

THE RELATIONSHIP BETWEEN URINARY INFECTION AND THE LATE
TOXAEMIAS OF PREGNANCY.

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THE RELATIONSHIP BETWEEN URINARY INFECTION AND THE LATE TOXAEMIAS OF PREGNANCY.

Introduction.

Much has been written about the aetiology of the late Toxaemias of Pregnancy, but up to the present, no authority has proved, beyond dispute, his own particular theory in this connection. In recent years several comprehensive surveys of the whole field have been made by competent observers, notably F.J. Browne (1, 2) and G.W. Theobald (3).

Among theories advanced as to the aetiology, one which has received a certain amount of prominence is that of J.P. Peters (4, 5). He claims that Pyelitis and Pyelonephritis are important factors in the causation of Pre-eclamptic Toxaemia and of Eclampsia. In support of his argument he quotes certain figures noted below.

1. Of 93 patients suffering from Pyelitis complicating Pregnancy 25 developed, before the end of Pregnancy, Hypertension or Oedema or both.
2. Of 320 patients with Toxaemia 41 had Pyelitis.
3. Of 25 autopsies in patients with vascular or renal disease that first manifested itself during Pregnancy 11 were found to have Pyelitis and Hydronephrosis.

His argument is based on the fact that, it is well recognised that dilatation of the ureters occurs during Pregnancy and becomes still more marked if Pyelitis supervenes (6). It is postulated that, in the presence of Pyelitis, and dilated ureters, ischaemia of the kidneys may occur with a consequent emission of renin, leading to Hypertension as in the Goldblatt (7) experiment. Supporting his argument are the experiments of Blalock (8) confirming those of Dill and Erickson (9) who found that, by obstructing the outflow of urine in dogs, sufficiently to cause Hydronephrosis, he was able to induce a state of Hypertension which was not abolished by denervation of the kidney. Hayes (10) found that Back Pressure phenomena, Hydronephrosis, and dilatation of the ureters were much more common in Pre-eclamptic patients and those suffering from Hyperemesis Gravidarum. By catheterisation of the ureters all these patients were cured, including 19 cases of Hyperemesis Gravidarum. In 6 cases of Eclampsia fits ceased a few hours after the ureters were drained.

In contradiction to this is the experience of Prather and

Sewell (11) who concluded from a study of their data, that Pyelitis was not a cause of Toxaemia of Pregnancy. According to Baird (12) patients with marked ureteral stasis with and without Urinary Infection have a normal or low Blood Pressure. He states that Pyelitis seldom developed in women in whom albuminuria and a rise of Blood Pressure had occurred during Pregnancy and that in a few cases in which Urinary Infection did develop during Pregnancy it had been transitory. Of the patients of Mussey and Loveday (13) who had Pyelitis of Pregnancy, only 3 of a total of 92 had accompanying or subsequent Toxaemia of Pregnancy. Out of 30 women who had Pyelitis of Pregnancy in one Pregnancy, none showed symptoms of this in subsequent Pregnancies and only 2 of these developed Toxaemia of Pregnancy. In their view "acute Pyelitis of Pregnancy, when treated promptly, is not prone to cause Pre-eclamptic Toxaemia or Eclampsia, and that, following one attack of acute Pyelitis of Pregnancy, the majority of such women do not exhibit symptoms of Renal disease". Finally, McLane (14) failed to find any higher incidence of Toxaemia among his cases of Pyelitis. The incidence was 10% among 98 cases of proved ante-partum Pyelitis, which was the same as in the whole clinic population.

The Problem.

It would, therefore, appear to be of some value if a fresh survey of a series of Pregnancies were made, in order that, if any new findings become, or confirmation of previous ones is made apparent, they can be assessed in the light of what is already known. This would be of greater importance if these observations were made in a part of the world where Toxaemia is known to assume larger proportions than in others.

The present work has been done in the light of these facts. The West Riding of Yorkshire is well known to have a higher incidence of Toxaemia of Pregnancy than many other parts of Great Britain. (Shaw (15)). The period covered is from 1st January 1944 to 17th August 1946. From 1st January 1944 to 15th June 1944 the figures are slightly less accurate than subsequent to this date as during this period all the urine specimens had to be examined at a central laboratory. Since then the Hospital's own laboratory was established enabling more frequent examinations to be made and the specimens did not suffer through transportation. The figures from 1st January 1944 to 8th March 1946 inclusive are based entirely on Hospital Records. All figures subsequent to 8th March 1946 constitute the writer's own personal cases, who have all been seen by him. All Hospital Records have been carefully checked by the writer and all doubtful cases eliminated in the final figures. The Hospital Diagnosis has not been accepted at its face value. If the facts as

recorded did not correspond with the diagnosis, this diagnosis was not accepted, but the diagnosis which corresponded with the facts as recorded has been made on a definite basis noted below. In this way, a number of doubtful cases of Pyelitis of Pregnancy and of Pre-eclamptic Toxaemia have been eliminated but it is hoped that, in this way, the fallible human factor at least, has been greatly diminished and the figures, in consequence, rendered more representative of the true facts.

Criteria.

From Records of Hospital Cases 1st January 1944 to 8th March 1946.

Diagnosis of Urinary Infection.

1. Any case in which there is written evidence of pathogenic organisms in a catheter specimen of urine on more than one occasion in spite of treatment.
2. Any case in which there is written evidence of pathogenic organisms and pus in a catheter specimen of urine on one occasion.
3. Any case in which there is obvious written clinical evidence of Urinary Infection in the absence of laboratory examination.

Diagnosis of Pyelitis.

1. Any case in which there is written evidence of Urinary Infection associated with tenderness over one or both kidneys and with or without pyrexia sustained over a period and in which the tenderness is not due to other cause shown.
2. Any case in which there is written evidence of Urinary Infection in which there is evidence in a catheter specimen of urine of Red Blood Cells and Casts on two or more occasions.
3. Any case in which there is written clinical evidence overwhelmingly in favour of Pyelitis in the presence of pyrexia reduced by the usual forms of treatment for Urinary Infection and in which the Ward Specimens have shown albuminuria and/or pus but in which Laboratory Specimens have not been available.

Diagnosis of Urinary Infection of Pregnancy.

