vomiting less frequent. Ht. and chest as before. A.T. 18,000.

12/8 Edges of membrane separating on left side of fauces. Vomiting ceased. General condition shows improvement. A.T. 15,000.

13/9 Membrane clearing well on left, but still marked on rt. side. Chest as noted. Bruising round sites of injections. A.T. 15,000.

14/10 Rt. side of throat still covered. Albuminuria. A.T. 15,000. General condition fair.

15/11 Faucial condition unchanged. Pulse and colour fairly Anti-streptococcic serum 15 cc. Good.

16/12 Glairy deposit on tonsils and fauces. Vomiting. Colour poor. Few urticarial wheals round injection sites. Albuminuria.

17/13 General condition improving. Throat swabbed with Hydrarg. Perchl. 1/10,000.

18/14 Albumin a trace.

20/16 Ht. sounds feeble. Reg. Tachycardia. AB within nipple L. Chest--few moist rales. Cough. Regurgitation of fluids.

21/17 Fauces clean. No regurgitation.

22/18 Regurgitation at intervals. Left otorrhoea.

23/19 Double otorrhoea. Child now attempts to sit up in bed.

26/22 Chest clear. Voice nasal.

7/11/22 Double int. strabismus.

34

25/52 Ht. sounds feeble. Colour poor. Bed blocks.
R strychinin gr. 1/100.

26/53 Condition improved.

4/12/22 Voice less nasal. Squint marked.

62

19/77 Voice clear. Eyes normal.

11/1/23 Walking well. No paralysees. Discharged.

91

Very severe faucial and nasal. Case 2.

M.M. Male aet. 5½. 4th day case.

23/10/22 Vomiting, sore, throat, cerv. adenitis, rhinorrhoea.

26 (no admission) Throat - mass of sloughing membrane, covering

4th day. Fauces and soft palate. Intense foetor. Profuse rhinorrhoea. Marked cerv. adenitis. ("Bull neck"). Colour poor. A.T. 24,000 units. (subcutaneously). Brandy 2 drs. 4 hrly.

27/5th Exudate - no apparent change. Epistaxis. Heart sounds pure. A.T. 24,000.

28/6 Exudate - as before. Epistaxis continues. Restless. Pulse tension fair. A.T. 24,000. Nares plugged with wool, soaked in adrenalin.

29/7 Colour improving. Epistaxis controlled by plugging. Pulse - tension fair. Erythema on forearms (blanket). A.T. 24,000.

30/8 Fauces - exudate resolving. Adenitis subsiding. Epistaxis now ceased. Albuminuria. Palate acting sluggishly. Some regurgitation of fluids. Ht. Sounds - tone good. A.T. 18,000. Anti-streptoc. serum 25C.C.

31/9 Exudate disintegrating. Albuminuria. Voice nasal.

1/11/22 10th Exudate much less. Voice very nasal. Throat swabbed. Hg. Prchl. VI/10,000.

4/13 Albuminuria. Scarlatiniform rash on abdomen.

5/14 Rash faded. Few streaks of exudate still present. Anti-strep. serum 25C.C. Foot of bed raised on blocks.

9/18 Fauces not yet quite clean. Pulse irregular.

12/21 Fauces clean. Double int. strabismus.

14/23 Ht. reg. Nasal voice. Strabismus. Fish diet.

21/30 Voice less nasal. Squint less marked. Tachycardia.

28/37 Ht. Sounds pure. Tachycardia.

2/12/22 41 Strabismus now accompanied by nystagmus-like movements of eye-balls. Deglutition difficult. Cardiac irregularity. Nasal feeding resorted to. ℞.Hypo. strych. gr. 1/60. Camphor. gr. 1½. ex ol. oliv. c.c.

3/42 Profuse salivation. Cardiac irregularity less marked.

5/44 Ht. regular. Pulse poor. Can swallow a little.

6/45 Slight parotitis (left). Pulse poor. Salivation. Atropin. gr 1/100. Rep. hypo. camphor.

7/46 Salivation continues. Rep. hypos.

8/47 Ditto. " "

9/48 Salivation less. " " " " " "

12/51 Salivation slight. Swallowing. Oral feeding resumed.

