A STUDY OF THE BLOOD CHOLESTEROL IN CHILDHOOD*

BY

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I. THE BLOOD-CHOLESTEROL LEVEL IN HEALTHY CHILDREN.

Previous investigations.—From a perusal of the literature it appears that the subject of the blood-cholesterol level in healthy children has not been attacked systematically hitherto. Much work has been done on the normal percentage of cholesterol in both the whole blood and the plasma of adults, though many differing methods have been employed. More estimations have been made on the blood of babies under two than on older children, but the effects of age and sex have not been studied in any detail. Some division into age groups has been attempted, but a variety of methods of estimation has been adopted and rather variable results obtained, so that before beginning any work on morbid children, it was essential to have a table of normal values, obtained by the same method as that used in the other work.

Normal percentage in adults.—Taking a review of the literature the normal adult value, as given by different workers, is fairly uniform.

Bloor who quotes the average of figures given in the literature as being 170 mgm. per cent, gives results which are slightly higher. His own values are 210–240 mgm. per cent, for women and 190–250 for men. Denis has somewhat similar values: 167–225 for women and 192–255 for men. Chauvaffd, Laroche and Grigaut give the normal as 150–180, and MacAdam and Shiskin are in close agreement with results of 133–191, the average being 161 mgm. per cent. Wade also considers the normal value to be 165. Hunt’s figures are slightly higher (177 mgm. per cent.).

Normal percentage in children.—The normal percentages for children quoted in the literature show a very much wider variation. Some of these figures apply to whole blood and others to plasma, which may in part account for some of the discrepancies.

Gordon and Cohn, using Bloor’s method on serum, give the average for cord blood as 89; in the first week of life as 87; and afterwards up to two years as 110–190 mgm. per cent.

Manicatide, Bratesco and Rusecco using Grigaut’s method on serum give an average of 131 under four months, and 116 from four months to one year. Their average they took as 125 mgm. per cent, for all babies whether artificially or breast fed.

Baylac and Sendrail using Grigaut’s method on serum give 149 as the average, which is in agreement with Baranski’s results of 150 mgm. per cent. Simone gives values of 67–105, and Varone’s results are also rather lower than the average, giving 115 as normal for infants.

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leading
obtained
by
is
now
allowed
extraction
to
sound
health
simple,
paratively
amounts
mixing
After
time
blood,
using
first
of
pure
prepared
filter
paper
thimble
a
is
conveniently.

It
is
described
in
the
Bausch-Lomb
colorimeter
obtained
easily
accordingly
was
required
of
numbers
of
methods
one
under
the
whole
operation
and
very
expensive.
The
colorimetric
methods
employed
give
slightly
higher
results
than
the
gravimetric,
but
on
the
whole
they
are
accurate.
In
the
present
investigation,
large
numbers
of
estimations
had
to
be
performed
and
a
reasonably
rapid
method
was
accordingly
essential;
and
as
the
patients
were
children,
a
simple
method
of
obtaining
the
required
small
quantity
of
blood
was
necessary.
The
method
described
by
Leiboff
appeared
to
fulfil
these
stipulations
the
most
conveniently.
A
small
amount
of
blood
only
is
needed,
the
apparatus
is
comparatively
simple,
and
there
is
very
little
opportunity
for
experimental
error
to
occur.
The
results
appear
very
consistent
and
thus
justify
the
adoption
of
this
method.

