

University of Glasgow.

Thesis for the Degree of M.D.

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Title.-

Albuminuria and Nephritis occurring
in connection with Scarlet Fever in combination
with Varicella, the Varicella occurring during
the Acute Stage or during the period of Convalescence.

Presented by

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When acting as one of the Assistant Physicians in the City of Glasgow Fever Hospitals at Belvidere, and Kennedy Street, during the years, 1893 and 1894, several outbreaks of Chicken Pox occurred amongst the Scarlet Fever patients, in the wards of which I had charge during the period referred to, occasioned chiefly by patients admitted incubating the disease. And amongst those so affected I remarked, that decided Albuminuria, and Acute Nephritis occurred in a considerable proportion, and in several cases, that the Nephritis was markedly severe.

Accordingly I set myself the task of endeavouring to find out whether the occurrence of Chicken Pox during the acute attack of Scarlet Fever or following soon after, had any causative relationship to the occurrence of Albuminuria, and of Nephritis, or of rendering ^{attack of} an Nephritis which would have ensued in the natural course of events, more severe.

The following questions therefore occurred to me as worthy of investigation.

1. As to whether the occurrence of Albuminuria, and Nephritis in the cases under consideration

was of the nature of a coincidence, and would have occurred in the ordinary course of Scarlet Fever, or whether the development of Chicken Pox was a factor in determining the appearance of the renal symptoms, or if already existing, it contributed to render the renal condition of more serious import.

2. If so, are we to regard this as generally applicable to cases of Scarlet Fever occurring in combination with Varicella.

3. If this be found to be true of such cases, can any cause be assigned for the increased tendency for the renal functions to become impaired, or for the degree of impairment to be greater than if it occurred in connection with Scarlet Fever alone.

In looking into the literature of the subject I find no definite record of any inquiry into the question of the significance attaching to Albuminuria and Nephritis occurring in connection with Scarlet Fever in combination with Chicken Pox, although Henoch, who has placed on record four cases of Chicken Pox in which Nephritis occurred as a complication, mentions that serious consequences may arise from

the combination of Varicella with other diseases — Scarlet Fever, Measles, and Diphtheria. (1)*

In virtue however of the great differences which Scarletinae Nephritis presents both as regards the relative frequency of its occurrence, and as regards the degree of severity, it seems to me a matter fraught with much difficulty to determine whether the disease superimposed, as it were, namely Chicken Pox plays any part in determining the occurrence of Albulinuria or Nephritis, or in rendering what would otherwise be an attack of moderate severity, one of grave import.

There can be little doubt that in the majority of instances Chicken Pox by itself, runs a comparatively mild course, and is seldom attended with danger.

The temperature, which in most instances keeps within a limited range, occasionally reaches a height of 103° or 104° F., and it may be even higher; it however quickly recedes. In cases attended with high temperature the eruption is usually copious, the individual papules and vesicles being numerous and the rash extensive, and an erythematous blush is frequently present.



* vide References pages 86 and 87.

Moreover the contents of the vesicles in these cases early undergo a purulent change.

Deep ulcers may form at the seat of the pustules situated in parts specially exposed to pressure, for example, on the back of the scalp; over the sacrum, etc.. Actual gangrene of the skin and subcutaneous tissues may take place.

In one such case which I met with in private, as the result of a slough over the left side of the occiput, the deep cervical glands became involved, and an extensive abscess formed on the left side of the neck, which burrowed underneath the sterno-mastoid muscle, so that it became necessary to make an incision in front and one behind that muscle, in order to secure efficient evacuation of the cavity, and drainage. It should be mentioned that the child was seven months old, and was ill-nourished.

Dr. MacCombie states that Pleurisy, secondary abscesses, and Pyaemia, may follow an attack of Varicella, and death ensue, and that such complications and sequelae are usually observed in unhealthy and ill-nourished children.

A Haemorrhagic form of the disease is also described, in which haematemesis, and melena, are said to occur along with haemorrhage into the

Cutis under the vesicles; so that while the disease most frequently follows a mild and uncomplicated course, it does not invariably do so. (2.)

Still until recently the complications and sequelae of Varicella were regarded as unimportant. It has been found however not to be so devoid of harm, or even of danger, as was generally supposed, especially in the case of very young children.

One of the complications stated to occur is Nephritis. As mentioned above, notes of four such cases are recorded by Henoch. (3) Oedema, accompanied by albumenuria set in from 8-14 days after the appearance of the eruption of Chicken Pox. In most, the eruption was copious, and accompanied by fever. In one, the youngest, a child, aged 2 years, it proved fatal. In this case there was evidence of syphilitic disease. In the others, recovery took place from 15 to 32 days later.

G. W. Rachel (4) records a case of Varicella in which Nephritis, and oedema of the feet, and face, were observed during the eruptive stage. The urine was moderately albuminous for 12 days. A careful search for evidence of Scarlet Fever was made, but nothing to vindicate that that

disease had been present, was found.

Of seven cases kept under observation for several weeks by the same author, symptoms of Nephritis were noticed in one, the youngest, a child aged 6 months. On the third day the vesicles showed signs of drying, and the febrile symptoms were subsiding. There were a few large patches over the left buttock, and sacrum, formed by vesicles becoming confluent. At this time it was noticed that very little urine was voided; there was however no discomfort connected with the act of miction.

The feet and hands were swollen. The swelling was so marked on the dorsa of the hands, that the fingers could not be flexed; they were immovably fixed in extreme extension, with the thumb adducted. The pupils were moderately contracted. The child was restless, and refused to use the feeding bottle. The fonticilles gave the impression of high tension of the contents of the brain.

On the sixth day the oedema was less, the skin on the dorsum of the hands still pitted on pressure. Very little urine was passed.

On the seventh day a specimen of urine was obtained for examination. A moderate amount of albumen was obtained on boiling. The quantity of

7.

urine passed was greater, and the edema entirely gone.

On the twelfth day a trace of albumen was still present.

On the fourteenth day the urine was normal. The author concludes by saying, that possibly the severity of the attack had something to do with the occurrence of Nephritis, as it was the only one of the seven cases in which the eruption showed a tendency to become confluent, especially over the chest, and neck. In the six other cases no signs of nephritis were found.

Similarly other observers have placed cases of Varicella attended with Nephritis on record.

Hoffmann (5) Rasch, (6) Semtschenko, (7) and others. The last-mentioned noted that the Nephritis occurred on the third day.

In accepting the testimony of these observers we are forced to conclude that Nephritis may, and does occur as a complication, in connection with Varicella alone; and that it may show itself during the first few days of the disease — as in the cases furnished by Rachel, and Semtschenko, or at a later date — as in those by Henoch, and that

in the case of unhealthy children it may assume a severe form.

The conclusion then to be drawn from the evidence before us is that Varicella by itself, may under certain circumstances exercise a selective and beneficial influence on the kidneys, thus resembling to some extent Scarlet Fever, Diphtheria, and Measles, although differing from those diseases in being more seldom attended by evidence of impairment of the functions of the kidneys.

Of the infectious diseases just mentioned, Scarlet Fever is the one in which Nephritis holds the chief place as a complication, or sequela, in virtue of ^{its relative} frequency, and significance.

And one of the principal features of the scarlatinal process, to the significance of which much attention has been devoted, is the presence of albumen in the urine. (8) (9) (10) (11)

It may appear in such small amount in the course of Scarlet Fever, as to be just perceptible as a faint cloud on applying the heat test with acetic acid; or the whole column may quickly coagulate. All gradations are found between these two extremes. Accordingly at this point of our inquiry ^{it is necessary} to define clearly what we mean by the term 'Albuminuria', and what by Nephritis.

Authorities differ widely in regard to the significance they attach to each, clinically and pathologically.

As is well known, a trace of albumen sometimes appears in the urine during the febrile state; it is common to the various diseases attended with pyrexia. It is transitory, disappearing with the receding temperature, and is followed by no signs

of alteration of the renal functions. To this febrile form of Albuminuria however we do not refer, although when it occurs in connection with Scarlet Fever it may be a matter of extreme difficulty, or impossibility to say whether or not the Albuminuria is due to certain changes in the kidneys incident to Scarlet Fever. For thus early in the disease, that is to say during the first few days, or during the acute stage, albumen sufficient only to show a faint or deep cloud may appear in the urine, and remain present for several days.

There may be no symptoms, or signs besides this referable to the kidneys. Inasmuch however as the albumen may suddenly become greater in amount, and blood suddenly appear, or a more gradual increase in the amount of the albumen take place, and inasmuch as symptoms indicative of pronounced renal changes, such as pallor of the face and lips, puffiness under the eyes, restlessness, sickness and vomiting, may set in subsequently, I think we are warranted in regarding these slight forms of albuminuria, in which only a very small amount of albumen is regularly detected even for a short period, as representing certain departures from the normal

renal condition differing only in degree from those found in the more severe forms of the renal affection.

(The different phases of the pathological condition will be considered at a later stage.)

I believe therefore that we must look upon this condition, i.e. Albuminuria, whether occurring late or early in the disease, as implying certain changes in the kidneys other than functional disturbances.

Further support is given to this view by the fact that at a later stage, that is to say, during the third week, and for several weeks thereafter — — the period during which the severe affection of the kidneys most frequently occurs, a trace of albumen may be present on two, or three occasions in succession, and disappear, to reappear once, or often for brief periods during the time that the patient is in hospital.

Moreover, albumen in larger amount, or blood, may suddenly make its appearance, and after one or perhaps two days, either or both may as suddenly disappear, to reappear abruptly after a lapse of some days, and after remaining present for a brief period may again disappear as abruptly

as they came.

Again, it is a fact worthy of note in this connection that Scarletinal Nephritis, ~~which may~~
~~it~~ may occur without any ^{albumen} ~~waste~~ being detected
 in the urine, although careful search has been
 made, or it may be detected at one period,
 and subsequent examination may fail to reveal
 its presence, and yet, when examined post mortem,
 the kidneys may present the appearances peculiar
 to genuine Nephritis of Scarletinal origin.

