May 1

Dear Sir,

I am replying to your letter of [date]. Also from the Matriculation ticket I hand herewith an investigation of the brain of children, its nervous centres and its central areas and processes.

Yours truly,

A.W. Fuller
April 1903.

For the approval of the Faculty of Medicine for the degree of M.D.

This THESIS is submitted

by Arthur William Fuller M.B. Ch.B.
The object in writing this Thesis is threefold:

Firstly to estimate the average amount of urine passed in 24 hours by children of average health of the ages of six months up to twelve years inclusive.

Secondly. The estimation of the total urea usually passed in the urine of children when in health.

Thirdly. The quantitative estimation of the Purin-bodies in the urine of children of the ages mentioned.

The results obtained are recorded in a table and are in relation to age and to body weight. A full and complete record of the diet has been kept during each experiment. The great bulk of the cases were taken from healthy workhouse children belonging to the Parish of Lambeth, S.E., but a few cases were taken from The Royal Hospital for Children and Women, Waterloo Road, S.E., (only those beyond suspicion of disease being selected) and three of the children were obtained from private sources. The mode of procedure adopted in order to obtain the samples and to arrive at the estimation of the total urine passed by the child in twenty-four hours was as follows:-

The child was required to empty its bladder
at a given time - say 12.00 noon. This sample was not saved, but all the urine passed up to and including that passed at the same hour next day was kept - well mixed and a sample taken of the mixed urine. The urine total was measured and recorded in cubic centimetres. Each child was also carefully weighed at the time of the experiment.

Urea is the chief nitrogen containing constituent of the urine and its amount was ascertained by means of Gerrard's ureometer, all urine containing albumen being rejected except one sample which contained a very slight trace; this was boiled and carefully filtered before being tested.

The Purine bodies although containing a comparatively small quantity of nitrogen are of great interest from the point of view of Proteid Metabolism and the estimation of Uric Acid, and I am not aware that they have been estimated systematically and in this manner before.

The Purine Bodies used to be called Xanthine bases or nuclein bases because they are derived from Nuclein, or Alloxuric bases because they contain in combination two radicles one of Alloxan and the other of urea. Latterly they have been shewn to be derivatives of a substance called Purine by E. Fischer.
They consist of the following amongst others

(Purine C₅H₄N₄).

Monoxy purine or Hypoxanthine C₅H₄N₂O
Dioxy purine or Xanthine C₅H₄N₂O₂
Amino-purine or Adenine C₅H₄N₄NH
Amino-Oxy purine or Guanine C₅H₄N₂O₂NH
Trioxy purine or Uric Acid C₅H₄N₂O₄

Theobromine (Dimethyl Xanthine) Caffein Theine
(Trimethyl Xanthine), substances which are present
(in quantities varying from 1 to 3 per cent.) in
cocoa, coffee and tea respectively, are also Purine
derivatives. Purine itself (C₅H₄N₄) has not as yet been discovered in the body.

The quantity of Purine bodies found in
the urine bears a direct relation to the amount
of the Purine contained in the food eaten and is also affected by the extent of the nuclein
cleavage in the metabolic processes of the body.
The former group have been named exogenous the latter endogenous purine. The Purine bodies may
be fully precipitated by Nitrate of Silver in Ammoniacal solutions, or by cuprous oxide in the
presence of Sodium bisulphite.

They exist in all forms of meat extracts and in flesh meats of all kinds.
The potato and other vegetables such as the beetroot contain them. Oats also contain them.

The specifications of uric acid and the other Purin bodies upon the various tissues of the body are of great interest and importance.

(1) In relation to the question of diet in children during the early years of life;
(2) in regard to the cessation of the processes of growth, the maintenance of Adult life and the gradual decline of bodily activities.

The estimation of Purin substances in food have been made by several observers - Kossel, Burian und Schur, Offer und Rosenquist and more recently by Dr. Walker Hall of Manchester who arrives at the following conclusions:

(1) As the methods available for the estimation of purin-bodies in animal organs were unsatisfactory, both as to technique and results, modifications were introduced and a reliable process worked out.

(2) In food-stuffs, the purin-bodies occur in two forms "free" and "bound". Both the glandular and muscular tissues contain approximately equal amounts of "free-purins", but the glandular tissues yield very large and the muscles only very small quantities of "bound-purins" (nucleins).
(3) The estimations of the Purin bodies contained in meats show that considerable quantities are present, but that little difference exists between the amounts contained in white and dark meats.

Certain vegetable foods have been found to contain Purin bodies. Amongst these are peas, beans, oatmeal, asparagus and onions. This furnishes a reason for the high uric acid excretion which follows their ingestion.

(5) From several varieties of beer and porter Purin bodies have been isolated, and their percentage amounts estimated. Their presence may account for the harmful influence of these beverages in gout, and for some of the pathological changes which occur in Chronic Alcoholism.

(6) Experiments upon the action of the Purin bodies upon carbohydrate metabolism show that caffeine induces an increased elimination of CO₂. Uric acid and Hypoxanthin are inert in this respect.

(7) The continued daily injection of Hypoxanthin into rabbits hinders their growth, causes degenerative changes in the liver and kidneys, alters the cellular relations and contents of the blood and marrow and produces slight changes in the intima of the smaller blood-vessels.
Feeding experiments with fish, fowl, beef haricot beans and beer, under appropriate conditions, shew that the urinary purin is increased in all these cases; that this increase corresponds with 50 to 60 per cent. of the Purin bodies ingested with the food; that the purin is principally in the form of Uric Acid, and that the increase of Urinary Purines reflects the metabolic activity of the individual in regard to "nucleins".

The forces may contain unabsorbed nucleins as well as certain purin substances from the digestive forces and cell-nuclei, and estimations of these bodies should be included in all metabolic experiments.

