
Urinary Potassium Excretion in Newborns With and Without Icterus Neonatorum*

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The precise mechanism underlying the common 'physiological' jaundice of the newborn remains uncertain (Goldbloom and Gottlieb, 1929; Billing and Lathe, 1956; Lathe and Walker, 1957; Nelson, 1964). This study was based upon a previous suggestion that increased haemolytic activity operates in some cases, and that an increased urinary potassium concentration is one expression of this, continuing as long as abnormal haemolytic activity persists (Gotlieb and Pesach, 1962).

In an earlier investigation of newborn infants affected by icterus neonatorum (Gotlieb, Pesach, and Rimon, 1961), 16 out of 18 showed the presence of lysolecithin in serum after incubation with lecithin. Under the same conditions lysolecithin was shown in only 1 of 10 infants without icterus neonatorum. Further studies (unpublished) showed that the difference in serum lysolecithin concentrations between the two groups of newborns was smaller than previously reported, though still statistically significant. Lysolecithin, which is known to be a strong haemolytic agent, may thus be a causative factor in icterus neonatorum. More direct evidence is needed, however, to substantiate haemolytic theories of idiopathic icterus neonatorum.

Since erythrocytes have a high content of potassium (420 mg./100 ml. RBC, Wintrobe, 1961), and since the renal excretion of potassium in the newborn is apparently efficient (McCance and Widdowson, 1954; Tudvad, McNamara, and Barnett, 1954), a rise in urinary potassium concentration may serve as an index of haemolysis (Gotlieb and Pesach, 1962).

The present investigation was designed to re-appraise the significance of differences between potassium excretion in newborns with and without physiological jaundice.

Material and Methods

The study relates to 96 normal full-term newborn infants, divided into two groups. Infants suffering from haemolytic disease of the newborn were excluded. 89 infants were breast fed, and 7 were artificially fed; 3 in group I and 4 in group II.

Cord blood and venous samples were collected each morning during the first 4 days of life, and at the same time the newborns were observed for clinical jaundice. Bilirubin was determined by the Malloy and Evelyn method (1937). Our main criterion for the division into 2 groups was the behaviour of serum bilirubin during the first 4 days of life and not the clinical jaundice. Infants were divided into 2 groups as follows.

Group I (44 infants, 16 males, 28 females) consisted of all infants in whom the serum bilirubin level showed a fall on the fourth day after an initial rise during the first three days of life, i.e. the peak of serum bilirubin occurred during the third day. In 36 of these, this peak did not exceed 5 mg./100 ml., and in the remaining 8 it ranged between 5–7 mg./100 ml. (in 4 of these 8 jaundice was apparent).

Group II (52 infants, 33 males, 19 females) consisted of infants in whom the serum bilirubin level on the fourth day of life was either the same or higher than the level on the third day. Clinically this group comprised infants in whom jaundice on the fourth day was either static or still increasing.

Urine samples were collected at least once a day and the potassium concentration was determined by flame photometry. In addition, in 58 cases the total urine excreted over a 7-hour period (from midnight to 7 a.m.) was collected, and both the concentration and absolute amount of potassium excreted over this period were measured.

Results

The means, standard deviation, and standard errors in the serum bilirubin and urine potassium results for each group are shown in Table I, and the mean serum bilirubin levels of the two groups are shown in Fig. 1.

The trend of the curves for mean urinary
Urinary Potassium Excretion in Newborns With and Without Icterus Neonatorum

TABLE I
Serum Bilirubin and Potassium Concentrations, and Urinary Potassium Excretion in First 4 Days of Life in Both Sexes: Comparison of Groups*