(9.) (10) (12) (13)

From a consideration of these various circumstances then, I think we are fully justified in regarding the presence of this particular sign on several occasions in succession, although unaccompanied by any other symptom referable to the kidneys, as an evidence of slight renal changes, and as a condition which may at any time assume a more serious form; ^{at the same time} while bearing in mind the circumstance that transitory forms of slight albuminuria, such as occur during health more frequently than was at one time thought, may likewise present themselves during the course of the diseases under consideration (15).

We apply the designation Albuminuric, then

to the presence of albumen in the urine, varying in amount from that which is just sufficient to give rise to a faint cloud on boiling, and acidulating with a few drops of acetic acid, so that which is sufficient to produce a considerable deposit, when it is unattended by other symptoms, such as those mentioned, (page 10.) indicative of interference with the renal functions. The term *Albuminuria* then refers merely to one manifestation of an altered state of the renal functions; and in the absence of other signs confirmatory of decided changes in the kidneys, it is arbitrarily employed here to denote a condition in which the urine is free from blood or blood colouring matter; although as has been explained it is believed that the term used in this limited sense implies certain alterations in the kidneys akin to those found in severe forms of the renal affection, that it implies definite, if slighter changes, in those organs. (14) (16)

In thus defining the sense in which the term *Albuminuria* is employed, I have likewise indicated what is implied by the term *Nephritis*. As has already been pointed out, from the imperfect state of our knowledge regarding the relation between

the clinical and pathological aspects of the subject, any distinction such as that proposed, must be an arbitrary one.

The difficulty of determining the relationship between the presence of albumen in the urine, and the actual nephritic process, has I believe much to do with the widely different results arrived at, as regards the frequency and significance of Scarletinal Albuminuria, and Nephritis.

While other important factors are the character of the epidemic; (20) the particular mode, and also the regularity and frequency of testing the urine; while much must no doubt be attributed to the skill and care of the individual observer.

Subjoined are a few of the results arrived at by different observers, bearing on this point.

Out of 5443 cases of Scarlet Fever, Goodall found 8.47 per cent with Nephritis, that is in which albumen was present on more than one occasion, and not febrile (10)

Out of 4015 cases Gaiger found Albuminuria or Nephritis in 4.69 per cent. (17).

Sørensen found 20 per cent. out of 365 cases. (18)

Out of 180 cases R. J. Thomson found 62.2 per cent. (9)

Out of 91 cases F. Dittmar found 52.7 per cent. (11)

The above results show that no real comparison can be made, in the absence of some common basis.

Accordingly in my endeavour to discover whether any increase in the frequency of Albuinenuria and Nephritis after the occurrence of Chicken-Pox in the course of Scarlet Fever, took place; or whether the condition was in any way aggravated; I saw that it was necessary to institute a comparison between cases occurring at the same time, that is to say, during the same epidemics, and as far as possible under conditions which obtained throughout.

Accordingly I first sought to find ^{out} the proportion of cases of Scarlet Fever by itself, in which Albuinenuria and Nephritis occurred during a given period.

I next proceeded to find out the ratio which the number of cases in which Albuinenuria; and Nephritis

appeared when both diseases coexisted, bore to the total number of cases in which Scarlet Fever and Variola occurred in combination.

And in the third place I compared the results obtained in both cases.

The cases observed at Belvidere Hospital, and those at Kennedy Street Hospital were taken separately.

Those in which Albuminuria in the slightest form occurred on more than two occasions, together with those in which more decided evidence of the presence of albumen was found, were grouped along with those in which more pronounced symptoms, and signs of renal mischief were manifest, for the reasons given above.

The urine in each case was tested morning and evening during the first eight, or ten days, or until the temperature came down to normal, then once daily, till the end of the third week, the specimen being obtained chiefly in the morning. Afterwards the urine was examined every alternate day till dismissal, unless albumen, or blood, colouring matter was detected, or some other symptom or sign of Nephritis showed itself, in which case the urine was examined morning and evening till the disappearance of such ~~adventitious~~^{expansive} substance from the urine, and at least once daily.

for a week thereafter.

In those cases in which Chicken Pox occurred in addition to Scarlet Fever, the urine was examined morning and evening while the eruption was present, and once daily after the vesicles had dried until the crusts had separated.

In a large number of the cases of Scarlet Fever attended, and unattended with Nephritis, the examination of the urine was undertaken personally, while in those in which Chicken Pox occurred in addition special attention was paid to the examination of the urine during the period mentioned.

In a number of cases the uriniferous sediment was examined microscopically.

The number of patients in the City of Glasgow Fever Hospitals at Belvedere, and Kennedy St., suffering from Scarlet Fever, during the periods referred to, the years 1893 and 1894, was greatly in excess of any previous year, and this made it well nigh impossible to make such an examination either as systematic, or thorough, as one would have desired.

In testing for the presence of albumen the method practised was as follows. —

The reaction was taken, then the cold test with nitric acid was applied as being the one most expeditiously carried out, care being taken however to prevent the mingling of the two fluids, at the zone of contact.

With this the heat test with acetic acid was frequently combined, and if there seemed to be any fallacy, or any doubt as to the result the picric acid test was resorted to.

While for the purpose of detecting blood, and blood colouring matter, the guaiac test, and the microscope were employed.

The same conditions as regards diet were maintained throughout, and the same principles of treatment followed, namely purgatives; linseed poultices to the loins; packs; in severe cases with scanty urine, dry cupping; ^{severe and} protracted cases to avert the supervention of uræmic symptoms, nitro-glycerine; and in the event of uræmic convulsions occurring chloral suppositories and the administration of Chloroform.

All the cases enumerated below, including those in which Chicken Pox occurred in combination with Scarlet Fever, were, with one or two exceptions under my care till dismissed; and all are consecutive.

The usual period during which patients are kept in hospital is fifty six days, dating from the commencement of illness, accordingly my observations have reference to the occurrence of Chicken Pox concurrently with the Acute Stage of Scarlet Fever, or during the period between the termination of the acute stage, and that of the patients' residence in hospital.

Cases under observation at Belvidere Hospital.

Total number of cases of Scarlet Fever irrespective of the occurrence of Chicken Pox.	} 446.
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From that number, 52 must be deducted, made up as follows:-

Children 1½ years and under in which the urine was not obtained for examination.	} 11.
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Cases of unusual severity in which the urine was passed involuntarily and was not obtained for examination.	} 3
---	-----

Cases in which Chicken Pox occurred.	} 38.
--------------------------------------	-------

52.

After deducting 52 from the total number of cases
424 is left.

Of these 424 cases, 64 presented signs of
decided Albuminuria, and Nephritis,
that is 15.80 per cent.

While of the 38 cases in which Chicken Pox
occurred, 8 presented signs of decided
Albuminuria, and Nephritis;
that is 21.05 per cent.

Cases under observation at Kennedy St. Hospital.

Total number of cases of Scarlet Fever
irrespective of the occurrence of }
Chicken Pox. } 924

From that number 36 must be deducted,
made up as follows:-

Children $1\frac{1}{2}$ years and under in which
the urine was not obtained for }
examination. } 7.

(Carried forward from p. 20

7)

Cases of unusual severity on which the urine was passed unwillingly, and }
 Could not be obtained for examination. }

15.

Cases in which Chicken Pox occurred.

14.

Total

36.

After deducting 36 from the total number of cases 888 is left.

Of these 888 cases 125 presented signs of Decided Albuminuria, or Nephritis, or 14.07 per cent.

While of the 14 cases in which Chicken Pox occurred 4 cases presented evidence of Decided Albuminuria or Nephritis, or 28.24 per cent.

In either case the percentage of instances in which Albuminuria of a decided character, and Nephritis occurred subsequent to the appearance of Chicken Pox, or was accentuated, is much greater than the percentage of cases in which that complication or sequela occurred in connection

with Scarlet Fever alone.

I find moreover that the smaller of these two percentages of cases of Albuminuria, and Nephritis occurring in connection with the two diseases in combination, namely 21.05 per cent., is made greater than either of those given as occurring in connection with Scarlet Fever, in the North Eastern Hospital, belonging to the Metropolitan Asylums Board, during the corresponding years, the figures being as follow

	Total number of cases.	Percentage in which Albuminuria and Nephritis occurred.
In 1893.	3005	13.1 per cent.
In 1894.	2104	13.3 per cent.

Again, the smaller of the two percentages, namely 21.05 is also greater than the highest percentage of cases of Scarlet Fever with Albuminuria, and Nephritis recorded in the Annual Reports of the hospitals of the Metropolitan Asylums' Board, from the year 1888 to the year 1894 (both years inclusive.)

The highest was in 1889, when out of 3414 cases
~~there were~~ ^{if was} 20.5 ~~cases~~ per cent.

I do not however lay any stress on comparisons other than those made under conditions which are as far as possible the same throughout.

It may legitimately be urged that the number of cases adduced, in which a combination of the two diseases took place is very small. That is so, and for that reason I have no desire to attach more than the proper value to the purely statistical aspect of the question, which must I believe be considered along with the leading features of the actual cases involved, ere we can pronounce upon the merits of the question at issue.

I would however observe again in this connection that the cases above enumerated occurred consecutively during the same periods, and under like conditions, as regards environment, and régime, and the examination of the urine, also that care was taken to exclude as far as possible any source of inaccuracy such as might arise from doubtful diagnosis, especially as regards the presence of Scarlet Fever, and also in connection with the Varicellar attack.

And now I propose to submit the particulars bearing on the question at issue, of those cases in which Chicken Pox occurred in connection with Scarlet Fever, and in which the complications referred to ensued, or of existing beforehand, returned, or were accentuated, together with our analysis of, and comments on those cases.

The Cases are taken in chronological order.

*Series I. Consisting of 8 cases met with at
Kennedy St. Hos Belvidere Hospital*

*Case 1. J.R. age. 6 1/2 years; admitted on 1st day of illness.
Distinct rash generalized.*

*Faucis reddened; tumefaction of soft palate.
Trace of albumen in urine.*

*16th day. Trace of albumen present for the first five days,
then on the 13th and 14th days.*

*This afternoon patient began to complain of headache,
evening temperature was 103.6° F.*

*Only 15 oz. urine passed during the last 12 hours.
It was dark red in colour, and contained albumen
and blood, in considerable amount.*

*Copious sediment consisting of urates; granular debris;
red corpuscles, and also of epithelial, and hyaline*

Cards.

