Research

Diagnosis of paediatric HIV infection in a primary health care setting with a clinical algorithm

C. Horwood,[1] S. Liebeschuetz,[2] D. Blaauw,[3] S. Cassol,[4] & S. Qazi[5]

Objective To determine the validity of an algorithm used by primary care health workers to identify children with symptomatic human immunodeficiency virus (HIV) infection. This HIV algorithm is being implemented in South Africa as part of the Integrated Management of Childhood Illness (IMCI), a strategy that aims to improve childhood morbidity and mortality by improving care at the primary care level. As AIDS is a leading cause of death in children in southern Africa, diagnosis and management of symptomatic HIV infection was added to the existing IMCI algorithm.

Methods In total, 690 children who attended the outpatients department in a district hospital in South Africa were assessed with the HIV algorithm and by a paediatrician. All children were then tested for HIV viral load. The validity of the algorithm in detecting symptomatic HIV was compared with clinical diagnosis by a paediatrician and the result of an HIV test. Detailed clinical data were used to improve the algorithm.

Findings Overall, 198 (28.7%) enrolled children were infected with HIV. The paediatrician correctly identified 142 (71.7%) children infected with HIV, whereas the IMCI/HIV algorithm identified 111 (56.1%). Odds ratios were calculated to identify predictors of HIV infection and used to develop an improved HIV algorithm that is 67.2% sensitive and 81.5% specific in clinically detecting HIV infection.

Conclusions Children with symptomatic HIV infection can be identified effectively by primary level health workers through the use of an algorithm. The improved HIV algorithm developed in this study could be used by countries with high prevalences of HIV to enable IMCI practitioners to identify and care for HIV-infected children.

Keywords HIV infections/diagnosis; Acquired immunodeficiency syndrome/diagnosis; Child care; Primary health care; Delivery of health care, Integrated; Physicians; Algorithms; Comparative study; South Africa (*source: MeSH, NLM*).

Mots clés HIV, Infection/diagnostic; SIDA/diagnostic; Puériculture; Programme soins courants; Distribution intégrée soins; Médecin; Algorithme; Etude comparative; Afrique du Sud (*source: MeSH, INSERM*).

Palabras clave Infecciones por VIH/diagnóstico; Síndrome de inmunodeficiencia adquirida/diagnóstico; Atención primaria de salud; Entrega integrada de atención de salud; Médicos; Algoritmos; Estudio comparativo; Sudáfrica (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: العدوى بفيروس العوز المناعي البشري، تشخيص العدوى بفيروس العَوَز المناعي البشري، الإيدز (متلازمة العَوَز المناعي المكتسب)، تشخيص الإيدز، رعاية الأطفال، الرعاية الصحية الأولية، إيتاء الرعاية الصحية، متكامل، أطباء، خوارزمية، دراسة مقارنة، جنوب أفريقيا. (**المصدر:** رؤوس الموضوعات الطبية – المكتب الإقليمي لشرق المتوسط).

Bulletin of the World Health Organization 2003;81:858-866

Voir page 864 le résumé en français. En la página 864 figura un resumen en español.

يمكن الاطلاع على الملخص بالعربية في صفحة **865**

Introduction

Over 10.9 million deaths occur annually in children aged <5 years in developing countries (*1*); most deaths are caused by preventable and easily treated childhood diseases (*2*). Appropriate management of these conditions is one of the most cost-effective interventions to reduce the global burden of disease (*3*). The Integrated Management of Childhood Illness (IMCI) was developed by WHO and United Nations Children's Fund (UNICEF) to improve survival rates in children (*2*); it uses an algorithmic approach to provide guidelines for the diagnosis and management of sick children at the primary care level (*4*). The clinical signs on which the IMCI guideline is based (*5–8*) and its ability to help health workers identify and appropriately treat sick children have been assessed previously (*9–11*). IMCI has been adopted as a worldwide strategy for improving paediatric care in resource-poor settings, and since its introduction in 1995, it has been implemented in 37 African countries and 102 countries worldwide (*12*).