18/57 Swallowing well. Voice very slightly nasal. H.S.N.

14/1/23 84 Eyes normal. Voice clear. Pillow.

17/87 2 Pillows.

24/94 Allowed up in blankets ½ hour.

8/2/23 109. Walking well. No palsies. Discharged.

HAEMORRHAGIC DIPHTHERIA. (Case 3)

R.F. Female aet. 12yrs. 6mths., 3rd day case.

21.2.23 Vomiting, sore throat, headache, cervical adenitis.

23/on admission - Throat - marked exudate covering tonsils and pillars of fauces. Uvula oedematous. Marked cervical adenitis (chiefly left). Herpes round mouth and ext. nares. Pulse and colour fair. Foetor. Vomited shortly after being sent ward. A.T.24,000.

24/4 - Adenitis still more marked. Fauces as before. Ht. normal. Colour good. A.T. 24,000. Anti-strep. serum 25 cc. Brandy 2 drachm. p.r.n.

25/5 - Exudate has grown since yesterday. Adenitis still marked. Ht. tone good. A.T. 24,000. Anti-Strep. 50 cc.

26/6 - Adenitis slightly less, but faucial condition unchanged. Petechial rash on chest. Few petechiae on knees. Colour fair. Ht. good. Liver enlarged to umbilicus. A.T.24,000.

27/7 - Exudate shows signs of separating. Adenitis less. Petechiae more numerous. Albuminuria. Colour fair. Ht. sounds clear. A.T.24,000. Anti-strept. S. 25 cc.

28/8 - Exudate distinctly less. Taking feeds well. General condition improving. A.T.24,000.

1.3.23/9 Exudate disintegrating. Petechiae still present. Ht. as before. A.T.24,000.

2/10 - General urticaria, wheals well marked. Rash very irritating. Exudate clearing well. A.T. 12,000. Albuminuria continues. Temp. 100°.

3/11 - Rash faded. T. 101°. Exudate limited to a few streaks in tonsils. Slightly ulcerated surface left where exudate has separated.

4/12 - T. 100. 2. Urticarial rash again visible. Vomiting. H.S.N. No petechiae.

5/13 Rash faded. H.S.N. Allowed sponge cake, jellies. T.99.4.

6/14 - T.100.4. Fauces clean. Albuminuria.

7/15 - Secondary rash (urticaria) now well out. Slight left adenitis. Only a trace of albumen in urine. T.99. Lower hepatic border now only 1" below costal margin.

8/15 - Complaining of joint pains in shoulders and knees. Axillary and inguinal glands enlarged.

11/18 - No joint pains now, but complaining of slight sore throat. Left adenitis (cervical). T. 100. Albumin a trace.

11/18 - (evening) Epigastric pains. Dyspnoea. H.S.N. Few rales over left side of chest in mid-axillary line. Bed blocks. Rectal salines. Poultices to left side of chest.

12/19 - No pains. No adventitious sounds in chest.

13/20 - Complaining of abdominal pain. Liver normal. Nothing elicited on palpation. No tenderness.

14/21 - Not complaining. Colour good. H.S.N. Off blocks.

16/23 - Fish diet.

20/27 - Ciliary paralysis. No strabismus.

21/28 - Palate sluggish. Nasal voice.

28/35 - Pupils reacting. Can read small print. Voice very nasal.

4.4.23/42 Voice less nasal. Full diet.

11/49 - Allowed one pillow.

18/56 - 2 Pillows. Voice clear.

23/61 - Sitting up. No paralyses.

VERY SEVERE FAUCIAL (Case 4).

J.E.G. Female, aet. 11½, 5th day case.

12/6/22 Sore throat. Cervical adenitis.

16 (on admission) Throat - membrane covering both tonsils. On rt. side it covers fauces and extends over hard palate. Considerable oedematous swelling. Cervical adenitis marked. Intense foetor. Few erythematous areas on arms. Pulse and colour fair. A.T.24-000. Liq.Adrenalin m X ex aq. Chlor. 4 hrly.

17/6 - Membrane - same distribution. Some dysphagia. Ht. sounds clear. Beats forcible. Trace of albumin in urine. A.T.24,000.