When the free purins are ingested they are rapidly oxidised and decomposed. About 50 - 60 per cent. of hypoxanthin leaves the body as urinary purin (principally uric acid) within 4 - 6 hours and the same percentage of uric acid appears in the urine after 8 - 10 hours. The bound purins however take 1 - 2 days before they are fully excreted.

The remaining 50 per cent. of the food-purin is excreted as Urea or as bodies intermediate between uric acid and urea.

By the quantitative estimations of purine bodies in food stuffs an exact forecast of the exogenous urinary purin is possible, and its amount can be limited when necessary by prescribing
a certain diet. From the total urinary purin the exogenous portion can be deducted and the endogenous amount obtained.

(13) The endogenous purin is partly derived from Leucocytes, but mostly from the cell changes which result from the maintenance of bodily functions, as its amount is proportional to the weight of the individual; in other words it bears a direct relation to the metabolic activity necessary for systemic purposes. Hence as the cell-nucleus is the dominating factor in metabolism the cleavage of cell-nucleins may incite the decomposition of proteid matter. It is possible that the endogenous urinary purin represents about one half of the total endogenous purin produced, and that the latter quantity indicates the extent of metabolic processes more completely than any other factors at present available.

(14) The general conclusions of the investigation point to the need for determinations of the endogenous purins in many diseases, either by the use of purin free food stuffs or by the aid of tables giving the percentage of purin in food stuffs and the necessary calculations therefrom. For this the Purinometer is proposed.

(15) The action of the purin bodies upon the alimentary system as demonstrated by Pawlow and later by Potapow-Procaitis, strongly contra-
indicates the employment of meat extracts or soups in hyperchloridæa. Dr. Walker Hall also shews that the blood pressure is not altered by purin bodies either immediately or remotely. Although Uric Acid may be considered more as one of the normal excretions than an extensive factor in the causation of disease, there are many conditions in which a knowledge of a patient's nuclein metabolism is of value. A period of diminished uric acid excretion precedes acute attacks of gout and if such alterations could be rapidly and easily observed, preventive measures might palliate if not avert the attack."

Several methods have been devised for the estimation of uric acid which need not be described here e.g. the one of Ritter, Hopkins, Ludwig-Salkonski, A. Jolles, Wöfler, Lewandowsky, Folin and Shaffer, and that of Walker Hall (which) is the one the writer has used and is as follows:

In the experiments recorded in this thesis only albumen free urine was used, but for other experiments if any albumen should be present it is necessary to precipitate and remove if by filtration

8.
Two solutions are used:

**No. I Solution** consists of

- Ludwig's Magnesium Mixture 100 c.c.
- Ammonia solution 20% 100 c.c.
- Tale 10 grm.

**No. II Solution** consists of

- Silver Nitrate 1 grm.
- Ammonia Strong 100 c.c.
- Tale 5 grm.
- Distilled Water 100 c.c.

To 90 c.c. of the urine 20 c.c. of No. I solution are added. An immediate precipitate of the phosphates falls and the clear fluid remains.

To 80 c.c. of the clear fluid 18 c.c. of solution No. II is added. The resultant precipitate is a mixture of Silver Chloride and Silver Purin. The former body is dissolved by the excess of ammonia. The filtrate is shaken until all white flakes disappear and the finely granular yellow-white precipitate remains suspended. If the Silver Chloride is not entirely dissolved strong ammonia is added drop by drop and the solution well shaken until no AgCl remains. These two processes which have first been described are best carried out by means of the "Purinometer".
It consists of three parts:

(1) A closed graduated tube.

(2) A stop-cock with above of the same diameter as the upper tube.

(3) A small glass reservoir of known cubical capacity.

The graduated tube is capable of being shut off from the broader part by the glass stop-cock. The upper part of the cylinder has a moveable glass stopper.

90 c.c. of urine are taken from the mixed urine of the twenty-four hours and poured into the graduated cylinder taking care to have the stop-cock turned off.

Solution I. is added and the resulting precipitant of Phosphates is allowed to fall into the lower part of the tube by turning on the stop-cock. The time for the fluid to become quite clear varies, but is never less than five minutes and seldom over half an hour, the powdered talc greatly helps the precipitate to settle.

When the phosphates have in this manner fallen to the lower end of the tube the stop-cock is turned off again and No. II. solution is added up to 100 c.c.
The Purinometer should be inclined vigorously backwards and forwards for about a minute in order to dissolve the Silver Chloride and to reduce the flakes to a finely divided precipitate. Place the apparatus in a cupboard away from the light and then read off the number of c.c. occupied by the precipitate twenty-four hours later. Dr. Walker Hall recommends waiting as long as this and the writer has followed these instructions, but considers that this time is unnecessarily long.

No tea or coffee were allowed during the experiment.

The following results were obtained by the methods which have just been indicated.

N.B. In the next few pages, a summary of the methods of working out the results at the end of these pages will be found. A table summarising the results obtained:
I. H. (M) aged 1 year, weight 23 lb.

Total urine 199 cc.
Area Percentage 2.1

Purin = 0.007

Total lree 2.1 x 199 = 4.17

Purin = 0.007 x 199

100

= 0.139

Experiment 1

I. H. (M) aged 1 year

Total urine 232 cc
Area Percentage 1.0 cc

Purin = 0.0078

Total lree 1 x 232

100

= 2.32

Purin = 0.0078 x 232

100

= 0.18

Experiment 2

I. H. (M) aged 1 year

Total urine 213 cc
Area Percentage 2.3

Purin = 0.0097

Total lree 2.3 x 213

100

= 17.89

Purin = 0.0097 x 213

100

= 0.206

Experiment 3
N. Desil, aged 2 years  
Body weight 20 lbs.  