Several clear vesicles have appeared on the head and chest.

14th day. Throat much improved, and glands less swollen.

Was sick during the night, when only 2 oz. urine were passed. No oedema nor dyspepsy.

18th day. Urine still very scanty; small amount of blood present, and considerable amount of albumen.

19th day. Was sick and vomited once during the day; has however been altogether more restful.

Slight general oedema of face; lower eyelids not markedly involved; no oedema in other parts seen. Urine contains less blood. Still very scanty and highly albuminous.

20th day. Sick once - in the evening; bowels moved freely; large quantity of urine passed during the day; temperature subnormal; pulse 80, of high tension; right ear has begun to discharge to-day.

22nd day. No sickness; 19 oz. urine passed during last 24 hours; still contains a small amount of blood; it is smoky, and of slight red tint.

No discharge from ear is less.

23rd day. No sickness; 20^{oz} urine passed in 24 hours. Still smoky; no red tint. Amount of albumen less.

24th day. Free from sickness; 23 oz urine passed; smoky; colour red; amount of albumen, same. pulse 80, of high tension; irregular.

25th day. Pallor of face, and puffiness of lower eyelids observed,

Blood and albumen present; albumen less in amount, almost corresponding to the amount of blood present.

26th day. Urine passed this evening straw-coloured; responded slowly to the test for blood;

27th day. Temperature normal, and frequently subnormal; pulse irregular.

41 oz. urine passed in 24 hours. Blood and albumen same in amount as on previous day.

28th day. 60 oz. urine passed; has slight smoky tint appearance; otherwise the same.

Pulse 65; irregular; no systolic murmur heard. Several vesicles on the head, and chest have become pustular, and are surrounded by hyperemic areas.

29th day. Condition of urine the same.

Oedema of the face, and puffiness of the eyelids still present. Pulse 65, not so hard, irregular; soft ventricular Systolic murmur, loudest at midsternal; also heard at apex. Accentuation

of second aortic sound.

34th day. Quantity of urine increasing; 43 oz passed in 24 hours; no response to Guaiac test; albumen very small in amount.

Systolic murmur scarcely heard; pulse more regular.

43rd day Upwards of 60 oz urine passed in 24 hours; blood can just be detected; amount of albumen small. Heart sounds, pure.

The pallor has disappeared from the face, and also the oedema.

59th day. Continued improvement; 40 oz. urine passed daily; absence of blood for more than a week; trace of albumen remains.

54th day. Urine abundant; blood present in small amount, from 53rd day, with small amount of albumen, more than would be accounted for by the presence of blood alone.

95th day. Has been improving steadily; entire absence of albumen since the 60th day.

Recovery complete; dismissed.

Case 2. R.R. age 4½ years; admitted on 1st day of illness.

Rash somewhat faint; distinctly seen on chest, abdomen, arms and legs.

Tongue coated with brownish white fur; fauces deeply injected; tonsils enlarged, bright red; accumulation of yellowish deposit on the surface of each.

Submaxillary glands on right side, enlarged.

Temperature on admission 101° F.

Heart sounds pure; normal in rhythm.

Urine contains urates in abundance, also a faint trace of albumen can be detected.

45th day. Pursued a mild course; no albumen present except faint trace on admission.

Has been convalescing satisfactorily and out of bed; an eruption of papules and vesicles appeared to-day on the head and face, and also on back, and chest; no red papulae, or erythematous rash present.

Morning temperature normal; evening temperature 100° F. Urine contains blood in small amount and albumen in amount apparently out of proportion to the blood.

46th day. Morning temperature 99° F. A few fresh vesicles seen in the same situation; eruption not abundant.

Face paler than before; no oedema, nor drophoy;

no diminution in the quantity of urine; albumen sufficient to form deposit, small amount of blood.
53rd day. Vesicles have dried, and crusts have almost all separated. Small amount of blood present until the 57th day, when albumen alone was present in small amount, as also on 52nd day.
63rd day. Urine entirely free from albumen since the 52nd day.

Nimisized, completely recovered.

Case 3. M. M. age 4 years. Admitted on 10th day of illness.

History of sickness, and sorethroat 9 days ago; swelling in neck noticed 6 days ago.

Dry papular condition of skin, especially on extremities.

Fauces, red and soft palate oedematous; tonsils enlarged, especially the left; darkly white fur on tongue.

Slight bilateral enlargement of glands at angle of jaw; cervical glands on left side also enlarged; and neck has a brawny feeling for some distance around the enlarged glands.

Temperature on admission 101.8° F.

Urine free from albumen.

11th day. Deep fluctuation in swelling on left side of neck. An incision was made and exudate given to a quantity of pus and serous fluid. Drainage was established and the wound dressed antiseptically.

18th day. Cavity in neck filling up by union of granulations; wound draining satisfactorily; temperature last evening was 102° F.; this morning 99° F.

Quantity of urine passed in 24 hours very small - only 4½ oz. Blood present in small amount; and albumen greater in amount than would be

accounted for by the small amount of blood.

27th day. An eruption consisting of papules and vesicles has appeared. It has the characters of the eruption of Chicken Pox. Febrile disturbance is slight. Albumen is larger in amount; blood, same in amount; and urine is very scanty.

24th day. Urine continues scanty; amount of albumen very considerable; blood stationary in amount.

54th day. Steady improvement has been taking place since last note; the urine is normal in quantity.

A trace of albumen remained until 3 days ago. Urine is now entirely free from albumen and blood. Wound is almost healed.

68th day. Dismissed, completely recovered.

4. January 1894 - February

Scarsell, S.
DAY OF
ILLNESS.
C. Pox.

DATE	29	30	31	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Scarsell, S.	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
DAY OF ILLNESS.	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M	M
C. Pox.	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E

107°
106°
105°
104°
103°
102°
101°
100°
99°
98°
97°

Temperature - Fahrenheit

Use.
sp.
wels.
Urine Oz., Alb,

Trace

Concret.
Secret.

Urine passed involuntarily.

Case 4. C. M. age 2 years. Admitted on 4th day of illness.

Fading rash with distinctive characters seen, and also a dry papular condition on trunk.

Reddening of fauces with oedema of uvula, and soft palate.

Tongue cleaning; presents the "strawberry" characters.

Slight bilateral enlargement of the submaxillary glands.

Temperature on admission 101.2° F.; pulse rapid.

8th day. The temperature keeps above 102° F.; restless; has a sunken aspect; profuse muco-purulent ~~expectoration~~ secretion on tonsils and posterior wall of pharynx; also yellowish patches of exudation seen on tonsils. Seropurulent discharge from nostrils & large number of papules and vesicles appearing on face, trunk, and limbs.

A trace of albumen appeared in the urine yesterday.

9th day. Patient becoming weaker; glands on either side of neck becoming hard and brawny; no deep fluctuation can be discovered; throat dusky red; secretion more viscid; discharge from nose purulent and offensive; pulse rapid and feeble.

A fresh crop of vesicles seen; vesicles of earlier

crop, drying. Eruption, copious. Red areas round many of the vesicles.

Since the 4th day of illness the urine has been passed involuntarily; previous to that no albumen was found in the urine.

16th day. Patient's condition becoming worse, although the temperature remains within moderate limits - ranging between 100° and 102.2° F. with morning remission; it was previously inverted. Pulse small, soft, and rapid.

Specimen of urine obtained to-day; albumen present in large amount; no blood detected.

19th day. Increasing weakness; since yesterday morning temperature has been rising higher, and higher. Pulse more feeble; no specimen of urine obtained since last note.

20th day. Hyperpyrexia; death.

A post-mortem examination was not obtained.

Case 5. R.P. age 6 years. Admitted on the 2nd day of illness.
Diffuse blush on trunk, and legs; red mottling
on forearms.

Fauces reddened; both tonsils enlarged; left much
more so than right. Creamy fur on tongue.

Submaxillary gland on left side enlarged.

Urine contains albumen, sufficient in amount
to form a deposit.

Temperature 103.2°F .

8th day. The temperature has been normal since
the 3rd day.

Urine is passed in sufficient quantity, - upwards
of 40 oz. daily; a trace of albumen has been
present continuously from the 2nd day.

No pallor of face; no oedema of feet or of face.

14th day. Faint trace of albumen for one or two days
alternating with absence of albumen for a like
period.

28th day. Submaxillary glands enlarged, and painful;
trace of albumen present; no blood.

44th day. Trace of albumen for one or two days alter-
nating as before with absence of albumen for
several days until to-day; albumen in larger
amount; no blood; no oedema nor dropsey.
no sickness.

56th day. Urine free from albumen on 54th and
55th days

Numerous red papules and vesicles on face, trunk,
and legs

Constitutional disturbance not marked.

Urine found to be again highly albuminous.

No blood present.

48th day. Urine now free from albumin for ten
days, and all crusts have separated.
Disinised, well.

Case 6. J. B. age 4. Admitted on 2nd day of illness.

Moderately bright rash seen on trunk, arms and legs.

Bilateral enlargement of submaxillary glands with tenderness.

Fauces reddened; tumefaction of soft palate, and pillars of fauces; tonsils also much swollen.

Tongue glazed and rather dry.

Urine contains a trace of albumen.

8th day. The urine has contained a trace of albumen till to-day when it was clear.

29th day. The temperature which has been almost normal during the past 8 days, rose this evening to 100.8° F. No complaint of sickness.

The urine contains a deposit of albumen; also blood in small amount.

40th day. Blood in small amount, and albumen sufficient to form a deposit, present till the 34th day.

On the 34th and 38th days blood was absent, and the albumen smaller in amount.

On the 39th day only a trace of albumen was present. It was clear to-day.

45th day. The urine has remained clear since the last note was made.

55th day. A number of isolated papules, and vesicles, having the characters of the eruption of Chicken-Pox appeared on the face, chest, abdomen, and legs. The temperature rose this evening to 104° F. Albumen returned in small amount; no blood present.

44th day. The eruption was moderately copious; the crusts have now separated.

The albumen remained present for 4 days. It has been clear since.

Dismissed, well.

Case 4. J. F. act. 4. Admitted on 2nd day of illness.

Moderately bright rash, punctate, seen on arms, legs, chest, and abdomen.

Fauces bright red; slight oedematous swelling of soft palate and uvula; tongue cleaning.

