An intradermal jet injector was used to administer combined diphtheria, tetanus, and pertussis (D.T.P.) vaccines to infants aged 2 to 12 months. A second dose was given one month after the first and a third six months after the second. Each dose was considerably smaller than the standard intramuscular dose. Blood samples taken one month after the third dose showed a satisfactory diphtheria and tetanus antitoxin response in all but a few cases. The antibody response to the pertussis component was not examined. Reactions were insignificant. Intradermal jet injection is proposed as a cheap, extremely rapid, and effective technique for D.T.P. immunization, especially suitable for use in remote areas where trained staff and facilities are few and many children require immunization.

References
patients are seen regularly at the monthly children's clinic, with
an attendance of 600-1,000 on any one day—a situation in which
the jet injector naturally comes into its own.
A consecutive series of 443 infants (226 male and 217 female)
between 2 and 12 months of age were admitted to the trial at
their first visit to the clinic, when they received their first dose of
D.T.P. It was intended that each child should have a second
dose after an interval of one month and a third after a further
interval of six months (Haire et al., 1966; Ministry of Health,
1967), but a number failed to attend for the subsequent doses
and for the final blood sample one month after the third dose.
Live attenuated poliomyelitis vaccine was given orally with the
first dose of D.T.P., B.C.G. (intradermally) and smallpox
vaccine (percutaneously) between the second and third doses,
and measles vaccine (when available) with the third dose of
D.T.P.
The first 259 infants (group 1) received alum-adsorbed
D.T.P. vaccine intradermally, the next 79 (group 2) received
unadsorbed D.T.P. vaccine intradermally, and the remaining
105 (group 3) received alum-adsorbed D.T.P. by intramuscular
injection. The age distribution of the three groups and the
table 1 - Size and Age Distribution of Groups at Various Intervals

<table>
<thead>
<tr>
<th>Age at Start of Schedule</th>
<th>Numbers at Time of</th>
<th>First Visit (x months)</th>
<th>Second Blood Sample (x + 7 months)</th>
<th>Third Blood Sample (x + 8 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 months</td>
<td>160</td>
<td>97</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>50</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7+ months</td>
<td>49</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 months</td>
<td>50</td>
<td>27</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>16</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7+ months</td>
<td>13</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 months</td>
<td>62</td>
<td>16</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>21</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>7+ months</td>
<td>21</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>443</td>
<td>198</td>
<td>136</td>
<td></td>
</tr>
</tbody>
</table>

numbers remaining after each interval are shown in Table I.
The adsorbed D.T.P. vaccine (Infagen) contained 20-26 Lf
units of diphtheria toxoid and 10-16 Lf units of tetanus toxoid
in each millilitre. The unadsorbed vaccine (Trivax) was the
standard B.P. preparation containing 65 Lf units of diphtheria
 toxoid and 12.5 Lf units of tetanus toxoid per millilitre. (The
dosages of pertussis vaccine are irrelevant to the present study
since the pertussis antibody was not measured.) The intra-
dermal jet injectors used (Panjet Mark 5, Schucoo International
Ltd.) (see Fig. 1) delivered a quantity of vaccine varying
between 0.05 and 0.08 ml at each injection. (More recent models
deliver 0.1 ml.) Each intradermal dose consisted of three jet
injectors given into the lateral aspect of the thigh, totalling
0.15-0.24 ml. The intramuscular dose (group 3) was 0.5 ml.
Blood for determination of antibody levels was collected at the
time of the first and third doses of D.T.P. and again one month
after the third dose. Each sample, consisting of 5 ml of venous
blood, was put into a sterile centrifuge tube and kept at room
temperature until the end of the clinic, when it was stored at
+4°C and sent next day in a cold box to Makerere Medical
School. There the serum was separated and stored at -20°C
before being sent to the Wellcome Research Laboratories in
England for titration of diphtheria antitoxin by the method of

Romer and Sames (1909), as modified by Glenny and Llewellyn-
Jones (1931), and tetanus antitoxin by the method of Glenny
and Stevens (1938). Pertussis agglutinins were not estimated
because these may give little or no indication of protective
immunity.