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(44 newborns: 16 M, 28 F)</td>
<td>(52 newborns: 33 M, 19 F)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>SD</td>
<td>SE</td>
<td>Mean</td>
</tr>
<tr>
<td>Serum bilirubin</td>
<td>(mg./100 ml.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st day</td>
<td>1-6</td>
<td>0-56</td>
<td>0-09</td>
</tr>
<tr>
<td>2nd day</td>
<td>3-4</td>
<td>1-44</td>
<td>0-22</td>
</tr>
<tr>
<td>3rd day</td>
<td>4-0</td>
<td>2-03</td>
<td>0-31</td>
</tr>
<tr>
<td>4th day</td>
<td>3-4</td>
<td>1-61</td>
<td>0-25</td>
</tr>
<tr>
<td>Urinary potassium</td>
<td>(mg./100 ml.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st day</td>
<td>133-4</td>
<td>49-3</td>
<td>7-42</td>
</tr>
<tr>
<td>2nd day</td>
<td>168-5</td>
<td>56-8</td>
<td>8-55</td>
</tr>
<tr>
<td>3rd day</td>
<td>133-5</td>
<td>47-8</td>
<td>7-20</td>
</tr>
<tr>
<td>4th day</td>
<td>90-7</td>
<td>47-8</td>
<td>7-20</td>
</tr>
<tr>
<td>Absolute 7-hour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>potassium excretion</td>
<td>(mg.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st day</td>
<td>6-9</td>
<td>4-11</td>
<td>0-79</td>
</tr>
<tr>
<td>2nd day</td>
<td>7-9</td>
<td>6-12</td>
<td>1-18</td>
</tr>
<tr>
<td>3rd day</td>
<td>6-7</td>
<td>4-38</td>
<td>0-84</td>
</tr>
<tr>
<td>4th day</td>
<td>4-2</td>
<td>3-10</td>
<td>0-60</td>
</tr>
<tr>
<td>Total</td>
<td>25-7</td>
<td>10-01</td>
<td>1-92</td>
</tr>
</tbody>
</table>

* For definition of Groups I and II see text.

potassium concentration was similar in both groups (Fig. 2), with the maximum concentration on the second day of life. But the greater concentration of potassium in group II (jaundiced) on the second, third, and fourth days, though not on the first day, was statistically significant (Table I).

In group I, 8 of the 44 newborns had a serum bilirubin level above 5 mg./100 ml. on the third

![Fig. 1.—Mean serum bilirubin in groups I and II during first 4 days of life.](http://adc.bmj.com/)

![Fig. 2.—Mean urinary potassium concentration in groups I and II during first 4 days of life.](http://adc.bmj.com/)
Gotlieb and Pesach

day (range 5–7 mg./100 ml.). In 4 of these clinical jaundice was apparent (9%). The remaining 40 in that group showed no clinical jaundice. In group II, all 52 infants showed clinical jaundice. The absolute urinary excretion of potassium in the 7-hour period was also greater in group II, with significant differences between the two groups, both for the total urinary potassium excretion during the four 7-hour periods, and for the individual 7-hour periods on both the second and fourth days (Table I and Fig. 3).

Because of the significant difference (p<0.001) in the sex distribution between the two groups, comparative studies were made separately for males and females (Tables II and III). Within each sex, the differences between the two groups were similar to those observed in the groups comprising both sexes.

**Discussion**

There seem to be no satisfactory criteria for defining physiological jaundice in a newborn. Widely different bilirubin levels have been suggested as representing upper limits of normal (Brennemann, 1965; Brown, 1962).

On examining daily serum bilirubin levels in 289 newborn infants, we observed that in the majority (86%) the serum bilirubin rose during the first 3 days of life. On the fourth day the situation may be modified in one of 3 main directions as follows: (1) Bilirubin decreases and the jaundice abates; (2) the bilirubin level of the third day is maintained on the fourth day, and jaundice generally remains just noticeable; (3) the bilirubin level continues to rise and jaundice becomes conspicuous.

It seems therefore that the ‘dynamics’ of the bilirubin concentration indicate the appearance or non-appearance of jaundice. A similar observation was mentioned by Ylppö as quoted by Davidson, Merritt, and Weech (1941).

It has been suggested that the serum potassium levels should serve as an indicator of haemolysis (Rappaport, 1949). However, upon examination of serum potassium levels in cases of icterus neonatorum and in infants with proven haemolytic

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**TABLE II**

*Serum Bilirubin and Potassium Concentration in First 4 Days of Life in Males: Comparison of Groups*

<table>
<thead>
<tr>
<th>Serum bilirubin (mg./100 ml.)</th>
<th>Group I (16 infants)</th>
<th>Group II (33 infants)</th>
<th>Group Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Means</td>
<td>SD</td>
<td>SE</td>
</tr>
<tr>
<td>1st day</td>
<td>1.8</td>
<td>0.65</td>
<td>0.16</td>
</tr>
<tr>
<td>2nd day</td>
<td>4.1</td>
<td>1.33</td>
<td>0.33</td>
</tr>
<tr>
<td>3rd day</td>
<td>4.7</td>
<td>1.75</td>
<td>0.44</td>
</tr>
<tr>
<td>4th day</td>
<td>4.1</td>
<td>1.57</td>
<td>0.39</td>
</tr>
</tbody>
</table>