Urine, clear.

6th day. Urine clear until to-day; contains both blood, and albumen, the former in small amount; the latter sufficient to give rise to a deposit; slight diminution in the quantity of urine passed.

13th day. Albumen still present in small amount.

No blood detected.

24th day. Quantity of urine has been increasing; no blood has been present since last note was made; but albumen has been present in the form of a trace for two or three days at a time, more than once. The temperature has been above 102°F . for the last two evenings; and to-day an eruption of vesicles, on chest, abdomen, arms, and legs appeared; albumen has reappeared in the urine, sufficient in amount to form a deposit; no blood detected.

36th day. Eruption was moderately copious; the crusts have separated. Albumen found during five days in succession and in decreasing amount; has been clear since then. Dismissed, well.

Case 8. C. S. act 8. Admitted on 2nd day of illness.

Moderately bright rash, diffuse, seen on limbs, and trunk.

Hyperaemia of fauces; moderate oedematous swelling of uvula, and soft palate; tonsils swollen and lobulated; tongue moist, clean at tip; papillae prominent.

Submaxillary glands on each side, enlarged.

Urine clear.

24th day. Course mild and uneventful up till this time.

A number of small red papules, and oval and rounded vesicles have appeared on legs, and anterior aspect of the body, and left side of the face; an erythematous blush on chest, abdomen, and back, seen.

The urine contains a small deposit of albumen; but no blood.

28th day. A few vesicles on the back are beginning to dry while fresh ones are appearing;

24 oz. urine passed in last 24 hours; albumen the same in amount.

56th day. Two days after last note was made, only a trace of albumen was present in the urine, this remained for two following days; it was clear afterwards.

Dismissed well.

Series II. Consisting of 4 cases
met with at Kennedy St. Hospital.

Case 9. M. M^c.A. age 6. Admitted on the 4th day of illness.
Rash well-defined, discrete, and moderately bright;
well out on chest and arms.

Faucial arch reddened; uvula ^{and} soft palate
oedematous; both tonsils swollen; accumulation
of muco-purulent secretion in pharynx.

Tongue, moist; general surface smooth, and studded
in front with swollen papillae.

Submaxillary glands on left side slightly enlarged
and tender.

Temperature on admission $101.8^{\circ}\text{F}.$

Urine clear.

6th day. Range of temperature moderate, highest
temperature till this evening being $101.8^{\circ}\text{F}.$; rose this
evening to $103.4^{\circ}\text{F}.$

Eruption of minute red papules, and vesicles has
appeared to-day; they are not numerous; and are
situated on the face, chest, and abdomen.

Urine, not scanty; free from albumen.

8th day. A fresh crop of vesicles has appeared to-day,
principally on the chest and abdomen; the others
are drying; no albumen present.

10th day. Temperature descending;

A trace of albumen was present in the urine morning and evening.

11th day. Albumen sufficient in amount to form a small deposit, this morning; in the evening only amounted to a trace.

24th day. The urine has now been clear for a week; one or two crusts still adherent.

56th day. All crusts have separated.

Dismissed, well.

Case 10. M. C. age 5½ Admitted on 2nd day of illness.

Discrete, well-marked rash seen on chest, abdomen, legs and arms; there are also seen a few pustules, several irregularly rounded crusts, and cicatrices on head, trunk, and limbs presenting the characters of a fading Varicellæ eruption.

Faeces reddened; both tonsils swollen and of deep red colour; accumulation of purpury deposit on each. Submaxillary lymphatic glands on each side are enlarged, and tender.

Urine, clear.

13th day. Temperature during the first few days was moderately high; it did not exceed 102.4° F.; and came down to normal on the 8th day.

The urine was clear until the 11th day.

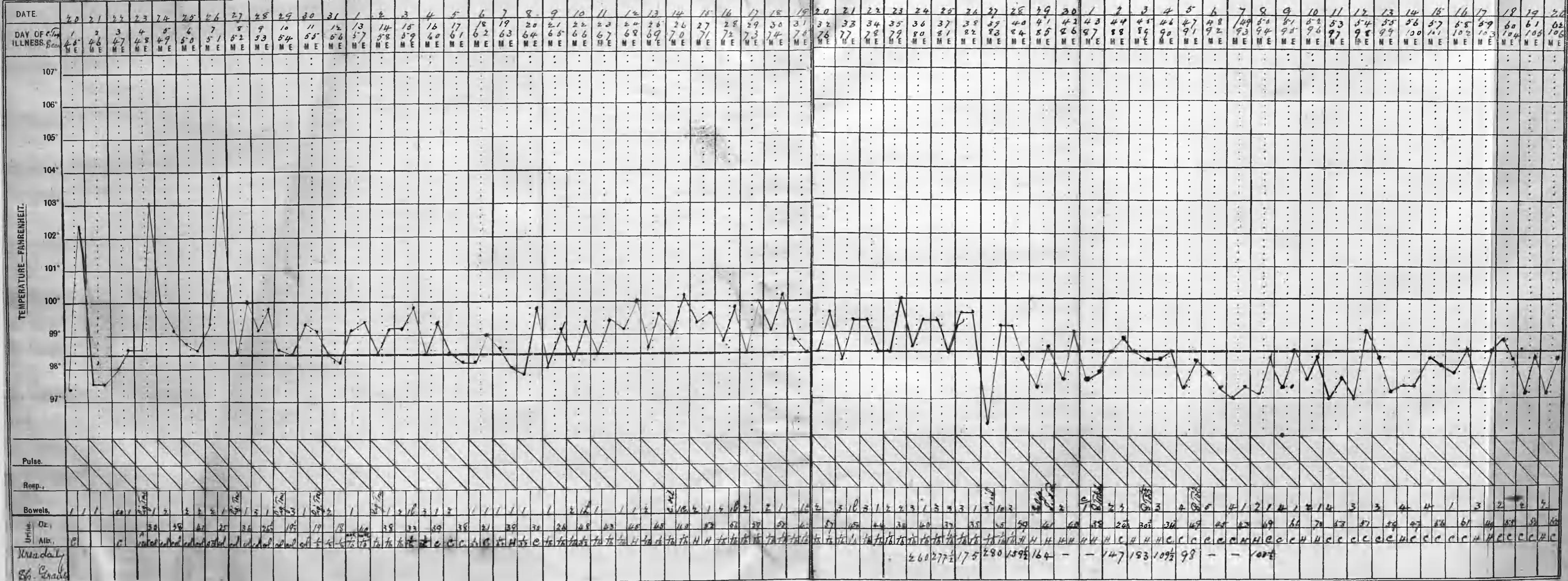
The pustules have dried forming crusts some of which have separated.

The urine is not diminished in quantity; has contained a trace of albumen, morning and evening since the 11th day.

14th day. A trace of Albumen persisted till yesterday.

Urine is now free from albumen.

57th day. Urine has remained clear; progress uninterrupted. Dismissed.



Case 11. J. S. act. 4. Admitted on the 3rd day of illness.
 Bright confluent rash, generalized;
 Hyperaemia of fauces; no obvious oedema of uvula
 or soft palate.

Tongue, moist, presents the "strawberry" characters.
 The urine contains a trace of albumen.

30th day. A trace of albumen was also present on the morning, and evening of the 4th day; has been clear since then; on the 3rd and 4th days the temperature exceeded 103° F in the evening.

Afterwards course uneventful; allowed up to-day.

45th day. Temperature became elevated this evening - 102.4° F.

A number of minute red papules, and vesicles appeared to-day. Some of the latter are rounded, and others elliptical or oval, and stand out of the healthy skin like beads; the eruption is characteristic of Varicella.

Urine found to be clear.

46th day. A few fresh vesicles seen to-day principally on chest and abdomen; the temperature is not elevated.

The urine is clear.

48th day. Groups of vesicles drying, and fresh ones appearing. The temperature has risen this

evening to 103°F .

A very considerable amount of albumen has appeared in the urine; coagulation of the whole column takes place on boiling, and adding acetic acid. No blood is detected; the quantity of urine is not diminished.

59th day. Was sick during the day and vomited.

The urine not diminished in quantity; has a crimson tint; the amount of albumen is very large - same as on 48th day. Blood is present in considerable amount. It appeared yesterday for the first time. Microscopic examination of the sediment revealed the presence of numerous red blood corpuscles, renal epithelial cells; hyaline tube casts; and granular debris.

55th day. Quantity of urine passed smaller - 19 oz. in the last 24 hours; dark red in colour; blood less, as also albumen; the latter is however considerable in amount ($\frac{1}{2}$ column.)

Vomited during the night; was sick and vomited several times during the day.

60th day. A larger quantity of urine passed - 39 oz. There has been no blood present for 3 days. The amount of albumen is much smaller - deposit of $\frac{1}{6}$ column. Free from sickness.

99th day. There is a tendency towards improvement in the condition of the urine; deposit of $\frac{1}{16}$ column. It has also been clear on three occasions, and there has been a trace of albumen on two occasions. Urine passed in sufficient quantity.

88th day. Further improvement in the condition of the urine; clear this evening; not more than a trace of albumen morning and evening since the 84th day.

102nd day. A much larger quantity of urine passed; has exceeded 40 oz.

With the exception of one occasion, it has been clear morning, and evening for a week.

120th day. Urine has been entirely free from albumen for upwards of 10 days.

Patient's general condition, good.

Dismissed, completely recovered.

Case 12. J. H. age 5 $\frac{1}{4}$. Admitted on 3rd day of illness.
 Moderately bright rash, discrete, present on chest
 and arms.

Fauces reddened; moderate degree of tumefaction
 of uvula, and soft palate; no deposit on the tonsils.
 Tongue clean, bright red; papillæ prominent.
 Submaxillary lymphatic glands on both sides
 slightly enlarged.

Urine clear.

10th day. The temperature became normal on the
 6th day of illness; and has been going on well
 till last evening, when the temperature rose to 107.2° F.
 Does not complain of pain or discomfort.

11th day. An eruption observed this morning on trunk,
 legs, and arms; and slightly on face, consisting of a
 considerable number of vesicles, and a few minute
 red papules. The vesicles are clear bead-like and
 oval or rounded, and are set ^{the} healthy skin.
 The eruption is typical of Chicken Pox.