18/7 - Membrane - edges separating from tonsils and uvula. Swallowing better. Adenitis less. Albumin cloud. A.T.24,000.

19/8 - Membrane disintegrating rapidly. Uvula still covered. Taking feeds well.

20/9 - Fauces nearly clean. Albumin cloud.

21/10 - Fauces clean. Light diet.

22/11 - Vomiting. Pulse irregular and poor in tension. Colour grey.

23/12 - Vomiting ceased. Ht. regular. Tone fair. No serum rash.

24/13 - Ht. regular. Colour fair. Voice clear. No serum rash.

25/14 - Complaining of faintness. Ht. regular. No rash.

26/15 - Ht. regular. 2nd sounds weak. Tone poor. No further vomiting. No rash.

27/16 - Ht. 1st Apical sound reduplicated. Tone poor. Pulsation outside nipple line. Has frequent syncopal attacks. Liver and spleen not enlarged. Albuminuria.

28/17 - Tachycardia. 1st apical sound reduplicated, 2nd sound weak. Rt. side of heart outside border of sternum. Liver not enlarged. Urine clear.

29/18 - Complaining of nausea and faintness. Liver palpable. Vomiting. Pulse thready. Oral feeding discontinued.

30/19 - Condition unchanged.

1.7.22/20 Tachycardia. Ht. as noted. Attack of faintness accompanied by extreme pallor this morning.

2/21 - Repeated syncopal attacks.

4/23 - Ht. as previously noted. Passed good night. Attacks of fainting less frequent.

5/24 - No recurrence of fainting.

7/26 - Voice nasal. Slight improvement.

9/28 - Ht. sounds clear.

(Evening) Fainting and Vomiting. Pallor. Lips blue.

10/29 - Ht. irregular. Sounds clearly heard.

12/31 - Condition unchanged. Inj. Camphor 1⅛ fr. en ol.oliv.

13/32 - Strabismus. Pharyngeal paralysis. Incontinence of urine. Rectal salines. Inunction with Ol. Morrhuae.

14/33 - Retaining salines. Quentity of Ol.Morrhuae absorbed, apathetic condition. Does not speak.

16/35 - Comatose condition, but pulse fair; face, arm and leg

paralysed on left side. (Left vocal chord ?).

17/36 - Diaphragmatic paralysis. Pupils dilated. Reacting.
Convulsive movements of head. Salivation.

(Afternoon) Died.

SEVERE FAUCIAL & LARYNGEAL (Case 5).

F.C.M. Male Aet 29. 7th day case.

20.11.22 Sore throat. Shivering. Cough.

26.11.22 (on admission) Pultaceous exudate covering tonsils, fauces and uvula. Cervical glands greatly enlarged. Coughs up shreds of membrane. Dyspnoea. Stridor. Slight recession. Partial aphonia. A.T.24,000. Brandy 4 drachms 4 hourly.

27/8 - Fauces very dirty. Bloodstained muco-purulent expectoration. Chest - diffuse bronchiolitis. Ht. normal. No stridor. Recession very slight. A.T.24,000. Anti-phlogistine to chest.

28/9 - Fauces clearing. Complaining of nausea. No dyspnoea but wheazy. Cough. Voice husky. A.T.18,000. Anti-strept. 25 cc.

29/10 - Exudate much less. General condition improving. Voice less husky. Cough less troublesome. Muco-purulent sanious expectoration. No casts. A.T.18,000.

30/11 - Area of serum injection, slight redness. Voice husky. Expectoration still blood stained, but less profuse. Ht. normal. A.T. 18,000.

1.12.22/12 Fauces not yet clean. Expectoration not blood-stained. H.S.N. Chest - few rales R. & L. A.T. 15,000.

3/13 - Trace of albumin in urine. Fish diet.

4/14 - Erythema abdomen. Fauces clean.

5/15 - Erythema very bright.

6/16 - Erythema multiforme - marked on trunk and limbs.

7/17 - Rash intensely irritating.

8/18 - T.99.6. Rash still out. Complaining of joint pains legs and arms. Ung. Methyl Salicyl. to joints.