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Description</th>
<th>Urine Volume</th>
<th>Protein Percentage</th>
<th>Protein Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Diet milk 10 oz, meal 15 oz</td>
<td>417 cc</td>
<td>1.0</td>
<td>0.117 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total urine = 1 x 417 = 417 cc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Protein = 0.117 x 417 = 0.48 g</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

N. D.  

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Description</th>
<th>Urine Volume</th>
<th>Protein Percentage</th>
<th>Protein Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>b</td>
<td>Diet milk 11 oz, bread 5 1/2 oz, oatmeal 2 1/2 oz</td>
<td>322.7 cc</td>
<td>1.8</td>
<td>0.225 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total urine = 1.8 x 322.7 = 578 cc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Protein = 0.225 x 322.7 = 0.72 g</td>
<td>100</td>
<td></td>
<td></td>
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</tbody>
</table>

N. D.  

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Description</th>
<th>Urine Volume</th>
<th>Protein Percentage</th>
<th>Protein Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>c</td>
<td>Diet milk 15 oz, vegetables, bread 5 oz, oatmeal 2 oz</td>
<td>397.46 cc</td>
<td>2.0</td>
<td>0.156 g</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total urine = 2.0 x 397.46 = 794.92 cc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total Protein = 0.156 x 397.46 = 0.62 g</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Experiments a)</td>
<td>Experiments b)</td>
<td>Experiments c)</td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>----------------</td>
<td>----------------</td>
<td>----------------</td>
<td></td>
</tr>
<tr>
<td>Child B (boy)</td>
<td>6 months, 2 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight</td>
<td>28.7 lb.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total urine</td>
<td>284 cc</td>
<td>298 cc</td>
<td>298 cc</td>
<td></td>
</tr>
<tr>
<td>Percentage</td>
<td>1.4</td>
<td>2.2</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Puree</td>
<td>0.0136</td>
<td>0.0249</td>
<td>0.0225</td>
<td></td>
</tr>
<tr>
<td>Total puree</td>
<td>0.39</td>
<td>0.66</td>
<td>0.596</td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>Bread 2 1/2 oz</td>
<td>Butter 1/2 oz</td>
<td>Butter 1/2 oz</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Milk 10 1/2 oz</td>
<td>Milk 12 oz</td>
<td>Milk 14 oz</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meat 1 1/2 oz</td>
<td>Meal 2 oz</td>
<td>Vegetable 4 oz</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vegetable 4 oz</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experiments</td>
<td>Body Weight</td>
<td>Test Milk</td>
<td>Total Urine</td>
<td>Milk Percentage</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
<td>-----------</td>
<td>-------------</td>
<td>----------------</td>
</tr>
<tr>
<td>A</td>
<td>21st 3lb</td>
<td>Dec 1st</td>
<td>280 cc</td>
<td>3.6</td>
</tr>
<tr>
<td>B</td>
<td>28th 30 lbs</td>
<td>Dec 1st</td>
<td>280 cc</td>
<td>3.3</td>
</tr>
<tr>
<td>C</td>
<td>35.5 lbs</td>
<td>Dec 1st</td>
<td>355 cc</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Chas B aged 3 yrs 4 mos.  

Total urine 511 cc  

Diet  
Bread 602  
Potatoes 302  
Pudding 50  
Minced Meat 400  

Total 1022

Per cent  

Total urine 0.0117 x 511 = 0.559
D. B (F) aged 3 yr 2 mms experiments

Body weight 284.2 lbs Bread 502

Area percentage 1.7 cc

Bulbs 10

Pulne 0.175

Vegetable 36

Pulne = \frac{340 \times 0.175}{100} = 0.586

Total pulp 340 cc

area = 5.78

Pulne 0.066

D. B

Experiment 6

Total pulp 360 cc

Bread 602 lettuce 10

Area percentage 2.2

Pulne 0.0234

Total pulp \frac{2.2 \times 360}{100} = 7.92

Total Pulne \frac{0.0234 \times 360}{100} = 0.842

D. B

Experiment 7

Total pulp 326.5 cc

Bread 82

Area percentage 2.9

Pulne 0.0117

Rusk 82

Total 152

Total pulp \frac{326.5 \times 2.9}{100} = 9.468

Pulne \frac{326.5 \times 0.0117}{100} = 0.038
AH (F) aged 4 years  

**Experiment a**

**Body weight** 231 6 lbs  
**Diet**  
**Breakfast** 10 oz  
**Lentil Percentage** 2.4  
**Lentils** 0.0117  
**Total lentils** $\frac{426 \times 2.4}{100} = 10.27$  
**Total lentils** $\frac{0.0117 \times 426}{100} = 0.49$

**Experiment b**

**Total lentils** 369 cc  
**Lentil Percentage** 3.1  
**Lentils** 0.0117  
**Total lentils** $\frac{3.1 \times 369}{100} = 11.43$  
**Total lentils** $\frac{0.0117 \times 369}{100} = 0.43$

**Experiment c**

**Total lentils** 312 cc  
**Lentil Percentage** 2.6  
**Lentils** 0.0097  
**Total lentils** $\frac{2.6 \times 312}{100} = 8.11$  
**Total lentils** $\frac{0.0097 \times 312}{100} = 0.302$
P.C. 3(M) 5 years 5 months

Body weight 281 lb

Total urine 397 cc

Urine percentage 4.0

Purine 0.156

Total area 4.0 x 397 = 15.88

Purine 0.156 x 397 = 0.61

---

P.C. E. (M)

Body weight 281 lb

Total urine 397 cc

Urine percentage 4.0

Purine 0.156

Total area 4 x 397 = 15.88

Purine 0.156 x 397 = 0.61

---

P.C. (M) aged 4 years

Total urine 397 cc

Diets:
- Purine 100
- Potato 10
- Rice 20
- Beer 140
- Milk 20

Purine 0.175

Total area 15.88

Purine 0.175 x 397 = 0.69
J. P. (M) aged 54 years

Experiment 1
Total urine 312 cc  Body weight 251.5 lbs
Urea percentage = 2.8  Diet: Bread 80 cc

Purine = 0.0136  Butter 10 cc
Total Urea $\frac{2.8 \times 312}{100} = 8.73$ meal 10 cc
Total Purine $\frac{0.0136 \times 312}{100} = 0.042$ meal 3 cc
Carrot 3 cc
Potato 5 cc
Pudding 4 cc