As
a
preliminary
precaution,
estimations
were
made
on
the
writer's
own
blood,
using
first
a
modified
Myers-Wardell
method
and
comparing
the
results
obtained
by
Leiboff's
method.
The
results
agreed
very
well
as
can
be
seen
in
the
following
list:

<table>
<thead>
<tr>
<th>Method</th>
<th>Estimation</th>
<th>Cholesterol mgm. per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myers-Wardell</td>
<td>1</td>
<td>156</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>156</td>
</tr>
<tr>
<td>Leiboff's method</td>
<td>1</td>
<td>153</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>169</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>160</td>
</tr>
</tbody>
</table>

Leiboff's method.—This
method
is
briefly
as
follows:

The
patient's
finger
is
cleaned
thoroughly
with
ether
and
pricked.
5
ccm.
of
blood
is
obtained
in
this
manner.
2
ccm.
of
this
blood
is
measured
out
and
run
on
to
a
special
prepared
filter
paper
thimble
end,
which
is
then
allowed
to
dry
at
room
temperature.
5
ccm.
of
pure
anhydrous
chloroform
is
poured
into
the
extractor
tube
and
the
filter
paper
disc
is
dropped
into
position.
The
tube
is
attached
to
a
reflux
condenser,
immersed
in
a
beaker
of
water,
and
extraction
allowed
to
proceed
for
twenty-five
minutes.
At
the
end
of
this
time,
the
extractor
tube
is
removed
from
the
condenser
and
cooled.
The
disc
is
taken
out
and
discarded.
Chloroform
is
now
added
exactly
to
the
5
ccm.
mark.
In
a
corresponding
extractor
tube
5
ccm.
of
a
standard
solution
of
cholesterin
in
chloroform,
containing
3
mgm.
cholesterin
per
5
ccm.
To
both
tubes
are
added
2
ccm.
acetic
anhydride
and
2
ccm.
concentrated
sulphuric
acid.
After
mixing
and
cooling,
the
extractor
tubes
are
placed
in
a
dark
cupboard
for
twenty
minutes.
By
this
time
the
colour
has
developed
and
the
contents
of
the
tubes
are
poured
into
the
cups
of
a
Bausch-Lomb
colorimeter
and
the
estimations
are
made.

Cases
investigated.—The
children
chosen
to
represent
the
normal,
were
sound
healthy
children
from
an
orphanage
in
the
vicinity.
They
were
all
leading
a
normal
life
of
a
more
or
less
standardized
type,
having
similar
amounts
of
exercise,
diet
and
school
work.

Fifty-nine
cases
in
all
were
studied,
including
twenty-six
boys
and
thirty-three
girls.
All
the
children
were
between
the
ages
of
thirteen
and
six
years.
## Table 1. The Cholesterol Level in 59 Normal Children