No sickness, nor headache.

Urine clear.

15th day. Fresh crops have been appearing daily; the
 eruption is copious, and semi-confluent; some of the
 vesicles are large and flattened, and umbilicated.
 Temperature has exceeded 103° F.

Urine has been entirely free from albumen until today, when albumen appeared in considerable amount. Blood also present, small in amount.

24th day. Many of the vesicles have become pustular; an erythematous rash is seen especially on the posterior aspect of the trunk.

The temperature has descended; remained low till this evening when it mounted quickly to 105.4° F. Albumen, larger in amount; ($\frac{1}{6}$ th column) also amount of Blood larger.

31st day. Slight improvement in the condition of the urine.

Albumen less in amount; also less blood; temperature running high, ranging between 103° F. and 104° F. pulse 120, not of high tension. Frequent vomiting; skin moist.

34th day. Increasing weakness; pulse 120 soft, and irregular. Respiration increased in frequency, 40. Dulness in both infrascapular, and lower axillary regions, where R.M. is very defective. Diarrhoea, with yellowish watery stools; became very restless during the night, and delirious; was very excited during the day; the vision became affected in a peculiar manner; patient spoke of seeing only one half of certain objects, for example,

he said he only saw ^{half of the} nurse's body, - she was standing in front of his bed; it was the left lateral half that he saw; On account of dyspnoea patient had to be propped in half-sitting posture.

There was oedema of the face, and of the arms, legs and trunk; patient becoming more prostrate, and urine becoming worse. Blood very considerable in amount giving the urine a ~~brown~~ ^{deep} red colour. Notable increase in the amount of albumen; tubercles present in abundance, epithelial and hyaline, chiefly the latter.

35th day. Became comatose; previous to this strabismus affecting left eye observed; rotated outwards. Did not regain consciousness; died same evening.

Permission was not granted to obtain post-mortem examination.

Number	Number of vehicles in traffic	Number of vehicles in traffic after onset of Vaseline	Character of traffic	Severity of disturbance	Result
1.	1st 16 min. 1/2 hr 1st - 60 and 13 pipe 16 min. 1st - 60 and 13 pipe 16 min.	1/2 hr 16 m to 60 m day Highways; moderately busy. 45 m to 52 m day. 45 m to 52 m day.	No vehicles	Slight and moderately obvious. Traffic disturbance moderate.	Complete Recovery.
2.	Neither	45 m to 45 m / 1st	No vehicles	Highways; moderately obvious. Traffic disturbance slight.	Complete Recovery.
3.	Nephritis, from 15% day.	22 m to 22 m - from 15% day.	Nephritis; severe.	Disturbance in severity. Traffic disturbance slight.	Complete Recovery.
4.	Neither.	30% to 30% 4?	Nephritis; severe.	Disturbance in severity. Traffic disturbance slight.	Fatal
5.	Allomimicra 2nd to 8m and 44 m to 54 m	35% to 35% / 1st	Allomimicra. Smaller no change to first attack. 35 m to 68 m day.	Disturbance obvious.	Complete Recovery.
6.	Allomimicra 1st to 8m	35% to 35% / 1st	Allomimicra; slight 35 m to 68 m day.	Disturbance moderately obvious.	Complete Recovery.
7.	Nephritis 6 m to 24 m	29% to 29% / 1st	Allomimicra; moderate. 24 m to 32 m day.	Traffic disturbance slight.	Recovery complete.
8.	Neither	24% to 29% / 1st	Allomimicra; moderate. 24 m to 32 m day.	Disturbance moderately obvious. Traffic disturbance slight.	Complete Recovery.
9.	Nephritis 22 m to 40 m	6 m to 33 m	Allomimicra; slight. 33 m to 40 m day.	Traffic disturbance slight.	Complete Recovery.
10.	Neither	1/1 m to 1/1 m	Allomimicra; slight. 1/1 m to 1/6 m day.	Traffic disturbance slight.	Complete Recovery.
11.	Neither	45% to 48% + 1st	Nephritis; severe and protracted.	Traffic disturbance slight.	Complete Recovery.
12.	Neither	11 m to 15 m 4 1/2	Nephritis; very severe. 15 m to 33 m day.	Traffic disturbance moderate.	Fatal

Of the 12 cases, in 4 Alburnuria, or Nephritis appeared for the first time, with or shortly after the onset of Chicken Pox, most frequently between the first and the fourth days.

Of these 4 cases two ended fatally, and in the case of the remaining five, in two severe attacks of Nephritis occurred, in a third an attack of moderate severity, and in the two which remained decided alburnuria for five and eight days respectively.

Of the two fatal cases, although a post mortem examination could not be obtained in either case, there can be no doubt that in one (case 12.) the renal affection was mainly, if not wholly responsible for the bringing about of the fatal issue.

The attack of Varicella was markedly severe, the vesicles being both abundant and large, and many becoming pustular. The constitutional disturbance was likewise great, and during this time the condition of the urine, with the exception of a brief interval of apparently slight improvement, gradually became worse, symptoms of a striking character indicative of the uraemic state, latterly presenting themselves. Hence a strong impression was made on my mind at the time that a close

connection existed in this particular case between the development of Varicella, and the intensity of the Nephritic process.

In the other case which proved fatal, without further information we are not justified in coming to any definite conclusion as regards the precise cause of the fatal issue. Here also it is to be noted that the eruption was copious, and the range of temperature high, and that the Nephritis occurred at the same period in the course of the Scarletinal attack, namely at the end of the second, or the beginning of the third week.

Of the five cases which still remain, in three, there were "early" attacks of Nephritis, or rather attacks of Nephritis which began early in the course of the Scarlet Fever, prior to the onset of the Varicella.

In one of these, a distinct accentuation of the signs peculiar to the renal affection took place after the eruption of Varicella appeared; and in the case of the other two, ~~even~~, an interval of three to fifteen days elapsed, during which the urine was free from albumen, followed in the one instance by albuminuria in slight form

lasting over several days, and in the other by Albuminuria moderate in degree and persisting for a similar period.

And while ⁱⁿ three out of the five cases Nephritis occurred prior to the onset of the Varicella, in the remaining two, Albuminuria occurred before that disease made its appearance; and on that disease appearing, in one case a severe attack of Nephritis set in, on the day on which the Varicellar eruption was first observed, lasting over forty four days; while in the other Albuminuria in a slight form returned, likewise on the first day of the Varicellar attack, lasting for twelve days.

It is to be noted that in both of these cases the eruption of Varicella was ^{markedly} ~~not~~ copious, nor was the febrile disturbance severe.

It will be observed also that the Albuminuria and Nephritis occurred most frequently ^{of all} on the first day of the Varicellar eruption, and with equal frequency on the 3rd and 4th days, and that only in one instance (Case 10) was it later in occurring — namely on the 11th day of Varicella.

With regard to the nature of the Varicellar attack it is to be remarked that of the six cases in which Nephritis, either very severe, or of moderate severity occurred in connection with the two diseases in combination, in three of these the eruption was copious, and the febrile disturbance considerable; in two ~~the~~ ^{the attacks} was moderately severe, and in one slight.

While of the six cases, in which Alburninuria occurred under similar conditions, in one the eruption was copious, and the febrile disturbance moderate;

in four the eruption was moderately copious, and the febrile disturbance slight in all but one, in which it was considerable; while in the remaining case the eruption was scanty, and the febrile disturbance slight.

And of the twelve cases, taken together, in which either Alburninuria or Nephritis occurred, in four the eruption was copious; in two of these the febrile disturbance was considerable, and in the remaining two, of moderate severity.

In five the rash was moderately copious; and of these, in one the febrile disturbance was considerable. In one it was moderate, and in the remaining three, slight.

In one the eruption was scanty, and febrile disturbance slight. (Case met with when vesicles were drying, and crusting and some becoming pustular.)

Or it may be stated more briefly thus.—

I. With regard to the rash,

In four cases it was abundant.

In seven cases it was moderately so, and

In one it was scanty, or apparently so.

II. With regard to the febrile disturbance,

In three cases it was severe

In three, moderately severe, and

In six, it was slight.

In the Nephritis peculiar to Scarlet Fever, as it is seen in hospital practice, oedema, in the experience of most recent observers is not of frequent occurrence. (9) (10) (16) Indeed Dr. Turner states that in his experience in those cases, marked oedema never occurs. And with the exception of one of the two

cases to be referred to I have not met with a case in which marked oedema, or anasarca occurred while the patient was in hospital. There was however in this particular instance, as we shall see, another cause which contributed to bring about the oedema, and to make it extensive.

Oedema was not a notable feature ^{of the cases} before us. It was present only in two cases (cases 1 and 12.) In the former there was a moderate degree of oedema of the face, and puffiness of the lower eyelids, and no oedema elsewhere.

In the latter, oedema of the face was present early, and to a marked extent, and at a later stage a condition of anasarca showed itself, with possibly also the presence of a certain amount of fluid, in both pleural cavities, as there was decided dulness in the infrascapular, and lower lateral regions in which situations the respiratory murmur was markedly deficient. The face and anterior and posterior aspects of the ^{trunk} were studded with vesicles, and pustules, some of which were of considerable size; and an erythematous rash was present on both aspects of the body, so that the oedema, was in part at least to be accounted for as has been indicated, by the numerous lesions in the skin;

season short a "serous saturation" of the lymphatic channels, and spaces of the subcutaneous cellular tissue (19.)

There were also the peculiar symptoms indicative of the uræmic state which occurred in this case, and which call for special note on account of their comparatively rare occurrence, although it would be outwith the scope of this paper to do more than allude to them.

The uræmic condition was ushered in by a state of nervous irritability, sensory, and motor; the boy's temperament underwent a change; from being quiet and docile, he became exceedingly fractious.

His intellect remained clear until coma ensued. On the day preceding the one on which he died, squinting of the left eye was observed, the left eye being rotated outwards. The movements were convulsive and occasional. This lasted for several hours, when the normal condition was resumed.

Next day patient spoke of not seeing properly, and on examination it was found that the defect of vision was binocular, and that there was approximately a loss of vision confined to the right half of each visual field. There was no accompanying paralysis. No ophthalmoscopic examination was made.