Experiment 2
J. P. (M)
Total urine 170 cc  Diet as above
Urea Percentage = 4.0
Purine = 0.0097
Total Urea $\frac{4 \times 170}{100} = 6.8$ meal
Total Purine $\frac{0.0097 \times 170}{100} = 0.16$

Experiment 3
J. P. (M)
Total urine 284 cc
Urea percentage 3.4  Diet as above
Purine = 0.0097
Total Urea $\frac{3.4 \times 284}{100} = 9.656$
Total Purine $\frac{0.0097 \times 284}{100} = 0.27$
<table>
<thead>
<tr>
<th>H(H) aged 5</th>
<th>Experiment a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>Diet</td>
</tr>
<tr>
<td>Total urine</td>
<td>227 CE</td>
</tr>
<tr>
<td>Area Percentage</td>
<td>3.4</td>
</tr>
<tr>
<td>Parum</td>
<td>0.0136</td>
</tr>
<tr>
<td>Total area</td>
<td>3.4 x 227 = 7.718</td>
</tr>
<tr>
<td>Parum</td>
<td>0.0136 x 227 = 0.03</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H(H) aged 5</th>
<th>Experiment b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total urine</td>
<td>255.5 CE</td>
</tr>
<tr>
<td>Area Percentage</td>
<td>3.9</td>
</tr>
<tr>
<td>Parum</td>
<td>negligible</td>
</tr>
<tr>
<td>Total area</td>
<td>3.9 x 255.5 = 9.964</td>
</tr>
<tr>
<td>Parum negligible</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>H(H)</th>
<th>Experiment c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total urine</td>
<td>284 CE</td>
</tr>
<tr>
<td>Area Percentage</td>
<td>3.7</td>
</tr>
<tr>
<td>Parum</td>
<td>0.0117</td>
</tr>
<tr>
<td>Total area</td>
<td>3.7 x 284 = 10.508</td>
</tr>
<tr>
<td>Parum</td>
<td>0.0117 x 284 = 0.332</td>
</tr>
</tbody>
</table>
Experiment D

EAH (F) age 3 yr
Total urine 312 cc Diet urinary 142 cc
area percentage 3.9
Pawne = .0136
Total area $3.9 \times 312 = 1236.2$ cc
\[
\frac{1236.2}{100} = 0.33
\]

Experiment E

EAH (F)
Total urine 369 cc Diet urinary 152 cc
area percentage 3.4
Pawne = .0117
Total area $3.4 \times 369 = 1255.6$ cc
\[
\frac{1255.6}{100} = 0.42
\]
### Experiment A

<table>
<thead>
<tr>
<th>Item</th>
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<tbody>
<tr>
<td>Body Weight</td>
<td>231.968</td>
</tr>
<tr>
<td>Total urine</td>
<td>620 cc</td>
</tr>
<tr>
<td>Urea Percentage</td>
<td>2.95%</td>
</tr>
<tr>
<td>Urea Total</td>
<td>18.290</td>
</tr>
<tr>
<td>Parine</td>
<td>0.0218</td>
</tr>
<tr>
<td>Water</td>
<td>102 cc</td>
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</tbody>
</table>

### Experiment B

<table>
<thead>
<tr>
<th>Item</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total urine</td>
<td>568 cc</td>
</tr>
<tr>
<td>Urea Percentage</td>
<td>2.8%</td>
</tr>
<tr>
<td>Urea Total</td>
<td>15.924</td>
</tr>
<tr>
<td>Parine</td>
<td>0.0225</td>
</tr>
</tbody>
</table>

### Experiment C

<table>
<thead>
<tr>
<th>Item</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total urine</td>
<td>511 cc</td>
</tr>
<tr>
<td>Urea Percentage</td>
<td>2.95%</td>
</tr>
<tr>
<td>Urea Total</td>
<td>15.074</td>
</tr>
<tr>
<td>Total Parine</td>
<td>1.04</td>
</tr>
</tbody>
</table>
E. G. (F) aged 6 years  
Body weight 3.51 lbs  
Area percentage 3.1  
Parine: 0.0078  
Total area: 5.11 ce  

Mutton with 1/2 pint  
(3 1/2 oz meat 1/6 lb vegetables)  
1/2 pint milk  
Milk pudding: Sago 6 oz  
Hults: 102  
Cereal 1/2 pint  
Milk 1/2 pint  

---

E.G. aged 6  
Body weight 3.51 lbs  
Area percentage 3.7  
Parine: 0.0019  
Total area: 5.08 ce  

Sm. Sm.  
37 21  
100 100  
Parine: 0.0019 x 5.08 = 0.0179

---

E.G. aged 6.  
Total area: 3.97 ce  
Area percentage: 2.9  
Parine: 0.0136  
Total area: 2.9 x 3.97 = 11.51

Parine: 0.0136 x 3.97 = 0.0539

---

Experiment a  
Experiment b  
Experiment c
Experiment 1

L. S. (F) aged 7 years

Body Weight: 231 lbs.

Total urine 454 cc, Diet: Bread 5 m. crust ¾ m.,
Cereal 100 cc, Meat 3 oz., Carrots 3 oz., Potatoes 5 oz., Safy 4 oz.