Any case in which there is written evidence of signs and symptoms developing during and not before Pregnancy which would have led to a diagnosis of Urinary Infection in the Non-pregnant woman.

Diagnosis of Pyelitis of Pregnancy.

Any case in which there is written evidence of signs and symptoms developing during and not before Pregnancy which would have led to a diagnosis of Pyelitis in a Non-pregnant woman.

Diagnosis of Pre-eclamptic Toxaemia.

1. Any case in which there is written evidence of a combination of Hypertension, Oedema and Albuminuria developing after the 20th week of Pregnancy subsiding during the post-natal period. For this purpose Hypertension is defined as a Blood Pressure persistently above 135/90 in a patient whose normal Pressure is below 130/85 or in proportion thereto.
2. Any case in which two of the above signs have been obvious during part of the last 20 weeks of Pregnancy and in which Headache, Dizziness, Dimness of Vision, Spots in front of the Eyes or other of the minor signs or symptoms is noted, clearing in the post-natal period.
3. Any case in which one of the main signs noted above has been obvious during part of the last 20 weeks of Pregnancy and in which two or more of the lesser signs and symptoms are noted in gross degree, clearing up in the post-natal period. For this purpose "part" is taken to mean at least two successive occasions at ante-natal visits or a period in Hospital or on several ante-natal visits not necessarily successive. By "subsiding" is meant some degree of return to normal not necessarily complete during the period of the Case Record.

Diagnosis of Eclampsia.

1. Any case in which there is written evidence of a definite history of fits associated with some of the signs and/or symptoms of Pre-eclamptic Toxaemia.
2. A definite history of a fit or fits occurring in the immediate Pre-natal period without other signs of Toxaemia and without any history suggestive of any other diagnosis clearing up in the post-natal period or dying with suggestive autopsy findings.
3. A definite history of a fit or fits occurring in the Delivery or immediate post-natal period clearing up during the post-natal period or dying with suggestive autopsy findings and without any history suggestive of any other diagnosis.

4. Any case in which there is written clinical evidence highly suggestive of Eclampsia but in which records are not sufficiently complete to be entirely convincing.

It is to be noted that the above schema is only for guidance in the mode of selection and in practically all cases sufficient evidence of a laboratory nature and/or of a clinical nature was available to clinch the Final Diagnosis.

Personal Case Records.

Similar general principles have been employed in sorting out my own personal cases but in these cases all diagnoses are supported by definite clinical and laboratory proof. No case which is doubtful has been considered as coming under Pyelitis, Pre-eclamptic Toxaemia or Eclampsia, but some cases which do not fulfil all the criteria for a complete Pre-eclamptic Toxaemia but in which there are signs and symptoms highly suggestive of this diagnosis are classified under the term Mild Pre-eclamptic Toxaemia.

Where term Urinary Infection + Toxaemia or the term Pyelitis + Toxaemia is used both in the Hospital Case Records and in the Personal Case Records this is to be taken to mean a coincident condition or a condition in which both have occurred but in which the former has preceded the latter.

Where Urinary Infection occurred in the Lying-in Period and there is a preceding Toxaemia, the infection is neglected unless there is a suggestive history of preceding Urinary Infection, as, in such a case, the infection will have no bearing on the figures and has, probably, been of a very transient nature due to the passage of a catheter in the early puerperium. This happening has been very rare and the infection has, in all cases, cleared within the six-day period of the sulphathiazole course given as a routine in these cases.

The only Controls which it has been possible to obtain, have been all other Female Hospital Admissions between the ages of 16 and 45. This is not entirely satisfactory as all these cases have been ill, whereas, the pregnant women have been, in most cases, quite normal in health, apart from their pregnant state.

A search for a Control Series through the Index Medicus as far back as 1935 has not revealed any article giving representative figures of the incidence of Pyelitis in the general Female Population, much less in a selected Group of this part of Humanity. Only one article by Shure (16) has been of any help in this connection and this is a study of autopsy specimens and, therefore,

suffers from the same drawbacks as my own figures. However, as it covers a much larger cross-section of the female population, it is of some value in checking the general incidence as some, at least, of these cases died as a result of accident or of some acute cause, whereas, mine cover, more or less, chronic sickness. In the case of these figures, it is unfortunate that the author subdivides his records into Age Groups which, while covering the Age Groups in the present study, yet covers down to birth and up to fifty at the same time. It is, however, highly probable that the error due to the inclusion of the Under sixteen Group is cancelled by the inclusion of the 45-50 Group which contains a much higher percentage of Pyelitis and Hypertension.

In the Records, the Total Admissions to the Hospital, subdivided into the different Groups has been given, in order that, a clear view can be obtained of the relative size of the Group under consideration. In this connection, it is to be emphasised that the Hospital draws its clientele from a wide area of the West Riding of Yorkshire and is not confined to one small circumscribed part of the County. Moreover, the Pregnancies almost entirely are unselected as only a small number of emergencies come into the Hospital. The others are ordinary booked cases from several communities in the West Riding.

For the purpose of this survey the Age Group 16-45 has been taken to represent the period of fertility. Only one case aged 46 has been included in the Pregnancies. It is realised that fertility can occur at both earlier and at later ages but, as a line had to be drawn, this one was decided on, as all except one of the Pregnancies were included in the Age Group.

The criteria are modified from the article by King (17) in which he subdivides Pre-eclamptic Toxaemia into Mild and Severe with a somewhat more marked cleavage than I have achieved. For the purpose of this work it is not necessary to have so distinct a line at such a high level since, if the relationship is to account for anything, incipient Toxaemia must be noted as well.

Tables.

The following pages contain a Series of Tables based on the results of my own observations. A list of these is given below.

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of Toxaemia, Urinary Infection of Pregnancy and Pyelitis of Pregnancy.

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Table I.

Record of Cases admitted to Hospital between 1st January 1944 and 8th March 1946 inclusive.