<table>
<thead>
<tr>
<th>Age</th>
<th>Mgrm. per cent.</th>
<th>Age</th>
<th>Mgrm. per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 years, 8 months</td>
<td>145</td>
<td>13 years, 11 months</td>
<td>137</td>
</tr>
<tr>
<td>13 .. 6 ..</td>
<td>142</td>
<td>13 .. 1 ..</td>
<td>134</td>
</tr>
<tr>
<td>12 .. 9 ..</td>
<td>142</td>
<td>13 .. 0 ..</td>
<td>131</td>
</tr>
<tr>
<td>12 .. 0 ..</td>
<td>146</td>
<td>12 .. 8 ..</td>
<td>142</td>
</tr>
<tr>
<td>12 .. 8 ..</td>
<td>142</td>
<td>12 .. 6 ..</td>
<td>132</td>
</tr>
<tr>
<td>12 .. 2 ..</td>
<td>157</td>
<td>12 .. 1 ..</td>
<td>137</td>
</tr>
<tr>
<td>11 .. 11 ..</td>
<td>143</td>
<td>11 .. 10 ..</td>
<td>127</td>
</tr>
<tr>
<td>11 .. 9 ..</td>
<td>145</td>
<td>11 .. 10 ..</td>
<td>135</td>
</tr>
<tr>
<td>11 .. 9 ..</td>
<td>142</td>
<td>11 .. 10 ..</td>
<td>135</td>
</tr>
<tr>
<td>11 .. 0 ..</td>
<td>140</td>
<td>11 .. 10 ..</td>
<td>133</td>
</tr>
<tr>
<td>10 .. 9 ..</td>
<td>142</td>
<td>11 .. 9 ..</td>
<td>128</td>
</tr>
<tr>
<td>10 .. 0 ..</td>
<td>142</td>
<td>11 .. 9 ..</td>
<td>134</td>
</tr>
<tr>
<td>10 .. 0 ..</td>
<td>138</td>
<td>11 .. 4 ..</td>
<td>125</td>
</tr>
<tr>
<td>9 .. 10 ..</td>
<td>133</td>
<td>10 .. 11 ..</td>
<td>142</td>
</tr>
<tr>
<td>9 .. 5 ..</td>
<td>132</td>
<td>10 .. 5 ..</td>
<td>126</td>
</tr>
<tr>
<td>9 .. 3 ..</td>
<td>137</td>
<td>10 .. 5 ..</td>
<td>125</td>
</tr>
<tr>
<td>8 .. 11 ..</td>
<td>132</td>
<td>10 .. 4 ..</td>
<td>125</td>
</tr>
<tr>
<td>8 .. 11 ..</td>
<td>136</td>
<td>10 .. 3 ..</td>
<td>137</td>
</tr>
<tr>
<td>8 .. 5 ..</td>
<td>139</td>
<td>9 .. 11 ..</td>
<td>129</td>
</tr>
<tr>
<td>8 .. 4 ..</td>
<td>131</td>
<td>9 .. 9 ..</td>
<td>137</td>
</tr>
<tr>
<td>8 .. 4 ..</td>
<td>131</td>
<td>9 .. 3 ..</td>
<td>142</td>
</tr>
<tr>
<td>7 .. 11 ..</td>
<td>133</td>
<td>8 .. 9 ..</td>
<td>129</td>
</tr>
<tr>
<td>7 .. 11 ..</td>
<td>132</td>
<td>8 .. 2 ..</td>
<td>133</td>
</tr>
<tr>
<td>7 .. 7 ..</td>
<td>136</td>
<td>8 .. 2 ..</td>
<td>129</td>
</tr>
<tr>
<td>7 .. 7 ..</td>
<td>133</td>
<td>8 .. 0 ..</td>
<td>135</td>
</tr>
<tr>
<td>6 .. 11 ..</td>
<td>133</td>
<td>6 .. 5 ..</td>
<td>133</td>
</tr>
<tr>
<td>6 .. 11 ..</td>
<td>130</td>
<td>6 .. 7 ..</td>
<td>125</td>
</tr>
<tr>
<td>6 .. 7 ..</td>
<td>125</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TABLE 2.

AVERAGE BLOOD CHOLESTEROL FOR EACH AGE GROUP.

<table>
<thead>
<tr>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>Mgrm. per cent.</td>
</tr>
<tr>
<td>13</td>
<td>144</td>
</tr>
<tr>
<td>12</td>
<td>144</td>
</tr>
<tr>
<td>11</td>
<td>142</td>
</tr>
<tr>
<td>10</td>
<td>140</td>
</tr>
<tr>
<td>9</td>
<td>132</td>
</tr>
<tr>
<td>8</td>
<td>134</td>
</tr>
<tr>
<td>7</td>
<td>134</td>
</tr>
<tr>
<td>6</td>
<td>129</td>
</tr>
</tbody>
</table>

CHART II.

THE RANGE OF VARIATION AT EACH AGE.
(max. per cent. cholesterol minus min. per cent. cholesterol).
BLOOD CHOLESTEROL IN CHILDHOOD

Results.—Table 1 and Chart 1 show the results obtained in each case graduated according to age.

Table 2 shows the average readings of the blood cholesterol for each age group.

Discussion.—Table 1 and 2 show the results obtained and for greater ease of explanation these have been expressed in the form of graphs also (Charts I and II). From a consideration of the figures given, some facts of importance emerge.