Results
The distributions of diphtheria and tetanus antitoxin titres in
the blood samples taken (A) before immunization (excluding
those cases in which no further samples were obtained), (B)
six months after the second dose, and (C) one month after the
third dose are set out in Tables II and III. Five children (three
from group 2 and one each from groups 1 and 3) have been
eliminated from the final analysis. They were found to have
measurable tetanus antitoxin titres (over 0.5 unit/ml) in their
pre-immunization serum samples and this was taken to indicate
previous exposure to D.T.P. immunization (four were over 8
months of age). All three groups showed, in general, satisfactory
responses to the diphtheria and tetanus components by the time
of the third bleeding, one month after the third dose. There
were, however, some individuals who responded poorly to both
diphtheria and tetanus after the intradermal adsorbed D.T.P.
(group 1). The number of patients in group 3 from whom a third
blood sample was obtained was too small for valid comparisons
to be made; at the time of the second sample, when such com-
parisons were possible, the antibody titres were poor and in-
adequate in all three groups.

On statistical analysis the only significant difference between
the results of the immunization procedures was found in the
tetanus antitoxin titres at the second bleeding, when the mean
response in group 1 was poorer than in groups 2 and 3 (P <
0.001). A possible explanation is that owing to a tendency for
the adsorbed triple vaccine to froth when administered by the
intradermal injector, only a proportion of the dose was injected.
This frothing occurs also with measles vaccine and is thought to

FIG. 1—The Panjet injector.

<table>
<thead>
<tr>
<th>Age at Start of Schedule</th>
<th>Numbers at Time of</th>
<th>First Visit (x months)</th>
<th>Second Blood Sample (x + 7 months)</th>
<th>Third Blood Sample (x + 8 months)</th>
</tr>
</thead>
<tbody>
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<td></td>
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<td></td>
</tr>
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<td>97</td>
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<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>50</td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7+ months</td>
<td>49</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 months</td>
<td>50</td>
<td>27</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>4-6 months</td>
<td>16</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7+ months</td>
<td>13</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 3</td>
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<tr>
<td>1-3 months</td>
<td>62</td>
<td>16</td>
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<td>4-6 months</td>
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<tr>
<td>7+ months</td>
<td>21</td>
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</tr>
<tr>
<td>Total</td>
<td>443</td>
<td>198</td>
<td>136</td>
<td></td>
</tr>
</tbody>
</table>

TABLE II—Diphtheria Antitoxin Titre Distributions

<table>
<thead>
<tr>
<th>Diphtheria Antitoxin (Units/ml)</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-005</td>
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<td></td>
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<tr>
<td>0-005-0-01</td>
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</tr>
<tr>
<td>0-01-0-02</td>
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</tr>
<tr>
<td>0-02-0-05</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0-5-0-01</td>
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</tr>
<tr>
<td>0-1-0-2</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0-5-1</td>
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<td></td>
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</tr>
<tr>
<td>0-10-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TABLE III—Tetanus Antitoxin Distributions

<table>
<thead>
<tr>
<th>Tetanus Antitoxin (Units/ml)</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-02-0-05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-05-0-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1-0-2</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0-5-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-10-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A = Pre-immunization sample. B = Six months after second dose. C = One
month after third dose.
* Subjects from whom no subsequent samples were obtained are excluded.
be the main reason why measles immunization given by intra-
dermal jet injection is so uncertain. It should also be borne in
mind that the vaccines were of different manufacture. The effect
of nutritional status on antibody response was checked by
examination of the infants' weight charts. Most of the children
received at least their first two doses of vaccine before the age
of weaning and therefore before the period of "weight faltering"
and early malnutrition. Of the 109 children in group I from whom
the third blood sample was obtained, 50 were below 80%,
and four below 60% of the expected weight for age on one or
more visits (usual last one or two). There was no significant
diminution of antibody response in these children.
Immediate reactions to the intradermal injections could not be
documented, but few were reported at the next visit. One of us
(K.M.W.) has adopted this technique of immunization as a
standard procedure with adsorbed D.T.P. and has never had any
severe untoward effects reported to him. Small indurated marks
about 5-7 mm in diameter were observed one month after each
dose but had disappeared entirely in three to four months. In
one underweight child an ulcer about 15 mm in diameter
developed at the site of one of the injections one month later.
Unfortunately, no record was made of this and the type of
vaccine used is therefore not known. The lesion had healed by
the next visit.