1944.															
Month	Admissions					Pregnancies									
	Pats.	Women.				Tot	'Toxaemias		'Urine Infection		+ Toxaemia		'Tot	'lit	
		'Total	'al.	'16-45 Age Grp'	'Urin. Inf'		'alone	'Pre-eclampsia	'al.	'Pyel.	'alone	'Pyel.			'al.
Jan	217	103	78	1	0	65	0	7	6	1	1	0	0		
Feb	153	86	69	1	0	50	0	0	4	0	0	0	0		
Mar	181	102	79	2	0	51	0	1	4	2	1	0	0		
Apr	195	101	78	0	0	70	0	4	11	2	1	2	0		
May	174	97	76	0	0	58	0	0	6	0	0	0	0		
Jun	165	94	74	1	1	64	1	0	8	2	1	0	0		
Jul	229	118	92	5	3	82	1	1	2	1	0	0	0		
Aug	284	144	118	2	0	100	0	8	9	1	0	1	0		
Sep	264	143	111	2	1	101	1	8	9	1	0	1	1		
Oct	180	84	65	1	0	50	0	1	4	1	0	1	0		
Nov	212	111	93	1	0	80	0	8	12	1	1	3	2		
Dec	237	117	82	2	0	70	0	4	7	3	1	1	1		
Total	2284	1300	1005	18	5	841	3	42	82	15	6	9	3		
1945.															
Jan	289	155	122	1	0	107	1	11	13	2	0	3	1		
Feb	230	109	84	0	0	71	0	8	10	0	0	3	1		
Mar	228	124	95	5	1	66	0	4	8	1	0	4	3		
Apr	210	117	79	2	0	65	0	6	4	3	3	3	3		
May	198	108	79	0	0	63	0	4	5	2	2	1	1		
Jun	238	124	87	0	0	72	0	1	8	2	1	1	0		
Jul	259	141	95	3	2	75	0	1	3	4	2	1	1		
Aug	208	106	70	0	0	55	0	1	3	2	1	2	2		
Sep	214	118	87	2	1	67	0	4	6	3	2	1	1		
Oct	268	144	106	5	2	76	0	3	4	1	0	2	0		
Nov	264	155	106	1	1	67	0	4	4	3	1	1	1		
Dec	253	129	93	2	0	69	1	2	3	4	3	2	0		
Total	2859	1531	1103	21	7	853	2	49	71	27	15	24	14		
1946.															
Jan	287	157	106	3	2	71	0	2	5	5	4	1	1		
Feb	295	149	96	4	1	68	0	1	3	3	2	3	3		
Mar/8	95	47	37	1	0	28	0	0	2	1	1	0	0		
Total	677	353	239	8	3	167	0	3	10	9	7	4	4		
Grand															
Total	5820	3184	2347	47	15	1861	5	94	163	51	28	37	21		

Table II.

Analysis of Table I showing Total Numbers of Cases of Toxaemia, Urinary Infection and Pyelitis of Pregnancy.

1944.	Toxaemias.				Pregnancies.		Urinary Infection.				
	Total	Total	Alone	Total	Pyel.	Total	Alone	+ Tox	Total	Alone	+ Tox
	841	136	127	9	4	24	15	9	10	6	4
1945.	853	146	122	24	14	51	27	24	29	15	14
1946.	167	17	13	4	4	13	9	4	11	7	4
Total.	1861	299	262	37	21	88	51	37	49	28	21

Table III.

Urinary Infection + Toxaemia of Pregnancy and Pyelitis of Pregnancy + Toxaemia of Pregnancy expressed as a percentage of the Total Cases of Toxaemia of Pregnancy. Analysis of Table II.

1944.	Toxaemia	Urinary Infection	Pyelitis
	100%	6.62%	2.94%
1945.	100%	16.44%	9.59%
1946.	100%	23.53%	23.53%
Total.	100%	12.37%	7.12%

Table IV.

Pyelitis of Pregnancy + Toxaemia expressed as a percentage of the Total Cases of Pyelitis of Pregnancy. Analysis of Table II.

<u>1944.</u>	<u>Pyelitis.</u>	<u>Pyelitis + Toxaemia.</u>
	100%	40.00%
<u>1945.</u>		
	100%	48.38%
<u>1946.</u>		
	100%	36.36%
<u>Total.</u>		
	100%	42.86%

Table V.

Total Urinary Infection of Pregnancy and Total Pyelitis of Pregnancy expressed as a percentage of the Total Pregnancies. Analysis of Table II.

<u>1944.</u>	<u>Pregnancies</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	2.84%	1.19%
<u>1945.</u>			
	100%	5.98%	3.40%
<u>1946.</u>			
	100%	7.78%	6.58%
<u>Total.</u>			
	100%	4.73%	2.63%

Table VI.

Urinary Infection of Pregnancy without Toxaemia and Pyelitis of Pregnancy without Toxaemia expressed as a percentage of the Pregnancies without Toxaemia. Analysis of Table II.

<u>1944. Non-toxic Pregnancies</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
100%	2.12%	0.85%
<u>1945.</u>		
100%	3.82%	2.12%
<u>1946.</u>		
100%	6.00%	4.66%
<u>Total</u>		
100%	3.27%	1.79%

Table VII.

Total Urinary Infection among Female Admissions of Age Group 16-45 and Total Pyelitis among Female Admissions of Age Group 16-45 expressed as a percentage of the Total Female Admissions of Age Group 16-45. Analysis of Table I.

<u>1944. Females (16-45)</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
100%	4.18%	1.49%
<u>1945.</u>		
100%	6.53%	3.25%
<u>1946.</u>		
100%	8.78%	5.85%
<u>Total.</u>		
100%	5.75%	2.30%

Table VIII.

Urinary Infection and Pyelitis among Non-pregnant Admissions of Age Group 16-45 expressed as a percentage of the Non-pregnant Admissions. Analysis of Table I.

<u>1944.</u>	<u>Non-pregnant (16-45)</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	10.99%	3.05%
<u>1945.</u>			
	100%	8.40%	2.80%
<u>1946.</u>			
	100%	11.11%	4.17%
<u>Total.</u>			
	100%	9.67%	3.08%

Table IX.

Comparative Table showing (a) Urinary Infection and (b) Pyelitis expressed as percentages of their individual Groups as tabulated in the previous six Tables. This is the most important Table of this portion of the Series.