First, it is obvious that a consistent level of blood cholesterol is maintained throughout childhood. In the case of boys, this shows a steady and progressive rise towards puberty, with a rather more rapid increase from the age of nine onwards. From nine to ten years the curve is steep, but a more even level is maintained from ten to thirteen. In the case of girls the amount of variation at every age is markedly greater than that shown by the boys, and this is especially manifest between the ages of ten and thirteen when a definite degree of instability exists, the curve tending to show a drop at eleven with a subsequent rise at twelve. The whole curve is entirely different from that of the boys, a progressive rise from the time of the second dentition until puberty not being apparent.

A curve of the range of variability has been plotted (Chart II), and this shows very clearly the wide range of variation which occurs in girls, especially at the ages of ten, eleven and twelve. This may be regarded as being coincident with the onset of puberty.

It will be seen also from a consideration of the graphs that the cholesterol level in girls tends on the average to be somewhat lower than in boys at every age.

II. THE BLOOD-CHOLESTEROL LEVEL IN CHILDHOOD DURING DISEASE.

From a consideration of the literature, it is apparent that the blood cholesterol level is disturbed during the course of many diseases.

During the present investigation, many examples of various diseases have been studied, but chief among these have been patients showing various phases of rheumatic infection. The main object in view being to determine whether or not there is any abnormality in the cholesterol content of the blood during the course of juvenile rheumatism, estimations have been made in cases selected from all stages of the disease. It was hoped that this would show some facts of interest. In addition, an attempt was made to correlate the results with obvious foci of sepsis in teeth and tonsils, and also to compare them with a similar series of cases in which leucocyte counts were performed.
### Table 3.
**Group A. The cholesterol level in children suffering from acute rheumatism.**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age years</th>
<th>Clinical history</th>
<th>Mgrmn. per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>9</td>
<td>Vague pains; joints not affected; early carditis; tonsils — and infected</td>
<td>143</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>First attack of chorea; nil cardiac</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Recent acute arthritis; nodules present; nil cardiac; tonsils and teeth healthy</td>
<td>131</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>First attack of chorea; nil cardiac</td>
<td>125</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
<td>Pains; nil cardiac</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Acute chorea and pains; active recent carditis; tonsils — and septic</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Acute chorea (early); heart nil; tonsils — and septic</td>
<td>126</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Acute chorea; nil cardiac</td>
<td>125</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Acute articular rheumatism; nil cardiac</td>
<td>132</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Rheumatic fever in 1928; acute chorea; nil cardiac</td>
<td>130</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Acute chorea; nil cardiac</td>
<td>128</td>
</tr>
</tbody>
</table>

### Table 4.
**Group B. The cholesterol level in children suffering from chronic rheumatism.**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age years</th>
<th>Clinical history</th>
<th>Mgrmn. per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12</td>
<td>Chronic mitral stenosis; now has acute articular rheumatism</td>
<td>136</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Pains and established mitral disease</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Established mitral stenosis, and acute articular rheumatism; tonsils unhealthy; teeth bad</td>
<td>133</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Established mitral leak; acute articular attack; tonsils — and septic</td>
<td>154</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
<td>Established mitral stenosis</td>
<td>184</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Growing pains; established mitral regurgitation; tonsils —</td>
<td>144</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Established mitral lesion</td>
<td>163</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Chronic mitral stenosis</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&quot;Felt tired&quot; for one year; triple mitral bruits; tonsils not —</td>
<td>180</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Recurrent attacks of chorea</td>
<td>173</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Chorea; established mitral affection</td>
<td>153</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Recurrent chorea; tonsils — and septic</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Recurrent chorea; nil cardiac; tonsillectomy previously</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Recurrent rheumatism; nil cardiac; tonsils — and septic</td>
<td>150</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Established mitral leak</td>
<td>144</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Established double mitral and aortic lesions</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>Recurrent chorea; heart, early infection; tonsils healthy</td>
<td>166</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Recurrent arthritis with carditis; tonsils — and unhealthy</td>
<td>173</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Recurrent chorea; nil cardiac; teeth septic</td>
<td>177</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Established mitral stenosis; tonsils — and septic</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Established mitral lesion</td>
<td>154</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>Established mitral regurgitation</td>
<td>160</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Recurrent chorea; tonsils — and septic</td>
<td>154</td>
</tr>
</tbody>
</table>
BLOOD CHOLESTEROL IN CHILDHOOD

CHART III.