Discussion
These results are encouraging. They indicate that intradermal
D.T.P. in reduced dosage can stimulate antibody production to
levels similar to those obtained with the standard intramuscular
schedule when three doses are given. The use of the intra-
dermal injector enables a very rapid rate of immunization to be
maintained, the necessity of sterilizing needles and syringes
during the clinic being eliminated. The method is therefore very
useful in the field, where a presterilized instrument can be filled
with vaccine sufficient for 20 children. The reservoir can be
refilled with one syringe and needle as necessary.
General reactions to the intradermal injection of D.T.P. may
be less frequent than those after intramuscular injection, as is
the case with T.A.B. It would seem likely that the plain vaccine
is less reactive locally than the alum-adsorbed vaccine, which has
the additional disadvantage of a tendency to froth. To date,
hepatitis has not been found to be associated with the use of jet
injectors. Although occasionally a spot of blood was noticed
on the rim of the nozzle of the instrument, the jet of vaccine does
not touch this rim.

The importance of the good results obtained with this method
must be judged against the background of large numbers of
unimmunized children attending a clinic staffed by a single
doctor with few, mostly unskilled, locally trained assistants and
meagre facilities. The method is now in use in one or two clinics
in Uganda, but further monitoring of the safety and reliability
of the technique is still required. It might well be the method of
choice for routine immunization clinics in any part of the
world.

We would like to thank the Chief Medical Officer, Ministry
of Health, Uganda, for permission to publish this material. One
of us (P.M.B.) was in receipt of a grant from the Wellcome
Trust for the study of modifications of immunization schedules
applicable to developing countries. We acknowledge with thanks
the generosity of Dr. R. Dudgeon and Professor G. Dick.
The assistance of the staff of Kagogondo Hospital was willingly
and cheerfully given and the close liaison developed during the
conduct of the trial between ourselves and the hospital was
relinquished most reluctantly.

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Excretion of Urinary Casts after the Administration of
Diuretics

P. R. IMHOF, J. HUSHAK, G. SCHUMANN, P. DUKOR, J. WAGNER, H. M. KELLER

Summary
The administration of ethacrynic acid and frusamide to
healthy volunteers was regularly followed by the excre-
tion of hyaline casts, without any concomitant protein-
uria. Hydrochlorothiazide and chlorthalidone did not
themselves induce cylinduria but augmented that
provoked by acidifying agents. It was shown by the

indirect immunofluorescence method that the casts were
composed of uromucoid (Tamm-Horsfall mucopro-
tein), which is always present in the urine, usually in
solution, and originates predominantly from the tubule
cells of the ascending limb of Henle's loop. The urinary
excretion of Tamm-Horsfall mucoprotein was not
increased after the administration of ethacrynic acid.
This mucoprotein is precipitated and forms aggregates
when the concentration of electrolytes increases and
when the pH of the urine declines. The casts that appear
in the urine after strenuous physical exertion are of
essentially the same composition. Casts produced by
patients with kidney diseases, on the other hand, contain
various protein fractions derived from the blood as well
as mucoprotein. Cylinduria occurring during diuretic
therapy and physical exertion is of no pathological
significance, and the diagnostic value of byaline casts is
very much limited if their exact composition cannot be
determined.

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Pharmacology

District Hospital, Belp, Switzerland
H. M. KELLER, M.D., Assistant Professor, Physician-in-Chief