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**TABLE III**

*Serum Potassium Concentration in First 4 Days of Life in Males: Comparison of Groups*

<table>
<thead>
<tr>
<th>Urinary potassium concentration (mg./100 ml.)</th>
<th>Group I (16 infants)</th>
<th>Group II (33 infants)</th>
<th>Group Comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st day</td>
<td>119.4</td>
<td>28.2</td>
<td>7.05</td>
</tr>
<tr>
<td>2nd day</td>
<td>168.4</td>
<td>33.8</td>
<td>8.45</td>
</tr>
<tr>
<td>3rd day</td>
<td>140.3</td>
<td>45.5</td>
<td>11.38</td>
</tr>
<tr>
<td>4th day</td>
<td>89.4</td>
<td>48.8</td>
<td>12.20</td>
</tr>
</tbody>
</table>
processes, we found a rise of serum potassium in only about 30% of the cases examined. The rise in serum potassium during haemolysis seems to be transient, since the excess potassium is rapidly excreted by the kidneys (McCance and Widdowson, 1954; Tudvad et al., 1954). For this reason, it was thought that urinary potassium excretion might serve better than serum potassium levels as an index of haemolysis.

The profile of the curves of urinary potassium concentrations (Fig. 2) was found to be similar in both groups, with a peak on the second day of life. This peak may be related to an increased concentration of the small amount of urine excreted on that day (Smith, 1959).

There is a similar trend in the absolute potassium excretion during the 7-hour period (Table I, Fig. 3). There is no statistical significance on the first day, as in all the other comparable groups, and no significant difference on the third day, and this we cannot explain.

On the first day of life there is no significant difference between the urinary potassium concentration in the two groups. This might indicate that the metabolic or haemolytic reaction responsible for physiological jaundice begins only in extrauterine life.

It is known that the immature liver of the newborns has a limited capacity to conjugate bilirubin (Billing and Lathe, 1956; Lathe and Walker, 1957). While liver immaturity plays a dominant role in idiopathic icterus neonatorum, any haemolytic element present must be important, since the destruction of even an additional 1% of the total erythrocytes releases enough bilirubin to increase the serum bilirubin level significantly (Brown, 1962; Odell, 1968). However, the detection of an increase in haemolysis of this order is not possible with ordinary haematological methods.

Urinary potassium examination may be of assistance in the management of cases of jaundice due to haemolytic disease of the newborn. A low urinary potassium concentration or a fall in the urinary potassium concentration indicates that the haemolytic process is abating, and that the immature liver is likely to be able to deal with the conjugation of the small amounts of bilirubin still being produced. This consideration may help to avoid some unnecessary exchange transfusions (Gotlieb and Pesach, 1963).

**Summary**

Urinary potassium concentration was measured in 96 normal newborn infants during the first four days of life. In 58 newborns, an overnight 7-hour collection of urine was made, and potassium excretion was measured.

The subjects were divided into two groups according to the bilirubin pattern. Group I consisted of 44 newborns, where the bilirubin rose during the first 3 days of life and came down on the fourth day. Maximal levels of serum bilirubin above 5 mg./100 ml. (range 5–7 mg./100 ml.) were nevertheless identified in 8 of the 44 subjects. Except for 4, the infants of group I were non-jaundiced.

In group II (52 newborns) the level of serum bilirubin did not fall on the fourth day, either remaining stationary or rising; and all were clinically jaundiced.
The urinary potassium concentrations were found to be significantly higher in the infants of group II (jaundiced) compared with the group I (mainly non-jaundiced) infants for all days except the day of birth.

The absolute 7-hour excretion of potassium was also significantly higher in group II (jaundiced) on the second and fourth days, and in the total of all four days. These findings suggest a greater degree of haemolysis in infants with icterus neonatorum.

It is concluded that increased haemolysis may play some part in the aetiology of 'physiological' jaundice, and that the measurement of urinary potassium concentration may be a useful aid in the management of jaundiced infants.

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