The phenomena are partly no doubt to be explained by the action of toxic products on the central nervous system ^{nervous} causing excitation of the centres involved; but without further data we are unable to say whether or in how far other causes, such as plethora with its sequel anaemia of the brain, played a part in the causation of the phenomena referred to. (20)

But to return to the main object of our inquiry, namely the ascertaining whether or not Chicken-Pox occurring during the course of Scarlet Fever or convalescence therefrom, has any influence in determining the onset of Alburninuria, or Nephritis, or of rendering such a complication, if already existing, of greater significance, or of graver import. The inference to be drawn from a consideration of these two series of cases is that such an influence was operative in the cases in question, and that it showed itself in the development of the Alburninuria, or Nephritis in the majority of instances at the very outset of the Varicellar attack. And while I do not attach a great deal of value to the comparison of the number of cases of Alburninuria, and Nephritis occurring in connection with Scarlet Fever alone, ~~with~~ that of the cases of Alburninuria, and Nephritis

following the occurrence of Chicken Pox in ~~connection~~^{combination} with Scarlet Fever, by itself, when taken in conjunction with an examination of the principal features of the individual cases, I think it is an important adjunct to the information derived in that way.

The fact that in all the twelve cases either Albuminuria, or Nephritis showed itself, either immediately, or very soon after the onset of the Varicella, or that there was a return of the Nephritis or Albuminuria, or a decided accentuation of the signs of the renal ~~syphilitic~~ affection, following immediately on the appearing of the Varicellar rash, points, in these cases I believe to some influence superadded, which tended to the development of the complication in question, or to cause an increase in the intensity, of the renal condition.

Before venturing however to apply the conclusions, arrived at after a study of the two series of cases, more widely, I would further submit particulars of a third series of cases which occurred during two slight outbreaks of Chicken Pox, amongst patients suffering from Scarlet Fever, of more recent date, and in which special attention was directed to the condition of the urine. Both occurred

in the Hospital at Kennedy St., the one commencing in November 1894, and the other in May 1898. The former outbreak was limited to six cases, and all the patients who contracted the disease, with one exception, had been upwards of thirty days in hospital.

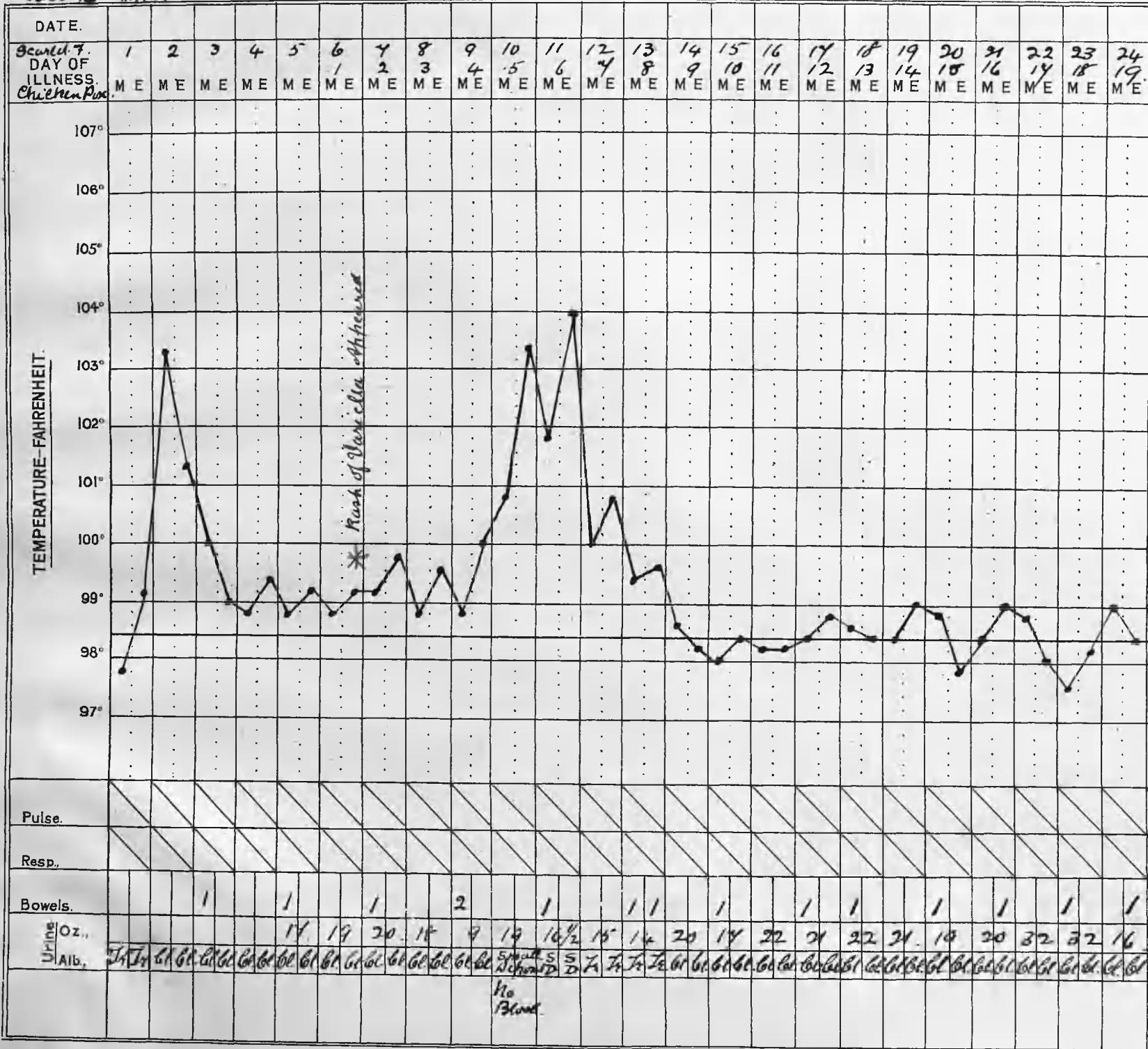
The patient who contracted the Varicella during the earlier period, was the one in whose case Albuminuria, in a decided form showed itself after the onset of the Varicella.

The rash of Varicella appeared on the 6th day of Scarletina, and ~~the~~ albumen made its appearance in the urine four days afterwards. The rash in this instance was very profuse, and general, affecting the head, trunk, and limbs, and the febrile disturbance was considerable. This case was the fifth of the series.

The latter outbreak comprised twelve cases.

In two of these the appearance of the characteristic eruption of Chicken Pox was ^{immediately} followed, in the one case by the return of Nephritis, the signs of the previous attack having a few days previously disappeared; and in the other after a lapse of several days, by Albuminuria in a slight form; no albumen having been present previous to this.

Case 13 M.C. a/c 2 8/12.



In the former of those two cases the Nephritis accompanying the attack of Varicella began on the forty-eighth day of Scarletina, and the second day of Varicella. The rash was moderately abundant, and chiefly limited to the chest and back. The febrile disturbance was not inconsiderable.

In the latter of the two, the Albuminuria made its appearance on the 23rd day of Scarlet Fever, and the eighth day of Chicken Pox.

The eruption was profuse.

The febrile disturbance moderately severe.

Subjoined are notes of the cases referred to, as obtained from the Ward Journals.

Series III

Case 13. M. C. adt 2⁸/12. Illness said to have commenced 3 days ago, although on account of the diagnosis being doubtful the child was placed in the Isolation Ward. Faint blush seen on Chest. Temperature 100.6° F. 13th day (?) Slight evidence of desquamation seen on feet; a trace of albumen found in the urine. 14th day. Child well until to-day; restless; temperature 104° F.; well-marked Scarlet Rash on chest.

Throat congested; tongue, clean.

6th day. Papules and vesicles of Varicella seen to-day.

7th day. The eruption has become very profuse over the whole body.

11th day. The temperature last night was 103.4° F., and patient was very restless. Albumen present in form of a trace on one occasion, on day of admission. Present this morning to the extent of a small deposit. No blood detected. On microscopic examination of the sediment epithelial casts, and renal epithelial cells undergoing fatty degeneration ^{were} found.

13th day. Vesicles drying; large number of crusts. A faint trace of albumen detected to-day.

15th day. Urine is now clear.

51st day. Urine has remained clear.
Dismissed, well.

Case 14. J. H. act 6. Admitted on the 5th day of illness.

Well-marked punctate general rash.

Tonsils, fauces etc., congested, and swollen.
Cervical glands normal.

Tongue clean, red, moist.

Temperature on admission 102° F.; pulse 144;
Respirations 48. Urine normal.

27th day. Going on well till yesterday; had diarrhoea

Temperature last night 99.6° F.; this morning 102° F.
 Cervical glands swollen; face pale, and puffy.
 Small deposit of albumen in the urine;
 blood in tolerably large amount.

23rd day. Passed 34 oz. urine in last 24 hours;
 slept well; skin not acting so well as before;
 sick three times yesterday; once after drinking, and
 twice spontaneously. Face pale and puffy.

24th day. Passed 15 oz. only; 1 loose motion; skin
 acting well; no complaint of pain; blood larger
 in amount; drinks well; sick during the night.

25th day. Passed 18 oz.; bowels loose; skin moist.

26th day. Passed 15 oz.; albumen $\frac{1}{2}$ column deposit.
 Blood smaller in amount; no vomiting; drinks well.

27th day. Only 4 oz. passed; more blood; vomiting
 frequent this afternoon.

28th day. Slept fairly well during the night;
 temperature this morning 102.3° F.; tends to be sick
 frequently; passed 9 oz. urine.

29th day. Urine passed 10 oz.; deposit of albumen $\frac{1}{2}$ col.
 Blood moderate in amount.

30th day. Urine passed 18 oz.; no vomiting;
 albumen the same in amount; trace of blood.

32nd day. Urine passed 28 oz.; deposit of albumen,
 $\frac{1}{8}$ column.

34th day Urine passed 36 oz.;

Haze of albumen present and trace of blood.

41st day. Urine passed 49 oz.; haze of albumen; no blood.

45th day. Urine clear; 50 oz. passed.

46th day. Rash of Variola seen to-day; a few papules and vesicles have appeared on the chest and back.

48th day. Urine clear in morning; in evening contains a deposit of albumen; trace of blood.