9/19 - T.101°. Complains of pains in chest (muscular). Joint pains continue. Rash.

10/20 - Albuminuria.

11/21 - No joint pains. Albuminuria. Haemorrhagic staining over areas where rash has been scratched.

12/22 - Rash faded.

15/25 - Urine clear.

31/1 - Ht. normal. No paralyses. Clothes.

18.1.23/59 Walking well. Discharged.

VERY SEVERE DIPHTHERIA (Case 6)

G.R. Female, aet 33, 3rd day case.

20.4.22 Headache, sore throat, cervical adenitis.

22.4.22 Throat - membrane on both tonsils, extending to soft palate (on admission) and uvula on left side. Cervical adenitis very marked on both sides. A.T.24,000. Adrenalin m X). 4 hourly.

23/4 - Membrane separating at edge of soft palate. Profuse rhimorrhoea. Left cervical adenitis accompanied by oedema of left side of face and chest. Ht. sounds soft. Urine - trace of albumin. A.T.24,000.

24/5 - Membrane showing signs of further disintegration. A.T.24,000.

25/6 - Some bleeding from raw surfaces where membrane has become detached. A.T.18,000.

26/7 - Membrane separating in masses. Pulse fairly good. Colour fair. Rhinorrhoea more profuse. Slight regurgitation of fluids.

27/8 - Uvula and left tonsil clear. Swallowing without regurgitation. Ht. regular. Tone improving. Liver and spleen not enlarged. Trace of albumin.

28/9 - Ht. regular. Adenitis subsiding.

29/10 - Voice nasal. Fauces nearly clean.

30/11 - Regurgitation of fluids. Blotchy erythema lower segment of abdomen. None elsewhere. Ht. regular.

1.3.22/12- Fauces clean. No hepatic enlargement. Spleen palpable. Voice nasal. Eyes react to light and accommodation. Rash faded.

3/14 - Nausea and chest pains complained of. Ht. regular 2nd sounds abrupt.

4/15 - Retching. Ht. as noted.

5/16 - Vomiting. Regurgitation of fluids. Very nasal. Ht. as before.

6/17 - Swallowing well.

1.6.22/43- Coughing. Salivation. Soft palate immobile. Oral feeding discontinued. Atropin gr. 1/100th., Strychnin gr. 1/60th Rectal salines.

3/45 - Salivation ceased. Oral feeding resumed.

7/49 - Ht. normal. Light diet.

30/72 - Ht. normal. 2 pillows.

31.7.22/103 Walking well. Discharged. No paralyses.

Case 7.

SEVERE DIPHTHERIA (Sensitized Patient).

E.A. Female aet 29. 2nd day case.

20/7/22 Headache, nausea, sore throat. Cerv. Adenitis (Diphtheria, treated with serum, 8 years previously).

21/7/22 (on admission) Fauces infected. Membrane covering tonsils, faucial pillars, and extending over soft palate on rt. side. Cervical glands considerably enlarged.

3 p.m. Desensitising Dose. Serum 1 cc.

10 p.m. Serum Urticaria on chest and arms. T. 101.4

A.T. subcutaneously 6,000 Units

Orally 3,000 "

11.20 p.m. A.T. 12,000 Units. No further reaction.

22/3 - No further reaction. Exudate less, but still considerable. H.S.N. Temp. 100.4. A.T. 21,000.

23/4 Exudate deliquescing. A.T. 15,000.

24/5 Membrane clearing well.

25/6 Left tonsil clean.

26/7 Urticarial rash marked - general.

Fauces clean.

27/8 Morbelliform rash. Headache and joint pains. Complaining of deafness. Temp. 101.6.

28/9 Rash still marked. Temp. 100.

29/10. Rash fading. Joint pains. Muscular pains in limbs. Not deaf to-day. Temp. normal.

31/12 - Not complaining.

27/39 Clothes.

30/42 Walking well.

1/9/22 Discharged. No paralysis.

SEVERE DIPHTHERIA (SENSITIZED PATIENT) Case 8.

D.G. Female aet 29., 2nd day case.

24/2/22 Nausea, pains in back and limbs. Sore throat. Headache.