Total urine percentage 2.6

Purine 0.0175

Total urine area - \( \frac{2.6 \times 454}{100} = 11.8 \)

- Purine area - \( \frac{454 \times 0.0175}{100} = 0.794 \)

Experiment 2

L. S.

Total urine 340 cc, Diet as above

Purine 0.0175

Total urine area - \( \frac{3.6 \times 340}{100} = 12.24 \)

- Purine area - \( \frac{0.0175 \times 340}{100} = 0.0595 \)

Experiment 3

L. S. Total urine 397 cc, Diet as above

Purine 0.0136

Total urine area - \( \frac{3.3 \times 397}{100} = 13.1 \)

- Purine area - \( \frac{0.0136 \times 397}{100} = 0.0539 \)
C D (M) aged 8 years

Experiment a

Body Weight 351 lb Diet Breads 12 m

Total Pumice 5.11 cc

area Percentage 2.8

Pumice .0205

Total area 2.8 x 5.11

Total Pumice .0205 x 5.11 = 14.3

CD (M) aged 8 yrs

Experiment b

Total Pumice 5.96 cc Diet a. above

area Percentage 2.4

Pumice .0185

Total area 2.4 x 5.96

Pumice .0185 x 5.96 = 11.02

CD (M) aged 8 yrs

Experiment c

Total Pumice 5.11 cc

area Percentage 3.1 Diet a. above

Pumice .0175

Total area 3.1 x 5.11

Pumice .0175 x 5.11 = 0.894
R.M. (F) aged 8 years

Experiment 2

Body weight 2.7 6/2 lb. Total urine

Area Percentage 3.6 = 483 ce

Purr. = .0195

Total Purr. = 3.6 \times 483 = 16.9

Purr. = .0195 \times 483 = .0941


Balls 12 oz. Potatoes 50 oz.

Cork as fruit Cabbage 30 oz

R.M. (F) aged 8 years

Experiment 1

Total urine 341 ce

Area Percentage 2.4 Diet as above

Purr. = .0117

Total Purr. = 2.4 \times 341 = 8.1841

Purr. = .0117 \times 341 = .0398

R.M. aged 8 years

Experiment 3

Body weight as above

Total urine 426 ce Diet as above

Area Percentage 1.7

Purr. = .0097

Total Purr. = 1.7 \times 426 = 7.242

Purr. = .0097 \times 426 = .0413
<table>
<thead>
<tr>
<th>B. B. (F) aged 9 years</th>
<th>Experiment a.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight 3 stone 6½ lb</td>
<td></td>
</tr>
<tr>
<td>Total Urine 596 cc</td>
<td>Dec. - Bread 12 oz.</td>
</tr>
<tr>
<td>Area Percentage 3.2</td>
<td>Butter 10 oz</td>
</tr>
<tr>
<td>Purine 0.185</td>
<td>Cocoa ½ pint</td>
</tr>
<tr>
<td>Total Area 3.2 x 596</td>
<td></td>
</tr>
<tr>
<td></td>
<td>19.07 meal. (10 fl.)</td>
</tr>
<tr>
<td>Purine 0.185 x 596</td>
<td>Cabbage 3 oz.</td>
</tr>
<tr>
<td></td>
<td>Potatoes 5½ lb</td>
</tr>
<tr>
<td></td>
<td>Milk pudding 5 oz</td>
</tr>
<tr>
<td></td>
<td>Milk ½ pint.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. B. (F) aged 9 years</th>
<th>Experiment b.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Urine 681 cc</td>
<td>Dec. 10 a.m.</td>
</tr>
<tr>
<td>Area Percentage 3.0</td>
<td></td>
</tr>
<tr>
<td>Purine 0.075</td>
<td></td>
</tr>
<tr>
<td>Total Area 3.0 x 681</td>
<td>20.48</td>
</tr>
<tr>
<td>Purine 0.075 x 681</td>
<td>1191</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. B (F) aged 9 yr.</th>
<th>Experiment c.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Urine 454 cc</td>
<td>Dec. 10 a.m.</td>
</tr>
<tr>
<td>Area Percentage 3.5</td>
<td></td>
</tr>
<tr>
<td>Purine 0.0097</td>
<td></td>
</tr>
<tr>
<td>Total Area 3.5 x 454</td>
<td>15.89</td>
</tr>
<tr>
<td>Purine 454 x 0.0097</td>
<td>0.0440</td>
</tr>
<tr>
<td>Name</td>
<td>Sex</td>
</tr>
<tr>
<td>----------</td>
<td>------</td>
</tr>
<tr>
<td>J. N. (F)</td>
<td>F</td>
</tr>
<tr>
<td>J. N. (F)</td>
<td>F</td>
</tr>
<tr>
<td>J. N. (F)</td>
<td>F</td>
</tr>
</tbody>
</table>

**Note:**
- Lactation: 3% of total urine
- Purée: calculated as a percentage of total urine
- Body Weight: 4' 11.5
- Purée calculation: $\frac{396 \times 0.0078}{100} = 0.0296$
- Purée calculation: $\frac{369 \times 0.0097}{100} = 0.0357$
- Purée calculation: $\frac{312 \times 0.0078}{100} = 0.0243$
Experiment 1

**E.H.** aged 10 yrs
Body height 45 11/8
Total urine 454 cc Del Breas 50

<table>
<thead>
<tr>
<th>area Percentage</th>
<th>1.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraffin</td>
<td>0.136</td>
</tr>
<tr>
<td>Total area</td>
<td>$1.8 \times 5.14 = 8.07$</td>
</tr>
<tr>
<td>Paraffin area</td>
<td>$\frac{0.136 \times 454}{100} = 0.61$</td>
</tr>
</tbody>
</table>

Experiment 2

**E.H.** (F) aged 10 yrs
Total urine 341 cc Del as above

<table>
<thead>
<tr>
<th>area Percentage</th>
<th>3.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraffin</td>
<td>0.117</td>
</tr>
<tr>
<td>Total area</td>
<td>$3.5 \times 341 = 11.93$</td>
</tr>
<tr>
<td>Paraffin area</td>
<td>$\frac{0.117 \times 341}{100} = 0.39$</td>
</tr>
</tbody>
</table>