49th day. 39 oz. urine passed; deposit of albumen, and blood in considerable amount.

50th day. Faint haze of albumen; blood less.

53rd day. Haze present to-day, but no blood.

54th day. Urine free from albumen and blood.

58th day. Continued improvement; allowed up on 63rd day. Dismissed, well.

Case 15. L. D. age 6 Admitted on the 4th day of illness.

Initial signs sufficiently well-marked.

Little constitutional disturbance.

Temperature on admission 98.4 °F.

15th day. Ran a mild course.

Rash consisting of numerous papules, and vesicles has appeared; it is that of Chicken Pox. Evening Temperature high, 104 °F.

23rd day. The eruption has been very profuse; and

pustular; eruption is drying; temperature now almost normal.
the crusts are separating satisfactorily.

A trace of albumen detected in the urine for the first time.

26th day. The urine was clear to-day.

Urine remained clear afterwards; was dismissed well.

In the foregoing cases, likewise, the albuminuria or Nephritis occurring when the two diseases existed in combination, as has been mentioned, showed itself either immediately on the appearance of the Varicella, or within a few days of the commencement of that exanthem.

In all three cases the rash was abundant, and in one particularly so, and in all but the last the febrile symptoms were pronounced. I think then, that taking the cases of all three series together, we are warranted in forming the conclusion that there was some influence at work other than that attributable to the Scarlet Fever alone, that we have proof of an influence superadded with the inception of the Varicellar attack, although it may not in each case give evidence of its presence till some days have elapsed.

The fact also that Nephritis has, in certain

instances been found to occur as a complication of Varicella, according to the testimony of the observers alluded to, (page 5.) lends confirmation to the conclusions arrived at.

They therefore admit of wider application, and may be regarded as applying to cases of Scarlet Fever and Chicken Pox, occurring in combination, in general.

The conclusions arrived at may be expressed thus. -

1. That under certain circumstances when the two diseases co-exist there is a greater liability for a renal complication, or sequela to ensue, in the event of its absence prior to this, than when Scarlet Fever alone is present.
2. That, when such a complication has been present and the signs and symptoms have disappeared, there is a greater likelihood of such a complication returning in a mild or in a severe form.
3. That if the Varicella appear during the course of the Nephritis or Albuminuria, there is a greater likelihood for this complication to become aggravated.
4. That there is a greater tendency for the renal affection to assume a severe, or even a grave form.

What the circumstances are under which the renal disturbance is more apt to occur, or to be accentuated, can only to a limited extent be determined from the evidence before us.

In the first place the nature of the acute attack of Scarlet Fever as regards the liability to Albuminuria, or Nephritis, is an inconstant factor, inasmuch as there would appear to be no definite relation between the mildness or severity of the acute attack, and the occurrence of Albuminuria, or Nephritis as a complication or sequela.

And as regards the particular stage of Scarlet Fever or of convalescence during which the occurrence of Varicella is more likely to be followed by Albuminuria, or Nephritis, or by an accentuation of either if already existing, we would observe that in the majority of instances ~~the~~ ^{the} attack of Varicella began between the sixth, and twenty second days; but that severe cases of Nephritis occurred when the attack of Varicella made its appearance during the seventh week.

According to the particulars furnished by the cases submitted, of the circumstances relating to the Varicellar attack, the one which bears the closest relationship to the occurrence of Albuminuria, and

Nephritis, in connection with the combined diseases, as brought out by a comparison of the leading features of the cases, is the character of the rash, as regards its abundance, the tendency for the vesicles to become pustular, and extent of distribution. It would therefore appear that a copious eruption of wide distribution, in which many of the vesicles became large, and flattened, and tended to suppurate, and where an erythematous rash appeared, was most conducive to the development of Nephritis and albuminuria.

The degree of febrile disturbance would seem to be a circumstance of less importance. (Vide pp. 54, 59, 60)

The third and last question put forward at the outset of this paper as worthy of investigation in this connection, was,

Can any cause be assigned for the increased tendency for the renal functions to become impaired, or for the degree of impairment to be greater than if it occurred in connection with Scarlet Fever alone?

It will be necessary at the outset of this ^{part of the} investigation to direct our attention to the pathological condition of the kidneys, as it obtains in Scarlet Fever alone, and especially in its bearing upon the clinical features met with in albuminuria, and Nephritis, ^{in so far} or at least as the association between the pathological, and clinical aspects can be made out. It is to be observed however that certain difficulties stand in the way, and make this only to a limited extent possible. There is a great want of correspondence between the symptoms and signs present during life, and the appearances met with post mortem. Clinically the evidence as afforded by the usual methods of examining the urine may be that commonly associated with renal disease in a slight form, while, when the organs come to be examined, post mortem, the most pronounced structural lesions may be found. And marked structural changes in the kidneys, such as are usually found

associated during life with the usual symptoms and signs of Nephritis, are sometimes met with unlooked for at the post mortem examination, and when it was thought that this condition could be eliminated.

Again, the symptoms and signs which we are wont to interpret as indicating serious changes in the kidneys may be met with during life, and yet after death we may be surprised to find that macroscopically the organs differ little from the normal.

I am not disposed to adopt the view that renal changes are invariably present in the course of Scarlet Fever, though that they are very frequent is I think shown by the investigations of Klein who discovered the presence of definite Glomerulo-Nephritis in twenty-three consecutive cases, fatal at periods varying from two days to seven weeks. Gaiger asserts that in at least one case, that of a patient who died early in the course of Scarlet Fever from a cause foreign to that disease, careful microscopical examination revealed no evidence of Nephritis, either of the Glomerular, or Interstitial form. (8) And Bartels asserts that in many cases of Scarlet Fever, the urine contains no renal epithelium. While Wagner has found that in many cases of Scarlet Fever the kidneys were quite intact when submitted to examination, post mortem.

Certain changes be they slight or severe are

no doubt to be found in a large number of cases, although there may be only a slight form of albuminuria present during life, or the presence of albumen may not have been detected, although regularly sought for.

This is, I believe, the view we are warranted in adopting, in the present state of our knowledge, and on account of the frequency with which albuminuria, in a slight form is met with in the early, and also in the later stages of the disease.

And with regard to the pathological condition of the kidneys found in Scarlet Fever, many classifications have been adopted, according to the interpretations put upon the various appearances found.

Friedländer, who during four years made autopsies in 229 cases of Scarlet Fever recognises three distinct forms

(1) The Initial Catarrhal.

(2) The Interstitial Septic,

(3) Nephritis post-Scarlatinosa (the glomerular form)
with a very few mixed forms. (14.)

Turner recognises two varieties, due to separate causes, with intermediate forms. (16.)

While Sørensen on the other hand regards the conditions met with, as so many different stages of the same process. (18.)

While Fürbringer again, adopting the scheme

initiated by Reinhardt, and Frerichs distinguishes two types

(1) Diffused Nephritis

(2) Circumscribed Nephritis (Suppurative.)

with transitional and mixed forms. (20.)

Then there is the division based on the essential anatomical and pathological conditions, into

(1) Glomerulo-Nephritis } Interstitial changes may be

(2) Parenchymatous Nephritis } more or less present in each.

(3) Septic Inflammation

The first of these three last mentioned forms indicates by its name the particular structures that are chiefly affected, and is to be regarded as typical of the condition found in the kidneys of patients who have died of Post-Scarletina Nephritis. The term was applied by Klebs who brought the appearances referred to into prominence, and his observations have been confirmed by Charcot, Coats, and others. (21)

It is not so much with different modes of classification that we are concerned, as with the minute structural changes in the organs in question, and what we can learn from these regarding what has been taking place in the organs during life.

The earliest changes that occur in the kidneys during the course of Scarlet Fever are vascular.

The vascular system and the vaso-motor apparatus, are, as we can understand peculiarly exposed to the direct action of any irritant which has obtained access to the general circulation, and in particular, to that part of the vascular system belonging to the excretory organs, and therefore concerned in the elimination of certain waste products, and deleterious substances from the blood.

The general appearance presented by the kidneys, as they are seen when examined post mortem, in the case of patients who have died early in the course of the disease, is that of congestion, the organs being, moderately or greatly enlarged. The cortex is generally so pale, and slightly yellowish in colour, while the interlobular vessels are indicated by bleeding points, and there is also a zone of congestion visible at the bases of the pyramids. Miniate extravasations of blood are frequently to be seen here or in the cortex. The glomeruli appear as brownish dots studded through the somewhat pale cortex.

Similarly changes of a congestive type are apparent on microscopic examination, the Malpighian tufts and finer vessels of the cortex being notably swollen. These channels come to be narrowed and obliterated in parts, owing to hyaline changes in the endothelial cells of the internal layer, and to

an increase of the nuclei of the cells forming the middle layer. A proliferation likewise of the epithelial cells lining the interior of the glomeruli takes place, as also of the cells of the supporting connective tissue.

Besides this there is a marked infiltration of the glomerulus, and Malpighian tuft with leucocytes, which are also found invading the connective tissue in the immediate neighbourhood, and between the tubules. They have been observed to be very numerous at a point at which the afferent vessel enters the capsule, and around that vessel.

While these changes in and around the glomeruli may predominate, evidence of alterations in other respects may not be wanting; for example, the epithelium of the convoluted tubules, or of the calyx, or even of the straight tubules may undergo cloudy changes, and the lumen of the tubules may become filled up with epithelial cells undergoing fatty, or granular degeneration, or with hyaline ~~cross~~ material. Blood may be met with in the tubules, or in the glomeruli.

Along with these changes there may be an increase in the intertubular connective tissue, although this takes place usually at a later period.

The aggregation of leucocytes which has been

mentioned may cause compression of the afferent vessel, as it enters the glomerulus, or the tubules of the cortex may be pressed upon so that they become blocked; and as a result, if this takes place to any great extent we can understand how the urine may be notably decreased in quantity, or præuric symptoms supervene. (8) (21)

And founded on this an explanation has been offered for the appearance of the urine suddenly, in sufficient amount to form a deposit, and its sudden disappearance after remaining for one or two days, in this way, that casts which may have been plugging uriniferous tubules involved ⁱⁿ ~~by~~ the inflammatory process, may become dislodged by the pressure of the fluid excreted, and subsequently become fixed, while other individual excretory channels have not been involved, or only to a slight extent in the inflammatory process.