25/12/22 (on admission) Fauces deeply injected. Exudate on rt. tonsil and faucial pillars. Rt. cervical adenitis. T. 102.6. A.T.21,000.

Patient had previous serum 3 years before. (Anti Streptococci) but I was not aware of the fact.

Urticarial rash round injection site within half an hour of injection. Not complaining otherwise.

26/3 - Exudate has now covered both tonsils. A.T.15,000. Adenitis 4t. and Left. H.S.N.

27/4 - Membrane loosening at edges.

28/5 - Coughed up large piece of membrane. Membrane less on fauces, but still extensive on post-pharyngeal wall. A.T. 18,000.

30/7 - General urticarial rash. Irritation intense. Fauces clean. Adenitis subsided.

31/8 - Cervical adenitis (serum) Axillary glands enlarged. Glands painful. Nausea.

1/1/23/9 Adenitis less. Not so painful. Irritation of rash troublesome.

2/10 - Severe joint pains, wrists, elbows, shoulders, knees.

5/13 - Rash faded. No pains.

14/22 - Again complaining of joint pains. Angina redux.

15/23 - Pains less severe.

17/25 - No pains.

23/31 - Ciliary paralysis.

5.2.23/44 Vision normal. Palate sluggish. Coughs when swallowing.

8.3.23/75 Clothes - loss of power in rt. leg. No loss of sensation. No other paralyses.

22/99 - Walking well. Sensation delayed in both legs. Knee jerks absent.

5.4.23/103 Discharged. No paralyses.

SEVERE FAUCIAL (Case 9).

F.P. male aet. 8, 3rd day case.

3.12.22	Headache, Vomiting, Sore throat. Adenitis. Rhinorrhoea.
5.12.22 (on admission)	Throat - mass of membrane covering left tonsil and soft palate. Rt. tonsil also covered. Cervical adenitis (more marked on left). A.T.24,000.
6/4 -	Exudate as noted. Ht. sounds normal. A.T.24,000. Anti-Strept.Serum 25 cc.
7/5 -	Exudate separating at edges. A.T. 24,000.
8/6 -	Exudate clearing rapidly. Rt.tonsil clean. H.S.N. A.T. 12,000. Light diet.
11/9 -	Fauces clean. Urine - no albumin.
12/10 -	Marked general urticaria. Temp.99°
13/11 -	Rash still out and very irritating. R/ Ung.Para-mon-chporo-phenol.
15/12 -	Rash still present.
22/19 -	Ht. normal. Voice clear.
26/23 -	Circinate rash well out on trunk and limbs. Urine clear. Temp. 100°.
27/24 -	Circinate rash replaced by marked general urticaria. Temp. 102°.
28/25 -	No urticaria. Another circinate rash appearing. Temp. 103°.
29/26 -	Rash less marked. T.101°.
30/27 -	Rash faded. Conjunctivae injected. Complaining of headache. Fauces clean. Inguinal glands enlarged. T.101°.
31/28 -	Puffiness under eyelids. No joint pains. Temperature normal. Trace of albumin in urine.

Case 9 Continued.

1.1.23/29 Oedema Less. Urine clear.

31/59 - Clothes.

12.2.23/71 Walking well. No paralysis. Discharged.

HAEMORRHAGIC DIPHTHERIA (Case 10)

M.E.W. Female aet. 10 5th day case.

29.1.23 Headache, vomiting, sore throat, rhinorrhoea.

2.2.23 (on admission) Throat - membrane covering and obscuring tonsils, fauces, soft palate. Hard palate almost completely covered. Uvula invisible. Foetor. Pronounced left adenitis. Profuse rhinorrhoea. H.S.N. Pulse poor tension. A.T. 24,000. Anti-strept. serum 50 cc.

3/8 - Exudate as noted. Foetor intense. Rhinorrhoea less. Some bleeding from mouth. H.S.N. Albuminuria. A.T.24,000. Anti-strept. serum 25 cc.

4/7 - Exudate - sloughing mass, but appears somewhat diminished. Adenitis slightly less. A.T.24,000. Anti-strept.S. 25 cc.

