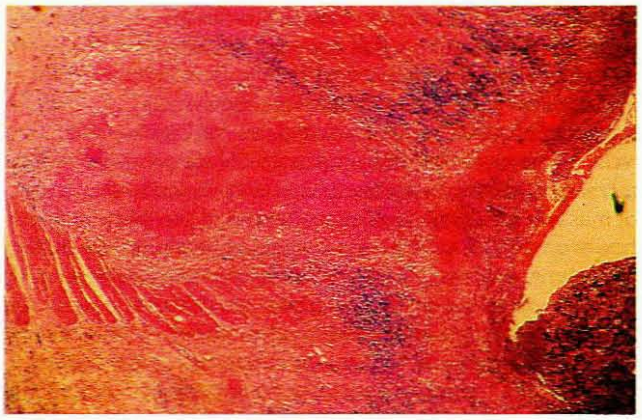

Fig. 1. A full-thickness biopsy of the terminal ileum shows features of granulomatous inflammation at the base of the ulcer.

Anatomical diagnosis. *M. tuberculosis* infection of the small bowel.

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SHORT REPORT

An analysis of DTP-associated reactions by manufacturer, batch, vaccinator, series number and infant weight

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Objectives. To determine whether two commonly used DTP batches manufactured by Rhône-Poulenc Rorer were more reactogenic than two commonly used batches manufactured by the South African Institute of Medical Research.

Design. Prospective study.

Setting. Six community clinics.

Patients. Infants routinely scheduled for their first three DTP immunisations.

Main outcome measures. Local and systemic adverse reactions following immunisation with DTP.

Results. Local reactions were significantly more common with both Rhône-Poulenc Rorer products.

Conclusion. All adverse reaction rates compared favourably with those reported by the Centers for Disease Control.

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Because of inadequate surveillance systems in many local authorities, it is impossible to substantiate a growing perception that the diphtheria-tetanus-pertussis vaccine, DTP-Meriéux, manufactured by Rhône-Poulenc Rorer, is more reactogenic than DTP manufactured by the South African Institute for Medical Research (SAIMR). Since this climate of uncertainty can eventually undermine the Expanded Programme on Immunisation, the validity of these perceptions was investigated by a study of the reaction profiles of four commonly used vaccine batches, suspected of unacceptable reactogenicity by some local authorities.

Literature

It is well known that whole-cell pertussis-containing vaccine is more reactogenic than most of the vaccines routinely used for immunisations.[1,2] The reported incidence of tenderness, erythema, swelling or induration at the injection site varies from 300 - 700/1 000 DTP doses, usually occurs within 48 hours of vaccination and is mostly self-limited.[1-6] A nodule may occasionally be palpable at the injection site for

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several weeks, but sterile abscesses have been reported occasionally (6 - 10 x 10^6 doses of DTP). Injection site abscess rates depend mainly on the sterility of vaccination practices. Rates of adverse events following immunisation (AEFI) are lowest when the vaccine is administered in the buttocks,[6] while subcutaneous administration at any site is particularly prone to cause local AEFI.

A variety of mild-to-moderate systemic effects frequently occur within 3 - 6 hours of DTP administration and can persist for 1 - 2 days[1,3,5-7] but appear to be without sequelae.[8] Fever of ≥ 40.5°C is rare and hypotonic hyporesponsive episodes even more so. The role of DTP in exceedingly rare neurological illnesses, e.g. prolonged convulsions, encephalopathy or sudden infant death syndrome, remains unclear.[1] The frequencies of local reactions and fever are known to increase with an increasing number of DTP doses, while mild-to-moderate systemic reactions decrease with an increasing number of doses.[5,6,9] Substitution of diphtheria-tetanus (DT) vaccine is advisable in cases of moderate-to-severe AEFI with DTP.

Subjects and methods

Three high-turnover clinics at both the Western Cape Regional Services Council (WCRSC) and Kraaifontein Municipality were selected. Infants aged 3, 4½ and 6 months, routinely scheduled for their first three DTP immunisations (DTP1, DTP2, DTP3), were prospectively enrolled from 1 June 1994 to 30 January 1995. All vaccine was provided by the Department of National Health (Western Cape). All vaccinations were administered intramuscularly in the deltoid area (23-gauge needle) and vials were stored and handled according to World Health Organisation guidelines.[7] Informed consent was obtained and contraindications as defined by the vaccine package inserts were adhered to.

At WCRSC clinics, infants randomly received either DTP-Meriéux batch K5315 or SAIMR batch G03509 and, at Kraaifontein clinics, DTP-Meriéux J5497 or SAIMR F08609. Methods of randomisation varied slightly between the two clinic groups in order to minimise clinic disruption. DTP dose numbers and batches were recorded on clinic cards to ensure vaccination with the same batch at consecutive visits. Each sister kept standardised personal immunisation records. Parents were requested to notify any one of the AEFI described to any sister at the clinic where vaccination was performed. Notifications were evaluated by clinic sisters according to a standard questionnaire and by direct observation. The Epi Info 6 statistical programme was used to analyse data.

Results

Table I summarises adverse events that followed within 48 - 72 hours of immunisation with the four batches, in comparison with AEFI rates reported by an authoritative source.[1] Redness in the 10 - 24 mm range was most prevalent (> 75% of cases) and the majority of cases had swelling in the 10 - 39 mm range (> 75% of cases). The majority of palpable masses were 10 - 24 mm in diameter (> 75% of cases).