The septic form is probably indirectly due to scarlatina, resulting from secondary infection, as it is most frequently associated with acute phlegmonous processes, and with severe diphtheritic affections, accordingly it will be unnecessary to do more than mention it here; it is to be remarked however that apart from the symptoms being masked by the general septic condition, the urine

does not usually contain much albumen, and as a rule no blood. (12) (16) (20)

The changes that occur in the form characteristic of Scarlet Fever involve chiefly on the one hand the vascular structures intimately concerned in excretion, and on the other, the epithelial elements of the excretory apparatus, and more particularly those of the capsule, and convoluted tubules. And while the latter usually occurs as a later condition it may coexist with the changes in the vascular structures mentioned, and the one or the other may predominate.

It will thus be seen that no correspondence can be established between particular periods in the course of Scarlet Fever, and the actual changes in the kidneys, and that it is likewise impossible to allocate particular symptoms and signs to particular periods in the course of the disease, or to connect them with particular pathological conditions or processes. (pp. 11-14.)

No real distinction can therefore be drawn between Albuminuria occurring by itself, and the collective signs and symptoms which constitute the type of Scutalinal or Post-Scutalinal Nephritis.

We have seen then what the particular structures and tissues are that are acted upon injuriously, and in what particular ways they are affected,

Consequently the question naturally arises. How are we to explain these changes?

The diffuse nature of the inflammation, and the circumstance that the principal structures involved are those concerned in the separation, and removal of irritating products or foreign substances from the circulatory system point to the cause as being some virus, carried thither by the blood.

The late Professor Coulis in his *Manual of Pathology*, 1883, p. 409, mentions that in cases of Scarlet Fever, colonies of Bacteria are sometimes to be seen in the papillaries, and uriniferous tubules of the Kidneys, and that it is not improbable that we have here to do with the specific organisms of the fever.

Pathogenic streptococci were likewise found by Hugstatter and Mannaberg. (20) Also by Turner, who however remarks that a considerable number of examinations were made with only a few positive results, most of the cases examined being of the septic type. As the result of his experiments he found micro-organisms more frequently present in the glomerular than in the septic form (16). And Wyssokowitch, as the result evidently of experiments carefully carried out, declares that the kidneys in an intact condition do not

excrete bacteria, but that the passage of such bacteria necessitates a local lesion in the renal parenchyma. And Fürbringer states that recent experiments carried out according to the Gram method, prove that the kidney in inflammation of infectious origin, can eliminate pathogenic germs, but that those germs can by no means be considered as primary agents of the disease. (20.)

So that while it was until a comparatively recent date thought that the micro-organisms themselves were the primary agents, with the advance which has taken place in Bacteriological chemistry, the trend of opinion is now in favour of their products, certain soluble alkaloids being the direct agents in producing the changes in the kidneys we have just been considering. These bacterial products or toxines, circulating in the blood may produce lesions in various organs, unassociated with the actual presence of the bacteria; the secretory cells of various organs, especially the liver, and kidneys are specially liable to be affected. Bloody swelling may be caused; it may give place to a fatty change, or necrosis with granular degeneration may take place. Hyaline changes in the walls of the arterioles may occur. Capillary haemorrhages take place frequently owing to the vessel walls

being abnormally permeable, and partly to changes in the blood plasma. (22.)

Many of these appearances are found in the kidneys in Scarlet Fever, so that there is a strong presumption that the renal inflammation is caused by soluble products of Scarletine microbes which have as yet not been identified.

We have seen then in what particular way the important structures concerned in secretion and excretion are damaged in the course of ^{the} Nephritis peculiar to Scarlet Fever. We will readily understand therefore how, at this particular time, or when resolution has to some extent taken place, a slight cause may be sufficient to aggravate the condition or to light up the acute process afresh, as would seem to have resulted in the cases described in which the two diseases co-existed.

And it has been shown that Varicella by itself may under certain circumstances give rise to inflammation of the kidneys. It is therefore quite natural to infer, that when those organs, and particularly the structures, and tissues most actively concerned in the eliminating of effete products from the system, are damaged in the process of inflammation, or have not recovered

from such a condition, they are specially vulnerable, and more so when as ~~as~~ ^{has been shown} there is a tendency —, although much less than in Scarlet Fever, Measles, or Diphtheria, for inflammatory changes in the kidneys to occur, in Varicella.

The aetiology of Varicella like that of Scarlet Fever is obscure. Having regard to the fact that in almost the whole of the cases examined, the signs referable to the affection of the kidneys made their appearance either immediately on the Varicella developing, ^{with one exception} or not later than the fifth day, that is to say while fresh crops were appearing I deemed it desirable to endeavour to find out whether any causative relationship could be established between the coming out of the eruption, and the appearance of those signs. Accordingly I made a series of bacteriological examinations in co-operation with Mr J. G. McColl Assistant Physician at Kennedy St Hospital.

Cultures were made from the contents of the vesicles chiefly during this period of the Varicellar attack, in the three cases belonging to the last Series, namely, Cases 13, 14, and 15, with the view of ascertaining whether any organisms of importance were to be found, which could have any influence, even indirectly, in bringing about the renal condition.

Two cultures in serum agar were made from each case, and from the same vesicle, and in one case (case 14) five additional tubes were inoculated from vesicles at a later period namely on the sixth day of the Varicellar attack. One of the vesicles which was becoming broader, and more mature was selected. The top of the vesicle was carefully removed, and the platinum loop after being sterilized was introduced into the middle of the vesicle, care being taken to prevent contact with the walls.

From the two stroke cultures subcultures on agar agar, glycerine agar, were made, and where necessary stock cultures, and potato cultures, with plate cultures, in addition.

I In Case 13 the cultures were made on the 5th day of the Varicella, and 1st of Nephritis.

- (1) In one tube no growth appeared.
- (2) In the other, two growths were seen, one white, and the other yellow.
 - (a) The former tended to follow the stroked surface, and consisted of minute drop-like parts, which appeared on the third day. They were pearly white and gradually merged into one another to form a band with wavy edges, and of the same breadth - about 2 m.m. throughout.

The culture presented similar characters on

Agar agar, but did not grow so well.

Hanied films were prepared and examined; it was found that the organisms were stained by Gram's method.

Growth found to be that of a species of Coccus; the cocci were grouped irregularly in masses, and in this respect as well as in size resembled the *Staphylococcus Pyogenes albus*, but otherwise, that is to say as regards its behaviour on culture-media it resembled the *Staphylococcus cereus albus*.

The cocci differed from those of a white culture, which Guttman who made a series of examinations of the contents of Vesicles in Varicella,^{describes} (23) in not showing any disposition to group themselves in pairs.

(b.) The yellow cultures were rounded, and gradually increased in circumference until they attained a diameter of 4 m.m. The growth was found to be that of *Sarcina lutea*.

II Case 14 Two cultures were made on the 2nd day of Varicella, and 1st day of Nephritis.

Two serum agar tubes were inoculated as before. No growth appeared on either.

Again on the sixth day five tubes were inoculated. In the case of three, no result. In the remaining two white growths appeared

in the form of narrow streaks of a dirty white colour, exactly like the growth of *Staphylococcus Pyogenes Albus*. It was found to liquefy gelatine - when inoculated on a sloped surface, in the manner peculiar to that organism, and in other respects to behave as that organism does.

The stained specimens showed cocci which answered fully to the characters of *Staphylococcus Pyogenes Albus*.

III. Case 15 Two serum agar tubes were inoculated on the eighth day of Varicella, and 1st day of Album in urea.

In one tube no growth seen.

In second, a greenish yellow culture appeared at the end of 48 hours.

Gelatine was slowly liquefied.

Stained films showed a coccus similar in mode of grouping, and in size, to *Staphylococcus Pyogenes Albus*.

In behaviour with respect to culture media, ^{and} appearance of the cultures it closely resembled the *Staphylococcus Pyogenes Citreus* if it was not identical with that organism.

Permission was not sought to conduct inoculation-experiments upon animals.

The organisms found were with one exception non-pathogenic, and probably penetrated into the interior of the vesicles from the outer surface.

Certain pathogenic organisms may find their way into the interior of vesicles or pustules, from the surface of the skin. In regard to this, Garlé, as the result of culture experiments, concludes that suppuration in the vesicles may be brought about in either of two ways, either through the instrumentality of pyogenic staphylococci which gain entrance from the surface of the skin, or of pyogenic streptococci which have penetrated from the blood vessels of the vesicles (24.)

It will have been observed that in two out of the three cases Alburnimuria, or Nephritis originated not later than the fifth day of the Varicellar attack, and that either complication occurred in thirteen out of the total number of cases, namely fifteen, ~~sets~~ from the first to the fifth day of the Varicellar attack.

It would seem therefore from this, and from the result of these examinations that the occurrence of one or other of those complications is not connected with any pyogenic change in the vesicles.

We therefore feel constrained to attribute it to the same cause which is in all likelihood

instrumental in producing the rash, and the febrile disturbance, and to believe that this cause is mainly operative in initiating a renal disturbance, of a mild or severe character, or in accentuating existing mischief in the kidneys, or in reviving the inflammatory process, when resolution was taking place.

And that in Uvaricella acu Scarlet Fever we have to deal with secondary agents derived from a specific virus, in the form of soluble alkaloids, which likewise show a predilection for the kidneys.

so that when both diseases co-exist, further mischief is readily engendered by those soluble alkaloids reaching the kidneys in a state of inflammation, or when recovering from such a condition and when the important structures and tissues previously referred to, are materially damaged or weakened by such inflammation.

With regard to the practical outcome of an investigation such as the present, what we desire most in regard to the treatment of Scarlet Fever patients is to anticipate at the earliest possible period the appearance of any of its numerous complications and sequelae, and to obtain some gauge as to their severity, and possible issue.

The results of the present investigation contribute to a slight extent towards this, and teach us, that while in a certain proportion of cases of Chicken Pox occurring during the acute stage of Scarlet Fever, or during the period of Convalescence no signs referable to the kidneys may appear, not to regard the co-existence of that disease with Scarlet Fever too lightly, but to keep a watchful eye on the condition of the urine, and if the attack of Varicella be severe, to be increasingly vigilant.

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