(a)
Urinary Infection

<u>1944.</u>	<u>Total Admissions</u>		<u>Pregnancies.</u>		
	<u>Non-pregnancies.</u>	<u>Total</u>	<u>Total</u>	<u>Toxic</u>	
	4.18%	10.99%	2.84%	6.62%	2.12%
<u>1945.</u>					
	6.53%	8.40%	5.98%	16.44%	3.82%
<u>1946.</u>					
	8.78%	11.11%	7.78%	23.53%	6.00%
<u>Total.</u>					
	5.75%	9.67%	4.73%	12.37%	3.27%

(b)

Pyelitis.

1944.	Total Admissions.				
	'Non-pregnancies.'		'Pregnancies.'		
	'Total'	'Total'	'Total'	'Toxic'	'Non-toxic'
	1.49%	3.05%	1.19%	2.94%	0.85%
1945.	3.25%	2.80%	3.48%	9.59%	2.12%
1946.	5.85%	4.17%	6.58%	23.53%	4.66%
Total.	2.30%	3.08%	2.63%	7.12%	1.79%

Table X.

Record of Cases admitted to Hospital between 9th March 1946 and 17th August 1946 inclusive.

Month	Admissions					Pregnancies							
	Pats	'Women'		'16-45 Age Grp'		'Toxaemias'		'Urine Infection'					
		'Tot'	'Preg'	'Tot'	'Tot'	'Ecl'	'Pre-'	'Alone'	'Alone'	'+Toxaemia'			
		'Tot'	'Preg'	'Tot'	'Tot'	'amp'	'eclamp'	'Tot'	'lit'	'Tot'			
		'al.'	'al.'	'al.'	'al.'	'M.'	'S.'	'al.'	'is.'	'al.'			
Mar	213	0	0	87	106	71	2	3	9	6	4	4	4
Apr	268	2	1	115	145	84	0	9	11	0	0	1	1
May	357	3	2	155	202	122	0	6	16	3	3	3	2
Jun	276	1	1	112	144	98	0	8	8	3	2	0	0
Jul	264	0	0	121	145	92	0	8	9	4	4	5	5
Aug	183	0	0	78	97	63	0	4	11	2	1	1	1
Grand													
Total	1561	6	4	668	839	530	2	38	64	18	14	14	13

Table XI.

Analysis of Table X showing Total Numbers of Cases of Toxaemia, Urinary Infection and Pyelitis of Pregnancy.

<u>Mar.-Aug. 1946.</u>		<u>Pregnancies.</u>									
		<u>Toxaemias.</u>					<u>Urinary Infection.</u>				
				<u>+ Urin. Inf'</u>			<u>Total</u>		<u>Pyelitis.</u>		
<u>Total</u>	<u>Total</u>	<u>Alone</u>	<u>Total</u>	<u>Pyel.</u>	<u>Total</u>	<u>Alone</u>	<u>+ Tox</u>	<u>Total</u>	<u>Alone</u>	<u>+ Tox</u>	
530	118	104	14	13	32	18	14	27	14	13	

Table XII.

Urinary Infection + Toxaemia of Pregnancy and Pyelitis of Pregnancy + Toxaemia of Pregnancy expressed as a percentage of the Total Cases of Toxaemia of Pregnancy. Analysis of Table XI.

<u>Mar.-Aug. 1946.</u>	<u>Toxaemia</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	11.86%	11.01%

Table XIII.

Pyelitis of Pregnancy + Toxaemia expressed as a percentage of the Total Cases of Pyelitis of Pregnancy. Analysis of Table XI.

<u>Mar.-Aug. 1946.</u>	<u>Pyelitis.</u>	<u>Pyelitis + Toxaemia.</u>
	100%	48.15%

Table XIV.

Total Urinary Infection of Pregnancy and Total Pyelitis of Pregnancy expressed as a percentage of the Total Pregnancies. Analysis of Table XI.

<u>Mar.-Aug. 1946.</u>	<u>Pregnancies</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	6.04%	5.09%

Table XV.

Urinary Infection of Pregnancy without Toxaemia and Pyelitis of Pregnancy without Toxaemia expressed as a percentage of the Pregnancies without Toxaemia. Analysis of Table XI.

<u>Mar.-Aug. 1946.</u>	<u>Non-toxic Pregnancies</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	4.37%	3.39%

Table XVI.

Total Urinary Infection among Female Admissions of Age Group 16-45 and Total Pyelitis among Female Admissions of Age Group 16-45 expressed as a percentage of the Total Female Admissions of Age Group 16-45. Analysis of Table X.

<u>Mar.-Aug. 1946.</u>	<u>Female (16-45).</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	5.69%	4.64%

Table XVII.

Urinary Infection and Pyelitis among Non-pregnant Admissions of Age Group 16-45 expressed as a percentage of the Non-pregnant Admissions. Analysis of Table X.

<u>Mar.-Aug. 1946.</u>	<u>Non-pregnant (16-45)</u>	<u>Urinary Infection</u>	<u>Pyelitis</u>
	100%	4.35%	2.90%

Table XVIII.

Comparative Table showing (a) Urinary Infection and (b) Pyelitis expressed as percentages of their individual Groups as tabulated in the previous six Tables. This is the most important Table of this portion of the Series.

<u>Mar.-Aug. 1946.</u>	(a)				
	Urinary Infection.				
	Total Admissions				
	Non-pregnancies.	Pregnancies.			
Total	Total	Total	Toxic	Non-toxic	
	5.69%	4.35%	6.04%	11.86%	4.37%

Table XVIII.

(b)
Pyelitis.

Total	Total Admissions.		Pregnancies,	
	Non-pregnancies.		Total	Toxic
4.64%	2.90%	5.09%	11.01%	3.39%

Table XIX.

Record of Cases admitted to Hospital between 1st January 1944 and 17th August 1946, inclusive.

Month	Admissions				Pregnancies			
	Pats.	Total	Women	16-45 Age Grp	Toxaemias	Urine Infection	Alone	+ Toxaemia
Grand	7381	4023	3015	53	19	2391	7	132
Total								

Table XX.

Analysis of Table XIX showing Total Numbers of Cases of Toxaemia, Urinary Infection and Pyelitis of Pregnancy.

1944-1946.	Toxaemias.				Pregnancies.			
	Total	Alone	+ Urin. Inf.	Pyel.	Total	Alone	+ Tox	Pyelitis.
2391	417	366	51	34	120	69	51	76

Table XXI.