5/8 - Exudate distinctly less. Petechiae on abdomen. Adenitis less. Toxaemic appearance. No liver enlargement. Albuminuria. A.T.24,000. Anti-strept. serum 25 cc. Bed blocks. Rectal salines.

6/9 - Fauces clearing. H.S.N. Area of punctures slightly reddened. Albuminuria. A.T.24,000. Anti-strept.Serum 25 cc.

7/10 - Fauces nearly clean but considerable collection of foetid purulent matter in post-pharynx. Has passed no urine for 24 hours. Ht. regular. Tone good. Liver not enlarged. Bruising round sites of injections. A.T.24,000. R/Hot stupes to loins. Anti-strept.Serum 25 cc. Sol.adrenalin m X b.d.s.

8/11 - 8 ounces of urine passed since yesterday. Breath very foul. Albuminuria. Retaining salines. No vomiting. Otorrhoea less. Ht. regular.

9/12 - Fauces - no membrane. Furrowed appearance where exudate has cleared. Pulse poor (54). Ht. feeble. Vomiting. Retaining salines. Camphor gr. 1½, strychnine gr. 1/60th. (hypo.)

10/13 - Retching. No vomiting. Retaining salines. Ht. sounds regular, but very faintly audible. Rep. Camphor.

11/14 - Cardiac irregularity. Sound almost inaudible. Pulse rate increasing (76) Extremities cold. Rep. Camphor & Strychinin.

12/15 - H.S. barely audible. Colour poor. Incessant retching and vomiting. Great precordial pain. Morphia gr. 1/8th.

(evening) Died.

SEVERE FAUCIAL DIPHTHERIA. Case 11.

F.C.W. Male aet. 5½. 5th day case.

4/10/22 - Headache, sore throat, cervical adenitis, Diarrhoea.

8/10/22 (on admission) Fauces injected. Exudate covering both Tonsils. Rhinorrhoea. Cervical adenitis rt. and left. Chest - Rales on both sides. No consolid. signs. A.T. 18,000.

9/6 Exudate more marked. Rhinorrhoea profuse adenitis increased. H.S.N. A.T. 18,000.

10/7 Fauces - exudate resolving. Adenitis marked H.S.N. A.T. 18,000.

11/8 Fauces clearing well. Colour fair. A.T. 12,000.

12/9 Exudate now limited to rt. side. H.S.N.

13/10 Fauces - only streak on rt. tonsil. Adenitis subsiding. General condition improving.

14/11 Tonsils clean. Mulo-purulint deposit on post. pharyn. wall. Colour good. H.S.N. Light diet.

15/12 Fauces clean. Albuminuria. No serum reaction.

16/13 Voice nasal. Albumin - trace. No serum reaction.

8/11/22 Vomited. H.S.N. Pulse and colour good.
35

14/41 Ht. irregular. Colour good. Tumidity of abdomen. Liver not enlarged. Voice continues very nasal.

27/54 Double int. strabismus. Voice continues nasal.
Ht. Regular.

5/12/22
63 Voice less nasal. Squint less.

19/77 - Eyes normal. Voice slightly nasal.

11/1/23
100 Voice clear.

10/2/23
130 Transferred to convalescent hospital.

SEVERE FAUCIAL DIPHTHERIA. Case 12.

G.S. Male Aet. 5. 4th day case.

9/4/22 Sore throat, vomiting, (Patient convalescent after an attack of scarlet Fever)

12/4/22 (on admission). Throat - membrane covering tonsils, pillars and post. pharyngeal wall "Bull neck". (Cervical Adenitis). Dyspnoea. Some stridor. No recession of chest wall. A.T. 24,000.

13/5 Fauces oedematous. Membrane of similar distribution. Ht. regular. A.T. 18,000.

14/6 Membrane still extensive. Glands as noted. No rhinorrhoea. Ht. regular, force and tone good.

15/7 Membrane disintegrating. Adenitis less.

17/9 Fauces clean.

21/13 Marked urticaria on face and arms.

22/14 Puffiness under eyelids. Rash general.

23/15 Oedemia of penis.

27/19 Oedemia subsided. Albuminuria.

28/20 Urine clear.

11/7/22 No paralyses. Discharged.
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