THE BLOOD CHOLESTEROL IN ACUTE AND CHRONIC RHEUMATISM.
(Average for each age group).

<table>
<thead>
<tr>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
</table>

TABLE 5.

THE CHOLESTEROL LEVEL IN CHILDREN SUFFERING FROM VARIOUS DISEASES.

<table>
<thead>
<tr>
<th>Age years</th>
<th>Sex</th>
<th>Disease</th>
<th>Mgrm. per cent.</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>F</td>
<td>Chronic nephritis; œdema +; blood urea +</td>
<td>... ... ... ... ... 165</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>Chronic nephritis</td>
<td>... ... ... ... ... 187</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>Chronic nephritis; no œdema; blood urea normal</td>
<td>... ... ... ... ... 200</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>Chronic nephritis; no œdema; blood urea normal</td>
<td>... ... ... ... ... 132</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>Chronic nephritis; no œdema</td>
<td>... ... ... ... ... 155</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>Asthma: idiopathic</td>
<td>... ... ... ... ... 148</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>Asthma: idiopathic</td>
<td>... ... ... ... ... 140</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>Asthma: idiopathic</td>
<td>... ... ... ... ... 130</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>Diabetes: no ketosis</td>
<td>... ... ... ... ... 147</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>Enlarged tonsils and adenoids</td>
<td>... ... ... ... ... 141</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>Enlarged tonsils and adenoids</td>
<td>... ... ... ... ... 174</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>Fidgety and nervous; no definite signs</td>
<td>... ... ... ... ... 153</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>Dystrophia adiposo-genitalis</td>
<td>... ... ... ... ... 150</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>Frigilatias ossium</td>
<td>... ... ... ... ... 150</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>Banti's disease</td>
<td>... ... ... ... ... 160</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>Chronic lymphatic leukemia</td>
<td>... ... ... ... ... 160</td>
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<tr>
<td>8</td>
<td>M</td>
<td>Hæmophilia</td>
<td>... ... ... ... ... Less than 120</td>
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This part of the investigation has been carried out on cases of juvenile rheumatism, but as this term embraces such a number of widely differing sets of symptomatology and consequently varied clinical pictures a little classification was necessary. The best division from the point of view of this paper seems to be into two large groups:

GROUP A.—Recent, acute, active rheumatism including muscular pains, swollen joints, pancarditis and chorea, usually associated with some degree of fever (Table 4).

GROUP B.—Rheumatism of a more chronic type, including recurrent chorea, myocarditis, endocarditis and established valvular lesions. Some of these cases were undergoing a secondary acute relapse and the picture becomes more complicated, but for the sake of clarity and ease of explanation, a short clinical history is appended to each case (Table 5).

In addition to the cases of rheumatic infection, some other diseases have been studied (Table 6). These form a heterogeneous group, including cases of chronic nephritis, idiopathic asthma, chronic lymphatic leukemia, fragilitas ossium and a few patients with chronic infected tonsils and adenoids. The cases of chronic nephritis were thought to be of interest in view of the increase in blood cholesterol reported in this condition; and the asthma cases represented specimens of an allergic condition. The cases with septic tonsils were chosen for comparison with cases of rheumatic infection in which similarly infected throats were present.