Urinary Infection + Toxaemia of Pregnancy and Pyelitis of Pregnancy + Toxaemia of Pregnancy expressed as a percentage of the Total Cases of Toxaemia of Pregnancy. Analysis of Table XX.

1944-1946.	Toxaemia	Urinary Infection	Pyelitis
	100%	12.23%	8.15%

Table XXII.

Pyelitis of Pregnancy + Toxaemia expressed as a percentage of the Total Cases of Pyelitis of Pregnancy. Analysis of Table XX.

<u>1944-1946.</u>	<u>Pyelitis.</u>	'	<u>Pyelitis + Toxaemia.</u>
	100%	'	44.73%

Table XXIII.

Total Urinary Infection of Pregnancy and Total Pyelitis of Pregnancy expressed as a percentage of the Total Pregnancies. Analysis of Table XX.

<u>1944-1946.</u>	<u>Pregnancies</u>	'	<u>Urinary Infection</u>	'	<u>Pyelitis</u>
	100%	'	5.02%	'	3.18%

Table XXIV.

Urinary Infection of Pregnancy without Toxaemia and Pyelitis of Pregnancy without Toxaemia expressed as a percentage of the Pregnancies without Toxaemia. Analysis of Table XX.

<u>1944-1946.</u>	<u>Non-toxic Pregnancies</u>	'	<u>Urinary Infection</u>	'	<u>Pyelitis</u>
	100%	'	3.49%	'	2.13%

Table XXV.

Total Urinary Infection among Female Admissions of Age Group 16-45 and Total Pyelitis among Female Admissions of Age Group 16-45 expressed as a percentage of the Total Female Admissions of Age Group 16-45. Analysis of Table XIX.

<u>1944-1946.</u>	<u>Females (16-45)</u>	'	<u>Urinary Infection</u>	'	<u>Pyelitis</u>
	100%	'	5.73%	'	3.65%

Table XXVI.

Urinary Infection and Pyelitis among Non-pregnant Admissions of Age Group 16-45 expressed as a percentage of the Non-pregnant Admissions. Analysis of Table XIX.

1944-1946.	Non-pregnant (16-45)	Urinary Infection	Pyelitis
	100%	5.26%	1.89%

Table XXVII.

Comparative Table showing (a) Urinary Infection and (b) Pyelitis expressed as percentages of their individual Groups as tabulated in the previous six Tables. This is the most important of the whole Series of Tables.

(a)
Urinary Infection

1944-1946.

Total	Total Admissions		Pregnancies.	
	Non-pregnancies.	Total	Total	Non-toxic
5.73%	5.26%	5.02%	12.23%	3.49%

(b)
Pyelitis.

Total	Total Admissions		Pregnancies.	
	Non-pregnancies.	Total	Total	Non-toxic
3.65%	1.89%	3.18%	8.15%	2.13%

Table XXVIII.

Various small Tables analysing a Series of Tables in an Article by Shure (16).

Approximate Total Female Autopsies. 5950

1. Age Groups	Pyelonephritis		Pyelonephritis + Hypertension	
	Total Cases	%age of Females	Total Cases	%age of Females
30 & under	23	0.38%	7	0.12%
31 to 40	31	0.52%	10	0.17%
41 to 50	28	0.47%	14	0.24%
Total	82	1.37%	31	0.53%

2. Pyelonephritis in Females and Pyelonephritis + Hypertension in Females expressed as a percentage of the Total Cases of Pyelonephritis in Females.

Age Group	Pyelonephritis Alone		Hypertension	
	Total	%age	Total	%age
30 & under	23	17.70%	7	5.34%
31 to 40	31	23.85%	10	7.63%
41 to 50	28	21.54%	14	10.69%
Total	82	63.08%	31	23.66%

Total Females in Control Groups. 359

3. Hypertension in Control Group of Females expressed in Age Groups and as a percentage of the Total Females in the Control Group.

Age Group	Hypertension	
	Total	%age Females
30 & under	6	1.67%
31 to 40	23	6.40%
41 to 50	31	8.63%
Total	60	16.70%

Study of the present Series.

The results of the present investigation have been tabulated above. Table I, which is a Record of the Work of the Hospital from 1st January 1944 to 8th March 1946, Table X, which is a Record of the Work of the Hospital from 9th March 1946 to 17th August 1946 and Table XIX, which combines these two Records in one single horizontal column, are analysed in the immediately following eight Tables. The results of these three separate analyses are combined in Tables IX, XVIII and XXVII respectively. These three Tables are, in consequence, the most important of their individual portions of the Series and Table XXVII, containing as it does, the combined analyses of the two and a half years' Record, is the most important of the whole Series.

(e) Pyelitis among Non-toxic Pregnancies, from the Records this works out at 1.79% over two years and three months, 3.39% during the period of the Present Record and 2.13% over the whole period.

It will be seen from these figures, that during the period of the Present Record i.e. 9th March-17th August 1946, the percentages of Pyelitis approximate to the percentages of Urinary Infection, whereas, in the Hospital Records, in all cases, the percentages of Pyelitis is considerably lower than the percentages of Urinary Infection.

This is due to three factors:

(a) The criteria for Pyelitis are severe and, therefore, a number of cases of true Pyelitis occurring during the period of the Hospital Record i.e. 1st January 1944-8th March 1946, are eliminated and called merely Urinary Infection, whereas, during the period of the Present Record a very much closer eye was naturally kept on all cases of Urinary Infection and, therefore, the number of cases of Pyelitis noted was higher, since the criteria were more often satisfied due to the Cases being under personal observation, than they could be when reliance had to be placed on other peoples' clinical records;

(b) During the first six months of 1944, as mentioned previously, there was no laboratory in this Hospital and urine and other specimens had to be sent to a central laboratory. In consequence, less were sent than would be at the present period and, therefore, it is possible that a number of cases were missed during this time;

(c) Further, during the period of the Present Record a definite routine was instituted so that, in all cases, urines were examined at stated intervals and in all cases where any suspicions arose, catheter specimens were examined by the laboratory. Thus, it is possible that more cases of Urinary Infection were likely to be spotted than during the previous period.

If these facts are accepted, it can be postulated that, in reality, the final percentage of Pyelitis during the period of the Hospital Record approached considerably nearer to the percentage of Urinary Infection than would appear from the Tables. If this is granted, then, in the final Table the percentage of Pyelitis also must approach closer to the percentage of Urinary Infection than would appear at present.