Experiment 3

**E.H.** (F) aged 10 yrs
Total urine 511 cc Del as above

<table>
<thead>
<tr>
<th>area Percentage</th>
<th>3.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraffin</td>
<td>0.156</td>
</tr>
<tr>
<td>Total area</td>
<td>$3.5 \times 511 = 17.83$</td>
</tr>
<tr>
<td>Paraffin area</td>
<td>$\frac{0.156 \times 511}{100} = 0.79$</td>
</tr>
</tbody>
</table>
L.M (F) aged 11 years Experiment A
Body weight 351 12½ lbs
Total urine 625 cc Diet Bread 14 oz
area Percentage 2.3 Butte 1½ oz
Parme. kefir+ milk ½ pint
Total area 2.3 x 625 = 14.37
Parme. 0.0136

L.M (F) aged 11 years Experiment B
Total urine 681 cc Diet as above
area Percentage 2.7 Milk ½ pint
Parme. 0.0136
Total area 2.7 x 681 = 18.38
Parme. 0.0136 x 681 = 0.092

L.M (F) aged 11½ years Experiment C
Total urine 568 cc Diet as above
area Percentage 3.85
Parme. 0.0185
Total area 3.85 x 568 = 21868
Parme. 0.0185 x 568 = 0.105
A. O. aged 11 yr, weight 38.1. 7/6. Experiment.

Total urine 710 c.c.  Diet:

Bread 1 3/4 lb.

Urea Percentage 3.5

Peei 0.0156

Total Urea 3.5 x 710 = 24.85

Peei 0.0156 x 710 = 11.07

A. O. aged 11. Experiment.

Total urine 511 c.c.

Urea percentage 4.1

Peei Percentage 0.0136

Total Urea 4.1 x 511 = 20.95

Total Peei 0.0136 x 511 = 0.689


Total urine 596 c.c.

Urea percentage 3.7

Peei 0.0175

Total Urea 3.7 x 596 = 22.05

Peei 0.0175 x 596 = 10.43
EB (M) aged 12 yrs  

Body weight 451 lbs

Total urine 284 ce

Total urine = \( \frac{3.7 \times 284}{100} \) = 10.5

EB (M) aged 12 yrs

Body weight 451 lbs

Total urine 596 ce

Total urine = \( \frac{3.7 \times 596}{100} \) = 22.05
| Age | Female average rainfall | Male average rainfall | Total rainfall | Sex | 3
|-----|-------------------------|-----------------------|---------------|-----|---
| 10'kilo | 3 | 6 | 9 |
| 18'kilo | 1.8 | 1.7 | 3.5 |
| 23'kilo | 3 | 6 | 9 |
| 26'kilo | 1.6 | 1.5 | 3.1 |
| 31'kilo | 1.5 | 1.4 | 2.9 |
| 33'kilo | 1.3 | 1.2 | 2.5 |
| 34'kilo | 1.2 | 1.1 | 2.3 |

*Total: 6.36*
This table gives a summary of the results of these investigations.

It has been shown that in order to obtain reliable information regarding the amount of urine, urea, or purin bodies it is not sufficient to take one 24 hours' sample, at least 3 must be taken from each case. The variation is often considerable from day to day and the urea which on one day shows a high percentage on the following day (and perhaps because of this) may have dropped to a correspondingly low ratio.

This remark also applies to the amount of urine which in many cases varies very considerably on different days, and the same applies to the purin estimation. In all sixty-three samples have been taken from healthy children so that the results have some claim to be regarded as fairly representing the normal urinary percentage composition, etc. of healthy English children.

GENERAL CONCLUSIONS: The amount of urine of course increases with the growth and development of the body, but the amount of urine passed per kilo of body weight (although presenting some variation in
different individuals due either to their constitution or their habits will be found not to increase.

The amount of urea passed per kilogram of body weight would appear to be increased about the second year, but after this it remains fairly constant up to the age of twelve years and the increase at the second year is probably only due to the greater quantity and variety of the food ingested.

The results of the investigations of the excretion of urinary Purins show that the amount excreted per kilo of body weight bears no relation whatever to the age or sex of the individual. And this is of great interest when it is coupled with the fact that there are comparatively great variations pointing as it does to idiosyncrasies in this respect, and it may be of value as indicating hereditary and constitutional tendencies in the individual.

The method adopted in this series of experiments has been as nearly as possible physiological. The children were fed on an ordinary and suitable dietary, were healthily employed and having regular exercise. The writer considers that the results obtained from specialised dietaries are apt to be misleading on account of the production of unphysiological conditions.
### Churchill's Tables

<table>
<thead>
<tr>
<th>Age</th>
<th>Height</th>
<th>Sex</th>
<th>Total Pounds</th>
<th>Amount</th>
<th>Weight by Age</th>
<th>Total Height</th>
<th>Pharynx</th>
<th>Rabbit</th>
<th>Total Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>16.8</td>
<td>M</td>
<td>5</td>
<td>55</td>
<td>2.2</td>
<td>7.87</td>
<td></td>
<td></td>
<td>31.3</td>
</tr>
<tr>
<td>4</td>
<td>16.9</td>
<td>M</td>
<td>31</td>
<td>29</td>
<td>2.7</td>
<td>8.67</td>
<td></td>
<td></td>
<td>17.6</td>
</tr>
<tr>
<td>5</td>
<td>16.7</td>
<td>M</td>
<td>17</td>
<td>392</td>
<td>2.6</td>
<td>10.19</td>
<td></td>
<td></td>
<td>23.3</td>
</tr>
<tr>
<td>6</td>
<td>20.9</td>
<td>F</td>
<td>2</td>
<td>405</td>
<td>2.7</td>
<td>10.94</td>
<td></td>
<td></td>
<td>34.2</td>
</tr>
<tr>
<td>7</td>
<td>22.6</td>
<td>M</td>
<td>4</td>
<td>564</td>
<td>1.1</td>
<td>6.2</td>
<td></td>
<td></td>
<td>26.9</td>
</tr>
<tr>
<td>8</td>
<td>26.2</td>
<td>M</td>
<td>20</td>
<td>652</td>
<td>2.2</td>
<td>13.82</td>
<td></td>
<td></td>
<td>27.8</td>
</tr>
<tr>
<td>9</td>
<td>27.5</td>
<td>F</td>
<td>25</td>
<td>731</td>
<td>2.3</td>
<td>16.81</td>
<td></td>
<td></td>
<td>27.9</td>
</tr>
<tr>
<td>10</td>
<td>27.2</td>
<td>F</td>
<td>15</td>
<td>768</td>
<td>2.1</td>
<td>11.28</td>
<td></td>
<td></td>
<td>27.9</td>
</tr>
<tr>
<td>11</td>
<td>36.4</td>
<td>F</td>
<td>7</td>
<td>766</td>
<td>2.3</td>
<td>16.83</td>
<td></td>
<td></td>
<td>26.3</td>
</tr>
<tr>
<td>12</td>
<td>36.4</td>
<td>F</td>
<td>8</td>
<td>829</td>
<td>2.8</td>
<td>23.21</td>
<td></td>
<td></td>
<td>22.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>134</strong></td>
</tr>
</tbody>
</table>