III. DISCUSSION OF RESULTS.

From a consideration of the known facts of the physiology and pathology of cholesterol in the animal body, it is apparent that a great amount of knowledge is not available upon these points. Conjecture is rife, but solidly established facts are relatively few, and even those known are difficult of correlation into a complete picture and many gaps are left unfilled. As this is the case, to draw sweeping conclusions from the results quoted would be unjustifiable and almost certainly fallacious. Some facts and points of interest do emerge, however, and these will now be considered.

For a full appreciation of these facts, a few observations on the physiology of the child are necessary. That the metabolism of the normal healthy child differs in many essential ways from that of the healthy adult is undoubted. On the whole, the balance of the child's biochemistry is very much more easily influenced by external factors and consequently is much more readily disturbed. The fact that growth is taking place rapidly means that the whole metabolism is in a constantly changing state, anabolism being much more marked than katabolism, although this is taking place to a less degree, and no organ of
the body remains static for any length of time. A review of the growth process is given in Abt's Pediatrics. The termination of the infantile and the beginning of the juvenile growth cycle at about the time of weaning is characterized by profound metabolic changes, the infant's body having to adjust itself to an altered diet and consequently to a change of materials for building up new tissues. Again, at the junction of the juvenile and adolescent growth cycles, there is a similar metabolic upheaval, and a relative instability of the growth process is shown. In the investigation quoted by Abt the increase of weight and stature, and the variability of each, in a number of healthy boys and girls was obtained. The boys showed a steady yearly increment of weight and height, while the girls gave a far less steady increment. The variability of weight of the boys, which was not great at any age, was slightly increased at the age of eight and nine years. The girls, showing at all ages a more marked variability, accentuated this slightly at the age of eight, but much more so at ten, eleven, twelve and thirteen years. The variability of height was not quite so obvious, and did not appear to affect any one age group more than another. It becomes apparent at once, that the two sexes show a marked difference in their response to the growth process (Chart IV).

Passing on from a consideration of the effect of growth, the basal metabolism may next be discussed. The basal metabolism appears to increase with age during babyhood, reach its maximum at the age of four years, and then fall gradually, reaching the normal adult value at about twenty years. It is a well recognized fact that a relatively high basal metabolism characterizes the period of growth. In this as in the growth process, the influence of sex is marked from early years, it being definitely lower in the female than in the male. Sonden and Tigerstedt (quoted by Abt) found that under like conditions in the young, the carbon dioxide output both per kilogramme of body weight and per square metre of surface, is considerably greater in males than in females.
This difference becomes less apparent with increasing age, until in old age it disappears completely. Benedict and Talbot also state that boys have a higher average metabolism than girls of the same weight.

A consideration of the differences between the blood of the adult and that of the child is illuminating also. At birth the specific gravity of the baby’s blood is equal to that of the adult, but thereafter it rapidly becomes less and remains at a lower level, the boys at all ages showing a higher specific gravity than the girls. Feldman\textsuperscript{17} considers that the specific gravity is not dependent on the number of corpuscles, but on their haemoglobin content, and this is low in childhood, rising gradually to the adult level at about puberty.

A further point of difference is the relative numbers of the cells of the blood. These are all greater in the child than in the adult, the red cells averaging 5,800,000 from 1—14 years, and the white cells 10,000—7,000 per c.mm.; also there is a relative lymphocytosis of 30—50 per cent. of all white cells, owing to a greatly increased activity of adenoid tissue in children in which the tonsils, thymus, lymphatic glands and spleen all take part.

As regards the chemical constituents of the blood, the non-protein nitrogen content, comprising urea, uric acid and creatinine are within the same limits as in the adult, but creatine behaves rather differently in the child. Feigl\textsuperscript{18} believes that there is a tendency revealed by the averages of his different age groups for the creatine and creatinine of the blood to increase with age from childhood onwards. Fonteyne and Inglebrecht\textsuperscript{19}, however, did not discover any relation of age to creatinine, but agreed that it influenced the amount of creatine. Rose\textsuperscript{20} showed that children of both sexes excrete creatine in relatively large quantities, and regard creatinuria as a normal accompaniment of the growth process. Rose thought this persisted in both sexes until or even after puberty, but Krause\textsuperscript{21} believes that boys cease to excrete creatine at the age of five or six years, while girls usually, but not necessarily always, continue to excrete it for some years longer. He believes that the excretion of creatine is entirely dependent on the balance maintained between its formation and destruction, and that the power of dealing with it is less well developed in the child than in the adult.