Be that as it may, it does not alter the relationship of the incidence of Urinary Infection and of Pyelitis in the various Groups examined. It will be noticed that the percentage of Pyelitis in Pregnancy and in all Female Admissions of child-bearing age is to all intents and purposes the same. Considering now, the Non-pregnant Admissions and Non-toxic Pregnancies, these also have a very close

Studying, therefore, these three Tables, we find that they bear a very close resemblance in that, comparing:

(a) the percentage of Urinary Infection in all Females of child-bearing age admitted, we find that, from the Records this works out at 5.75% over two years and three months as compared with 5.69% in the five and a half months of the Present Record and 5.73% over the whole period;

(b) Urinary Infection among Non-pregnant Admissions of child-bearing age, we find that, from the Records this works out at 9.67% over two years and three months, only 4.35% in the period of the Present Record and 5.76% over the whole period;

(c) Urinary Infection among Pregnant Admissions, we find that, from the Records this works out at 4.73% over the two years and three months, 6.04% during the period of the Present Record and 5.02% over the whole period;

(d) Urinary Infection among Toxic Pregnancies, we find that, from the Records this works out at 12.73% over two years and three months, 11.86% during the period of the Present Record and 12.23% over the whole period;

(e) Urinary Infection among Non-toxic Pregnancies, we find that, from the Records this works out at 3.27% over two years and three months, 4.37% during the period of the Present Record and 3.49% over the whole period.

Comparing now:

(a) the percentage of Pyelitis in all Females of child-bearing age, from the Records this works out at 2.30% over two years and three months, 4.64% during the period of the Present Record and 3.65% over the whole period;

(b) Pyelitis in Non-pregnant Females of child-bearing age, from the Records works out at 3.08% over two years and three months, 2.90% during the period of the Present Record and 1.89% over the whole period;

(c) Pyelitis among Pregnant Admissions, from the Records this works out at 2.63% over two years and three months, 5.09% during the period of the Present Record and 3.18% over the whole period;

(d) Pyelitis among Toxic Pregnancies, from the Records this works out at 7.12% over two years and three months, 11.01% during the period of the Present Record and 8.15% over the whole period;

resemblance and their percentages are lower than the percentages of either the Total Admissions or the Total Pregnancies.

It remains to examine the percentages of Pyelitis in Toxic Pregnancies. Here, there is a big difference for it is more than four times that among Non-pregnant Admissions and nearly four times that among Non-toxic pregnancies. That this is not due to chance must, surely, be self-evident as it has been found in two separate examinations, one of other peoples' records, the other of my own records and in each case the number of patients involved is considerable.

Examining now, the relationship of Pyelitis + Toxaemia of Pregnancy to Pyelitis of Pregnancy, it will be seen from the Records of Cases admitted during the period 1st January 1944-8th March 1946, that this is 42.86%, that during the period 9th March 1946-17th August 1946 it was 48.15% and that for the period 1944-1946 inclusive it was 44.73%

Again, if the factors mentioned above as causing the smaller percentage of Pyelitis during the period of the Hoospital Record are accepted, then it will be realised that the final percentage should have approximated to 48%. But, even if the figure of 44.73% is taken as the final figure it, in itself, is evidence of the close relationship of Pyelitis of Pregnancy to Toxaemia of Pregnancy. Again, these percentages are hardly likely to be due to chance since considerable numbers are involved and they have been found in two separate examinations, one of other peoples' records and the other of my own records.

Discussion.

Outlined in the first four paragraphs of this Thesis are the bare bones of a large volume of work on the relationship of Pyelitis and Pyelonephritis of Pregnancy to the late Toxaemias of Pregnancy. Whether the conclusions of the various authors are in favour or are against the hypothesis of a connection between these two scourges of the pregnant woman, there is no doubt that all of the workers in the field have had very much in the front of their minds the extreme probability of such a connection. The main reason for this has, no doubt, been a marked clinical impression that there was such a connection. Certainly, this worker started with such an impression. In conversation with other medical men interested in Obstetrics it has been noticed that a similar impression has been held.

The object of the present work has been to confirm or refute the theory of Peters (4,5) that there is a distinct relationship between Pyelitis of Pregnancy and the late Toxaemias of Pregnancy.

The result of this worker's investigations is that the figures given by Peters in support of his argument have been confirmed both from the Hospital Records and from the worker's personal Records.

Peters' figures for Pyelitis of Pregnancy given in Paragraph Two of this Thesis show that 26.88% developed Hypertension or Oedema or both. A total of 12.81% of his cases of Toxaemia had Pyelitis. Of his cases, who died with vascular or renal disease 44% had Pyelitis or Hydronephrosis.

It is unfortunate that a survey of the incidence of Urinary Infection, Pyelitis and Pyelonephritis has not been carried out among healthy young women serving in the Armed Forces throughout the late War. Had the results of such a survey been available the task of getting adequate controls for any experiments in this subject would have been that amount easier. As it is, inadequate controls only are available and, in consequence, it is difficult to draw a definite conclusion about the general incidence among women of these conditions.

I have attempted, by analysis, to make the figures of Shure (16) fit the case, but, it has to be pointed out, that he omitted to give the exact total of Females involved and also the total figures in the different Age Groups. It is, therefore, not possible to give percentages related to the total figures in each Age Group. Instead, I have given these figures as related to the total women autopsied. This figure is given as 5950 as it is stated that the totals of male and of female bodies were approximately equal.

It will be noticeable that Peters' figures correspond to a large extent with the others quoted below, given by Shure. Braasch (18) found that, of nearly a thousand patients picked at random, 20% had Hypertension, whereas, of 180 patients of both sexes suffering from Pyelonephritis, 26% had Hypertension. Oppenheimer (19) found that, in a series of autopsies, 24% had Hypertension as against 40% of 97 patients suffering from Pyelonephritis.