In total, significantly more infants experienced local (2.08 < RR = 4.16 < 8.34) and systemic (2.38 < RR = 6.84 < 19.67) reactions with batch J5497 than with F08609. Vaccination with DTP-Meriéux K5315 resulted in significantly more local reactions (1.47 < RR = 5.15 < 18.65) than vaccination with SAIMR G03509. DTP-Meriéux K5315 was no more reactogenic than SAIMR G03509 at any specific WCRSC clinic. Meriéux J5497 only caused significantly more total reactions than SAIMR F08609 at the largest Kraaifontein clinic (2.51 < RR = 5.07 < 10.26).

In total, AEFI cases and controls did not differ in terms of weight at birth, at DTP1 or at DTP2. In an inception cohort at the Kraaifontein clinics, the incidence of AEFI declined significantly with subsequent dose numbers of Meriéux J5497 ($P < 0.001$). The RR for a local AEFI with J5497 (N = 222), compared with F08609 (N = 183), was 4.12 at DTP1 (95% CI = 1.43; 11.84), 3.10 at DTP2 (95% CI = 1.04; 9.25) and 0.93 at DTP3 (95% CI = 0.13; 6.54).

The incidence of fever was excluded from all calculations, since thermometers were not used uniformly.

Table I. Rate (per 1 000 doses) of adverse events occurring within 48 - 72 hours of DTP vaccination, regardless of dose number

		Meriéux		SAIMR	
	MMWR*	J5497 (N = 629)	K5315 (N = 1 059)	F08609 (N = 748)	G03509 (N = 1 259)
Local					
Redness	330	6.3	1.9	2.9	0
Swelling	400	55.6‡	5.7‡	13.4‡	3.2‡
Subcutaneous nodule		12.7	4.7	3.2	2.4
Pain	500				
Systemic					
Fever > 38°C	500	14.3†	0†	5.3†	0†
Drowsiness	330	3.2	0	0	0
Fretfulness	500	17.6	1.9	1.4	0.8
Vomiting	66	3	0	0	0
Persistent, inconsolable crying > 3 hrs	10	3.2	0	0	0
Collapse	1.3				
Convulsions	0.57	1.6	0	0	0
Sterile abscesses	6 x 10^3	0	0	0	0
Fever > 40.5°C	3				

* Adapted from reference 1.
† Subjectively judged by parent.
‡ Sum of nodules, induration and masses.

Discussion

The local and systemic rates of AEFI with all the batches used in this study compared very favourably with those reported by the Immunisation Practices Advisory Committee of the Centers for Disease Control[1] (as indicated in Table I) and the International Children's Center in Paris.[11] Even the most reactogenic batch, DTP-Meriéux J5497, was clearly within acceptable levels and the majority of local reactions were relatively minor. At the Kraaifontein clinics, AEFI rates seemed to depend on the broad socio-economic level of the community served. The Kraaifontein clinic where two vaccinators were less prone to AEFI than their colleagues, suggests differences in vaccine administration technique among vaccinators. Contrary to international experience, the incidence of local AEFI for DTP-Meriéux J5497 decreased with increasing dose number, thus indicating that the more reactogenic individuals were at greatest risk of an AEFI at DTP1.

Conclusions

Our results prove that perceptions of 'unacceptable levels of AEFI' for the batches used are unfounded and in danger of compromising the goals of the Expanded Programme on Immunisation.[11] Improved surveillance at all levels to provide accurate data for rational decision-making, combined with increased levels of knowledge about what kind of AEFI are 'acceptable', could contribute substantially towards attainment of high DTP coverage.

The risk of an AEFI with DTP in this study was determined by the choice of vaccine manufacturer and batch, vaccinator, dose series number and the broad socio-economic group of the patient. More comprehensive studies are required to determine whether a link exists between AEFI and vaccine efficacy.

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HISTORY OF MEDICINE

Was Isaac diabetic?

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Isaac was the second of the three biblical patriarchs of whom Abraham and Jacob are the first and third. His position in the middle of this lineage may be responsible for his mediocre image in the eyes of some readers of the Bible, an image that is reinforced by the sense of his having been of a somewhat lethargic personality and not noted for the bursts of activity or feats of physical achievement associated with other famous biblical figures. This, together with the rest of the biblical account of his life, affords a tantalising opportunity to speculate on his medical condition, specifically the possibility that Isaac might have been diabetic.

Signs and symptoms

Diabetes mellitus and its complications encompass a multiplicity of signs, symptoms and secondary conditions, which include a constant need for water, increased appetite, lethargy and chronic fatigue, visual deficit due to cataracts or retinopathy, and sexual dysfunction including impotence. This paper asserts that a sufficient number of these conditions can be discerned in Isaac to make him a probable diabetic.

At the age of 40, Isaac married Rebekah (Genesis 25:20). Thereafter, the couple evidently experienced a long period of involuntary infertility, for Rebekah did not become pregnant until 20 years later when she was delivered of her twin sons, Esau and Jacob. Isaac was now 60 years old (Genesis 25: 26) — or was he? At this point, it may be appropriate to take a closer look at the question of Isaac's age. The Bible says that when he was 100 years old, and when 'his eyes were too dim to see', he called his eldest son Esau to give him his blessing, for 'behold, I am grown old, I know not the day of my death' (Genesis 27: 1-2). Given that such a blessing was normally bestowed when the giver was on his death-bed, Isaac must have felt very sick indeed, and it seems reasonable that, having reached a century, Isaac should be concerned about his mortality and should begin to think about bestowing his assets. But Isaac went on to live another 80 biblical years after this event! The Bible says: 'And the days of Isaac were 180 years. And Isaac departed this life, and died, and was gathered unto his people old and full of days; and Esau and Jacob his sons buried him' (Genesis 35: 28-29).

During the period after the blessing, Isaac's sons got married, had many children, and established themselves as patriarchs in their own right. Isaac even survived family tragedies such as the rape of his grand-daughter and a raging neighbourhood dispute that culminated in mass murder. Despite his own feelings, Isaac was evidently not

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