From the time of birth onwards the food of the child, consisting as it does mainly of carbohydrates, proteins, fats and salts, is comparable to that of the adult, but the use to which these substances are put differs somewhat. In the adult, protein is broken down and used to repair damage to vital cells, while fats and carbohydrates supply the necessary fuel. It has been shown also, by Cathcart, that carbohydrates are necessary for synthetic processes in the cells in connection with protein metabolism and do not act merely as sparsers of protein. In the child, however, anabolism is proceeding rapidly and a source of supply of energy which is easy of obtaining must be at hand. Substance metabolism is usually taken to mean chiefly the metabolism of proteins, since these constitute the essential substrata of living protoplasm. Salts rank next in importance, but fats and carbohydrates are regarded as being merely accessory. Abt considers it doubtful if the attitude of regarding the
fats and carbohydrates merely as fuel is correct. Lipoid matter, which is present in company with the fats, is of great importance structurally, especially in the building up of the nervous system.

From this brief summary of some of the points of difference between the metabolism of child and adult it is seen that the numerous factors taking part in the growth process seem to be responsible and that these appear to behave rather differently in the case of the boys than in that of the girls.

Some curves are reproduced (Chart 4) from Abt's work on paediatrics showing the variability of growth and height at different ages in boys and girls and from these it is seen at a glance that the variation in height is not marked at any age in either sex, but that there is an increased variability in the weight curve, which is much more evident in the case of the girls. It is interesting to compare this curve with that already given as indicating the variability of blood cholesterol at different ages.

In both of the latter curves the variations are rather more accentuated than in the case of the growth curves, but here again the girls show a wider range, and in each case this appears to show more at a year earlier than in the growth curve. For example, the two peaks of the growth variation are at eleven and thirteen years, while those of cholesterol variation are at ten and twelve years. It seems not unlikely that there may be a relationship between the two, and that this is not merely accidental, cholesterol possibly playing some important part in the process of growth. Further confirmation of this view is found in the work of Shope in America. He states that a number of investigators have surmised that differences in blood-cholesterol level occur in organisms of various ages and differing stages of development. Roffo experimenting on rats found that the blood cholesterol increased between three and five months of age, Baker and Carrel using chickens found a marked difference with age. Shope used for his investigations cattle, rabbits and guinea pigs all of varying ages. He found the variations with age to be of two types:—

(a) A marked and rapid increase from birth, lasting throughout the early life of the animal; and (b) a less marked but more gradual decline with advancing age. In all cases he found the changes in cholesterol content of the blood to be more uniform and regular in male than in female animals. In female guinea pigs, the blood cholesterol showed many irregular fluctuations which in many cases were unrelated to age, and Shope questions whether possibly cholesterol serves more functions in the female organism than in the male. These fluctuations are, in the case of female children fully confirmed in the present investigation, but their exact interpretation is not possible at the present stage of our knowledge of the functions of cholesterol in the body.