It will be seen from Table XXVIII, which is an analysis of Shure's figures, that the final totals for Hypertension have in each case been related to the Total Females in (a) the cases suffering from Pyelonephritis and (b) the Control Group. In this way it is possible to compare the relative percentages at the different Age Levels. It will be seen that, in all cases, the percentages in the Control Group are below those in the Pyelonephritis Group. From this, it may be argued immediately that there is some connection at least between Hypertension and

Pyelonephritis. This connection is noticeable in all Age Groups (for the sake of clarity I have omitted all but the Groups essential to my argument) but it is particularly noticeable in the earliest Age Group. Now, as from Shure's Table Six, it is evident that, in this Age Group, among the Controls, only 10% suffered from Hypertension, it is arguable that, were there no connection between Pyelonephritis and Hypertension, then the percentage of Hypertension in this Age Group should not be raised above this when the part of the Group suffering from Pyelonephritis is considered. On the contrary, examining Shure's Table Four we find that the percentage in this portion is 21.7% or more than double that in the Control Series. Similarly, in the following Group the figures are respectively 30.6% and 32.2%. It is only in the higher Groups that any appreciable increase is noted in the Controls as compared with the diseased cases. Again I must emphasise that these figures are all analysed from autopsies and that, therefore, one would expect the percentage of Hypertension to be even less in a Group drawn from the General population.

All these figures, which in all cases, show a definite increase in the percentage of patients having Hypertension when there is an infection of the pelvis of the kidney, support those of Peters in so far as the Hypertensive element of the late Toxaemias of Pregnancy is concerned. It would appear, therefore, that, if a further series of figures, culled from an adequate number of Pregnancies, gave a similar percentage of Toxaemia following Pyelitis and a similar number of cases of Toxaemic Pregnancies showed a similar percentage of Pyelitis, then there would be strong grounds for suspecting that the connection, as far as the other Toxaemic elements were concerned, would be based on fairly firm premises. It would remain then to discuss the probable factors involved and, from the literature, to try to establish the assumptions on a firm foot.

The results of my investigations which have been studied in the previous section give strong support to the findings of Peters and, in fact, in so far as the percentage of cases of Pyelitis of Pregnancy developing Toxaemia of Pregnancy is concerned in my series this is nearly double that of Peters.

On the assumption that the figures given by Peters supported by those quoted by me are of some significance it remains to be determined in what way the increase in Pyelitis of Pregnancy in cases of late Toxaemia of Pregnancy is related to the actual Toxaemia. It has been shown above that there is a very marked increase in the percentage of Pyelitis of Pregnancy in the cases of late Toxaemia of Pregnancy. From a study of the figures of other observers it is seen that the percentages found in these Tables are confirmed to a large extent.

According to Browne, in order that any theory of Toxaemia of Pregnancy can be sustained, it must satisfy one that it explains the following facts:

1. It occurs only in pregnancy or shortly after delivery.
2. It occurs chiefly in primigravidae.
3. It may occur in hydatidiform mole, where there is no foetus. It is relatively much more frequent in this condition.
4. It is not infrequently associated with accidental haemorrhage.
5. It is sometimes associated with bilateral cortical necrosis of the kidneys.
6. It may set in for the first time a few hours or more after delivery.

None of the current theories entirely satisfies all of these conditions. According to Tweedy (20) toxic protein derivatives entering the blood stream from the intestine are normally neutralised by tissue antibodies: in pregnancy extra toxins, derived from the foetus and placenta, overload the system and cannot be thus neutralised. Protein poisoning results. This does not explain post partum Toxaemia satisfactorily. Young (21) considers that toxic substances are, in fact, absorbed from the infarcted areas in the placenta, causing tissue poisoning with consequent Toxaemia. The studies of Trimble and Hill (22) discount this. In a very intensive examination of 640 placentae, they came to the conclusion that they could not recognise an acute type of infarct associated with Toxaemia of Pregnancy. Zangemeister's (23) Water-poisoning theory has been discounted by various observers. Rowntree's (24) experiments with dogs, in particular, are significant in that the only post mortem changes in dogs, poisoned by excess of water intake, is oedema of the tissues, whereas, in Toxaemia, widespread tissue changes are evident, notably, in the liver and kidneys. Paramore's (25) theory of increased intra-abdominal pressure is discounted by the fact that the renal blood flow is normal. The theory of Theobald (26), that the Toxaemia is an expression of a dietetic deficiency is very plausible but it does not explain the decrease in the percentage of cases of Toxaemia in Germany during the Great War in spite of the food blockade (Baader (27)). The findings of Hoffman and Anselmino (28), claiming an endocrine origin for Eclampsia, have not been confirmed. (Theobald (29), Levitt (30) and Hurwitz (31)). Other workers have produced conflicting evidence in this respect.

Goldblatt (7) found that, by occlusion of the renal artery by

an occlusion clamp, Hypertension occurred. This was due to the release of a substance called renin from the ischaemic renal cortex combining with a renin activator to form angiotonin, which acts directly on the blood vessels producing contraction of small arteries and arterioles. Corcoran and Page (32) found that renin affected especially the afferent arteries of the glomeruli. The rise of blood pressure, caused by this constriction, is almost entirely independent of the nervous system. (Pickering (33), Arnott and Kellar (34), Page (35)). In normal and Toxaemic Pregnancy, it has been shown that, renal blood flow is normal. (Chesley (36)). Renal ischaemia is not, therefore, the cause of the raised blood pressure of Toxaemia. Browne (1) considers that, in the face of the evidence, Oedema and Hypertension, by causing cerebral anaemia, play a chief part in the aetiology of Eclampsia and that these are complementary to each other. Thus Eclampsia may arise (a) if there is a sudden rise of blood pressure even if little Oedema, or (b) if there is much Oedema with little Hypertension. He also thinks that there is a part played by family predisposition.