**Note:** The table includes a total of 8 rows, with the final row summing the data.
It is interesting to note that these conclusions in respect to the total quantity of urine and urea contained in it are in agreement with the results obtained by Dr. Churchill, Professor of Pediatrics in the Chicago Polyclinic (Archives of Pediatrics '98, vol. vi. p. 646), (See table opposite).

Dr. Churchill mentions the fact that American children excrete a smaller amount of urine than those of Germany and Austria and some other countries. The observations of the writer show that the same remark applies to English children (or more correctly London children).

Vierordt's tables on this subject show an enormous difference in this respect but as his percentages were based on a very small number of cases they cannot be regarded as final.
### Vienot’s Table

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of cases</th>
<th>Average weight in kilograms</th>
<th>Total urine in 24 hours</th>
<th>No. of C.C. for each kilo of body weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5 boys</td>
<td>4</td>
<td>13.62</td>
<td>743</td>
<td>53.03</td>
</tr>
<tr>
<td>3-5 girls</td>
<td>4</td>
<td>14.73</td>
<td>708</td>
<td>48.00</td>
</tr>
<tr>
<td>6 boys</td>
<td>1</td>
<td>15.5</td>
<td>1209</td>
<td>78.00</td>
</tr>
<tr>
<td>7 boys</td>
<td>1</td>
<td>22.42</td>
<td>1055</td>
<td>47.06</td>
</tr>
<tr>
<td>11 boys</td>
<td>1</td>
<td>24.0</td>
<td>1815</td>
<td>75.64</td>
</tr>
<tr>
<td>13 boys</td>
<td>1</td>
<td>32.69</td>
<td>1758</td>
<td>23.12</td>
</tr>
<tr>
<td>Adults</td>
<td>63</td>
<td>1700 to 1800</td>
<td></td>
<td>28</td>
</tr>
</tbody>
</table>

As tending to confirm this it is evident that even in Adults the amount of urine passed in Germany and Austria is greater than in England and America.

- **Salkowsky** gives 1500 c.c. to 1700 c.c. as the average in Germany.
- **Jaksch** gives it as 1500 to 2000 c.c. in Austria.
- **Landois** and **Sterling** record the English average as 1000 to 1500 c.c. **Gautier** gives that of France as 1250 to 1300 c.c. and **Simon** that of Americans as 1000 c.c. to 1300 c.c.
Herz, after noting results from 60 children of both sexes from the ages of 3 to 14 years, found that from 500 to 1400 c.c. was the average daily amount and Camerer found from 619 to 1034 c.c. in individuals of from 2 - 11 years old. Parrot, Cruse, Camerer, Martin, Ruge and others state that from 200 to 500 grammes are the average diurnal quantity of urine passed by a child from 1 month to 2 years old. Dohrn and Martin, Ruge state the newborn infant passes in relation to every kilogram of body weight four times as much urine as the adult.

Holt by combining the results of the investigations of Schabanowa, Cruse, Camerer, Martin, Ruge, Berti, Schiff and Herter gives the following:

### TOTAL URINE

<table>
<thead>
<tr>
<th>Age</th>
<th>Grammes.</th>
<th>Ounces.</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 24 hours</td>
<td>0 to 60</td>
<td>0 to 2</td>
</tr>
<tr>
<td>Second &quot; &quot;</td>
<td>10 to 90</td>
<td>0 to 2</td>
</tr>
<tr>
<td>3 - 6 days</td>
<td>90 to 250</td>
<td>3 to 8</td>
</tr>
<tr>
<td>7 days to 2 months</td>
<td>150 to 400</td>
<td>5 to 13</td>
</tr>
<tr>
<td>2 to 6 months</td>
<td>210 to 500</td>
<td>7 to 16</td>
</tr>
<tr>
<td>6 months to 2 years</td>
<td>250 to 600</td>
<td>8 to 20</td>
</tr>
<tr>
<td>2 - 5 years</td>
<td>500 to 800</td>
<td>16 to 26</td>
</tr>
<tr>
<td>5 - 8 years</td>
<td>600 to 1200</td>
<td>20 to 40</td>
</tr>
<tr>
<td>8 - 14 years</td>
<td>1000 to 1500</td>
<td>32 to 48</td>
</tr>
</tbody>
</table>
In regard to the excretion of Urea.

Dohrn found 36 Milligrams of Urea in the bladder of a child who just born and Martin and Ruge determine the following quantities during the first 10 days of life 0.07683, 0.2504, 0.1358, 0.1817, 0.2567, 0.2267, 0.2284, 0.16240, and 0.1505.

Although the amount of Urea is very plentiful up to the end of first month (0.80 grms., per kilo of child) according to Parrot and amounting during the third week to 1 gramme and 1.89 grammes Dr. Fernandez Figueira of Rio de Janeiro says we may conclude that the amount is 1.7% and therefore less than in adults.