Passing on from the normal figures given, it is necessary to say a few words about the rheumatism curves, and the figures obtained from cases of other diseases. Here again, the results are not easy of interpretation. From Table 3 (Group A) it may be concluded that during the more acute phases of rheumatism, the blood cholesterol is not greatly disturbed. In the first two cases in Table 3 the figures are perhaps slightly higher than normal, but on the average the figures are within normal limits and do not show much variation,
ARCHIVES OF DISEASE IN CHILDHOOD

Turning to the results in the chronic rheumatism group (Table 4) very different figures are found. The general trend is for an average higher than the normal for any age, in many cases this being very marked. Cases having an acute attack superimposed on a chronic cardiac lesion show a lower cholesterol level than those with uncomplicated heart disease. No direct association with infected teeth or tonsils could be traced, some cases with chronic sepsis showing an increase in cholesterol and others none, but in this connection it is interesting to note that a case of chronically infected tonsils, without any rheumatic symptoms did give a very high result.

Kipp\(^{25}\) during his studies of pneumonia traced a relationship between the number of leucocytes in the blood and its cholesterol content, and in the present investigation many leucocyte counts were performed, but no parallelism could be made out. The average counts in both the acute and chronic cases of rheumatism were between the limits of 6,000 and 12,000 cells per c.mm. in a few cases rising to 15,000 per c.mm., but as has been stated already the normal may be regarded as lying between 7,000 and 10,000 per c.mm. so that these counts show a very mild grade of leucocytosis, and this did not appear to bear any relationship to the increased cholesterol in the more chronic cases. The haemoglobin content of the blood also has been thought to have an influence on the cholesterol content, but here again explanations break down, as many of these children have a marked secondary anaemia.

The most reasonable explanation which can be put forward at the present time with the amount of knowledge at our disposal is that of the growth process again. It is a well known fact that during the course of chronic juvenile rheumatism growth is much impeded, the children being thinner than normal and often under the average in size, and it may be suggested that possibly the excess of cholesterol in the blood would in the normal course play some part in anabolism, but that the disorganization of the growth process by the rheumatic condition leads to a slight degree of accumulation in the blood.

There is less interest attached to a consideration of Table 6 which comprises a group of cases suffering from fairly common diseases. Included in this series are five cases of chronic nephritis, one of which showed marked oedema. In four out of the five cases a greatly increased blood cholesterol was found, one case giving as much as 200 mgm. per cent., which was the highest reading recorded in the whole investigation. Three cases of idiopathic asthma, one of diabetes without ketosis, and one of chronically infected tonsils and adenoids, yielded normal results. Two cases of dystrophia adiposo-genitalis gave results rather higher than normal, as did a case of Banti’s disease and one of chronic lymphatic leukaemia. A single case of haemophilia gave a result which was too weak to estimate with the usual standard solution used in the colorimeter, and was therefore less than 120 mgm. per cent. The child, aged eight, was having a fairly severe hæmorrhage at the time the investigation was made.

No explanation of these results is attempted at the present time, but they are recorded, being of interest in that they confirm the results already published in the literature.
BLOOD CHOLESTEROL IN CHILDHOOD

General conclusions.

Estimations of the blood cholesterol of children of both sexes between the ages of six and thirteen lead to the following conclusions:

1. The average percentage of blood cholesterol in healthy boys increases as the age increases and the percentage in individual boys does not differ greatly from the average for that age.

2. The average blood cholesterol of healthy girls increases much less with age than that of healthy boys, and the percentage of cholesterol in individual cases often departs widely from the average for that age.

3. In acute juvenile rheumatism the average percentage of cholesterol in the blood is normal, but in chronic rheumatism it shows a definite tendency to be greater than normal. It is suggested tentatively that this abnormally high level is related to the disordered growth which frequently attends chronic juvenile rheumatism.

4. During the course of the parenchymatous type of chronic nephritis in children, the blood cholesterol rises, as in adults.

5. The blood cholesterol is normal in idiopathic asthma and in diabetes which is being controlled by insulin.

In conclusion, I wish to express my thanks to Dr. Dingwall Fordyce and to Professor Ramsden for much valuable criticism and advice.

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2. Denis, W., Ibid., 1917, XXIX, 93.
10. Simone, quoted by Baylac & Sendrail, vide supra.
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A Study of the Blood Cholesterol in Childhood

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