Having disposed of the various theories, it remains to discuss the possibilities in regard to Pyelitis of Pregnancy in its relation to the late Toxaemias of Pregnancy. It has been pointed out already that there is a definite increase in the incidence of Hypertension in the presence of Pyelitis and of Pyelonephritis, even in the Non-pregnant state. This increase probably is due to the release of renin from the ischaemic renal tubules from the dammed up ureters and kidney pelves. This theory is fairly well established as has been mentioned already. (Blalock (8), Dill and Erickson (9), Hayes (10), Shure (16)). Barnes and Browne (37) have shown, in a report on the observation of 1956 patients, of whom 915 were nulliparous, that Pregnancy, in itself, does not predispose to chronic Hypertension, that there was no significant increase in the blood pressure in Pregnancy and that Pregnancy does not aggravate a tendency to Hypertension. This report, therefore, also supports the theory that the cause of the increased incidence of Hypertension in Pyelitis is due to the Pyelitis itself, particularly in so far as Pregnancy is concerned, since Pregnancy, in itself, does not take the part of an activator. Further support of the Back-pressure theory is given by Chesley (38). This observer found that the uric acid clearance is reduced in Toxaemia to a marked extent. This diminution depends on two factors (a) a decreased rate of glomerular filtration and (b) an increase in tubular reabsorption. These two findings can be explained easily on the assumption that there is a decreased flow through the glomeruli and a back pressure in the tubule due to one or other factor, the most well-known one being raised intra-abdominal pressure due to the gravid uterus, the other being the one we are attempting to establish, namely, Pyelitis of Pregnancy.

Since my figures for the incidence of Pyelitis of Pregnancy in Toxaemia of Pregnancy and of the incidence of Toxaemia of Pregnancy in Pyelitis of Pregnancy are similar to those of Peters (4,5), it would appear that there is a definite relationship, not only in the Hypertensive element of Toxaemia, but also in the other elements of this condition. That it is only one of several factors in causation cannot be doubted since Pyelitis is only present in a proportion of cases of Toxaemia. Were it only the Hypertensive element that was involved, then the other signs of Toxaemia should not occur, but it will be noted that this is not the case and all the manifestations of Toxaemia may follow, as may the other signs and symptoms without Hypertension. Hofbauer (39) found that atony and dilatation of the ureter, while common in Pregnancy are uncommon in Pre-eclampsia. This is in conflict with the findings of Hayes (10). It provides, however, an interesting possibility in that, if the Pyelitis precedes or is co-incident with the early stages of Toxaemia then the ureters may become filled with a cast, of the pus etc., and, becoming completely blocked, cause an increased back pressure thus providing the Hypertensive element, while the pituitary element, postulated by Hofbauer, provides the other elements.

In order that the relationship of Pyelitis of Pregnancy to the late Toxaemias of Pregnancy may be sustained it should satisfy Browne's postulates mentioned earlier.

1. It occurs only in Pregnancy or shortly after delivery.

It has been shown above that Urinary Infection is less common in Pregnancy than in Non-pregnancies, particularly where Non-toxic Pregnancies are concerned, but that it is very much more common in Toxic Pregnancies. The dilatation of the ureters and the ureteral stasis (Hayes (10)) predispose to Urinary Infection of the kidney pelvis. If the ureteral and pelvic lumina become infected, damming up of the ureter by products of this infection will inevitably lead to production of the renin-angiotonin syndrome of Goldblatt (7). In the cases where this does not occur Toxaemic symptoms will not develop and this would account for the cases of Pyelitis in which no Toxaemic symptoms are evident. It is obvious, therefore, that where Pyelitis is a factor in the production of Toxaemia, the dilatation of the ureters is a predisposing factor.

2. It occurs chiefly in primigravidae.

The abdominal walls of primigravidae being much firmer than those of multiparae cause increased intra-abdominal pressure which, in the presence of Pyelitis, is much more likely to lead to blocking of the ureter by the products of the Pyelitis thus leading again to the production of the renin-angiotonin syndrome.

3. It may occur in Hydatidiform Mole, where there is no foetus. It is relatively more common in this condition.

Hydatidiform Mole, being in the nature of Pregnancy, leads to similar dilatation of the ureters with the same possible results. I have no figures as to the frequency of Pyelitis in this condition.

4. It is not infrequently associated with accidental haemorrhage.

The occurrence of accidental haemorrhage has no bearing on the relationship of Pyelitis of Pregnancy to Toxaemia of Pregnancy. The importance of accidental haemorrhage in Toxaemic States has been denied. (Hill and Trimble (22)).

5. It is sometimes associated with bilateral cortical necrosis of the kidneys.

Bilateral cortical necrosis can be explained by the renin-angiotonin syndrome of Goldblatt (7) produced by the Pyelitis of Pregnancy as mentioned above.

6. It may set in for the first time a few hours or more after delivery.

Frequently there is an oliguria following delivery. In the presence of an existing Pyelitis this may lead to blockage of the ureter with production of the renin-angiotonin syndrome of Goldblatt (7).

Conclusion.

From a study of my observations and from comparison with the work of others, I conclude that Urinary Infection and, in particular, Pyelitis and Pyelonephritis of Pregnancy are factors in the causation of the late Toxaemias of Pregnancy. That they are not the only factors is self-evident since in only a proportion of cases of late Toxaemia of Pregnancy is there any evidence of Pyelitis of Pregnancy and not all cases of Pyelitis of Pregnancy develop late Toxaemia of Pregnancy. But that they are important factors cannot be doubted since the percentage of cases of Pyelitis of Pregnancy developing Toxaemia of Pregnancy is so high (44.73%) in relation to the percentage of Pregnancies developing Pyelitis. (3.18%).

Summary.

1. A short discussion of the theory that Pyelitis of Pregnancy is associated with the late Toxaemias of Pregnancy is given. From the literature, views for and against this association have been stated.
2. The problem of the present work has been stated. The period of the observations and the problems surrounding the collection of these observations have been made clear.
3. A statement of the criteria adhered to in the collection of these observations both as regards Hospital Case Records and Personal Case Records has been made.
4. A Series of Tables derived from these observations is included. A number of Tables giving a Control Series from the work of Shure (16) has been included.
5. A study of the author's own observations has been made.
6. The different aspects of the problem have been discussed. A comparison between the author's results and those of others has been made. A short summary of the various theories regarding the aetiology of the late Toxaemias of Pregnancy with the objections thereto is included. Finally, a discussion of the theory of the relationship of Pyelitis of Pregnancy to the late Toxaemias of Pregnancy, particularly in regard to the criteria laid down by Browne (1), completes this section.
7. The conclusion is drawn, from the author's observations and from examination of the literature, that Pyelitis of Pregnancy does, in fact, bear a close relationship to the late Toxaemias of Pregnancy, and that, while it is not the only factor concerned, it is an important one, in so far as 44.73% of all cases of Pyelitis of Pregnancy develop late Toxaemia of Pregnancy.

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