Holt (1903) gives the following:

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Amounts</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st days</td>
<td>0.076 to 0.114 Grammes.</td>
</tr>
<tr>
<td>2-7</td>
<td>0.140 to 0.650 &quot;</td>
</tr>
<tr>
<td>1 - 2 months</td>
<td>0.90 to 1.40 &quot;</td>
</tr>
<tr>
<td>3 - 5 years</td>
<td>13.09 to 14.01 &quot;</td>
</tr>
<tr>
<td>5 - 13 years</td>
<td>16 to 21.03 &quot;</td>
</tr>
</tbody>
</table>

This estimate gives a considerably lower amount in the case of children of 3 - 5 years than the writer has found to be the case and also a slightly lower estimate in children of from 5 - 13 years.
of age.

Churchill found that not only were the average percentages higher than the average given for adults but individual cases show a remarkably high percentage of elimination of Urea, no less than 8 children having over 3 per cent, the highest being 3.7 per cent. and this observation exactly agrees with the results obtained in the present investigations.

Purdy and Foster also state that the excretion of Urea in children is relatively higher than in adults. The low percentage of early infancy is of course due to the quiescent state of the child but Martin and Ruge report wide variations in single specimens during the first 10 days of life varying from .6 per cent. to 1.9 per cent. Schiff also gives wide variations .28 to 1.7 per cent. during the first 14 days.

Vierodts' observations give from 1.1 to 2 per cent. for older children from 3 to 12 years old but this result is based on only 7 cases.

Vögel pointed out in 1863 that although the absolute quantity of Urea passed by both women and children is less than by men yet the relative quantity passed by children in relation to the body weight
of the adult is greater. According to Uhle's observations (1859) children pass for each Kilo of their body weight as follows:

**UREA**

From 3 to 6 years about 1.0 grammes.
- 8 to 11 " " 0.8 "
- 13 to 16 " " 0.4 to 0.6 grammes.

This result as regards the ages 8 to 11 years is in accordance with that of the writer of this paper.

Vögel says the quantity naturally varies in different persons and in the same person at different times according to the bodily constitution and the nature of the diet and the activity of the nutritive functions of the individual.

Moreover these numbers do not include the maximum and minimum quantities of Urea which occur in certain cases in perfectly healthy persons.

Maubauer in 1863 proved that the Urine of a healthy man fed on a mixed diet contained 2.5 to 3.2 per cent of Urea and that the amount varied directly as weight of body and quantity of food ingested but numerous other investigations give 30 to 40 grammes = 0.37 to 0.60 grammes per Kilo of body weight.
Lehmann found 58 grammes of urea in twenty-four hours under a purely animal diet and this dwindled to .15 grammes on a non-nitrogenous diet. The urea does not wholly disappear even when no food is taken.

It is beyond the scope of this paper to discuss the origin of the urea and the causes of its variation, though it may be mentioned that Franque of Würzburg as far back as 1855 established that it was affected by the amount of nitrogenous food ingested, and Vögel stated that in 1863, the amount of urea was an approximate measure of the degree of metamorphosis of Proteid Compounds going on in the body; both these views are probably correct.

**PURIN BODIES:** The conclusions arrived at by the writer as to the amount of the Purin bodies excreted have been briefly referred to in an earlier part of this paper. The results recorded show that although there is much variation per kilo of body weight, yet this variation bears no relation to the age of the child. Uric acid is included in the Purin series, and Holt says in the last (1903) edition of his work, that few observations have been made on the elimination of uric acid, but all authorities agree that it is much higher in the newly
born than at any subsequent period of life.

\[
\text{Proportion of Uric Acid to Urea}
\]

<table>
<thead>
<tr>
<th>Age</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martin &amp; Ruge</td>
<td>1 : 14</td>
</tr>
<tr>
<td>Herter</td>
<td>1 : 60</td>
</tr>
<tr>
<td>under 1 year</td>
<td></td>
</tr>
<tr>
<td>from 2-5 years</td>
<td>1 : 50 - 70</td>
</tr>
<tr>
<td>from 2-15 years</td>
<td>1 : 45 - 60</td>
</tr>
</tbody>
</table>

CONCLUDING REMARKS.

The writer in presenting the result of his investigations feels bound to allude to the fact that, since Medicine is not an exact science, it is important for Physicians in this country to have data to refer to which have been obtained in this country, for however much we may owe to foreigners and to their statistics it is impossible—as the accompanying tables show—for them to be accepted as indicative without modification of the normal condition of things that obtains in the people of our own country who are not only of another race but generally speaking live under other conditions.

It is interesting to find that the results of the present enquiry must nearly agree with those obtained from American children by Dr. Churchill.
The remarks of Dr. Figuetti cannot be passed by when he says that the diseases of the urinary system and of other organic local affections demand a practical knowledge of clinical urology, and this chapter of Infantile Semiotics is as important as it is generally neglected either because it is believed erroneously that disturbances of the urinary functions are infrequent in the child or because of the usual difficulty in collecting the urine for examination.

Dr. Gilchrist, Dr. Harper, Edward G. Clayton and others have recently pointed out that the urine of tuberculous patients shows unusually low proportions of phosphates and of urea. Dr. Harper strongly advocates the use of urea to supply the deficiency, but the writer cannot say that he has ever seen any improvement from its use clinically. The diminution of nitrogen in the urine may be taken as a proof that there is an interference with proteid metabolism but it seems to be a crude therapeutic that would supply it in the form in which it is excreted, and what may be a valuable hint from nature becomes of no value practically if it is to be interpreted after this fashion.

The writer feels confident that the estimation of the Urea and Purin bodies as well as of the other
constituents of the urine will be of service in the
determination and treatment of certain diseases, and
is hopeful that this towards the subject may be
of use in the evolution and advancement of our
knowledge of those early chemical changes that take
place in the human organism in the course of dis-
ease, antecedent as they are to those gross lesions
with which the Pathologist becomes so familiar,
and which after all are oftentimes only monuments
of the present deficient state of knowledge of the
slow and subtle processes whereby those organic
changes have been produced.
Thesis.