The existing IMCI guideline recommends referral for children with severe or recurrent illnesses, such as those that are

[1] Human Resource Development, KwaZulu-Natal Department of Health, South Africa. Correspondence should be sent to this author at Private Bag X54316, Durban 4000, South Africa (email: christiane@telkomsa.net).

[2] Ngwelezane Hospital, KwaZulu-Natal, South Africa.

[3] DOH Centre for Health Policy, University of the Witwatersrand, Johannesburg, South Africa.

[4] HIV-1 Molecular Virology and Bioinformatics Unit, Africa Centre and University of Natal, Durban, South Africa.

[5] Department of Child and Adolescent Health and Development, World Health Organization, Geneva, Switzerland.

Ref. No. **02-0416**

common in patients with HIV/AIDS; however, the specific identification and management of HIV/AIDS was not included in this guideline. In South Africa, HIV/AIDS is the leading cause of death in children, and it has reversed improvements in childhood mortality made over recent decades (*13*). Care for children with HIV/AIDS is putting a strain on health services (*14*) and increasingly is being shifted to the primary care level. Primary care health workers could provide the ongoing care that these children need, but such workers urgently need to gain appropriate skills. IMCI must now include the specific management of HIV infection as a major cause of morbidity and mortality in children (*15*).

In KwaZulu-Natal Province, South Africa, the prevalence of human immunodeficiency virus (HIV) is very high: 36.2% of women who attended government antenatal clinics in 2000 were HIV-positive (*16*). An algorithm for identification of children with HIV therefore was incorporated into IMCI. If a child is identified as possibly having HIV infection, IMCI includes guidelines for HIV serotesting and ongoing supportive management of paediatric HIV/AIDS. Antiretroviral drugs are not available currently for treatment of HIV infection in South Africa. This algorithm also has been adapted for use by several other African countries, but it was never evaluated formally. We report an evaluation of an HIV algorithm for identification of children with symptomatic HIV infection and show how data from this study was used to improve the algorithm.

Participants and methods

IMCI/HIV algorithm

IMCI comprises a series of guidelines for assessment and treatment of common childhood conditions that are important causes of morbidity and mortality (*2*). The health worker assesses the child through history and examination and classifies the child as needing referral, specific medical treatment, or advice on home management.

Screening questions were added to the routine assessment of every child to alert the health worker to the fact that a child might be at risk of HIV infection. If any screening questions were answered positively, the child was also assessed for symptomatic HIV infection (Fig. 1). This assessment was based on local clinical experience (*17–20*) and WHO clinical case definitions for paediatric acquired immunodeficiency syndrome (AIDS) (*21*).

Participants

The study was carried out in the paediatric outpatient department at Ngwelezane hospital in KwaZulu-Natal from January to April 2001. This is a district hospital, and approximately 200 children are seen weekly in the outpatient department; most of these are referred by the 19 outlying clinics. HIV counselling and testing is available with routine hospital services and is requested by clinicians where indicated, but it may not be easily accessible because of a shortage of counsellors. Long-term follow-up care is provided for a small number of HIV-infected children in the hospital outpatient department, but very little follow-up care is provided by first-level clinics.

All children aged 2–59 months who attended the paediatric outpatient department during working hours were considered for enrolment in the study. Children of known HIV serostatus and follow-up cases were excluded. For logistical reasons, the number of children enrolled each day was limited to 14.

Sample size was calculated with the formula used to compare two proportions (*22, 23*), on the basis of assumptions that the seroprevalence of HIV in the study population was 20% and that the sensitivity of diagnosis by the paediatrician would be 80% compared with an HIV test. We wanted to recognize a deviance of 15% between the doctor and the algorithm, at a 5% level of significance. The sample size thus calculated was 138 children confirmed as HIV-infected, so that the total sample required was 690.

Consent and ethical approval

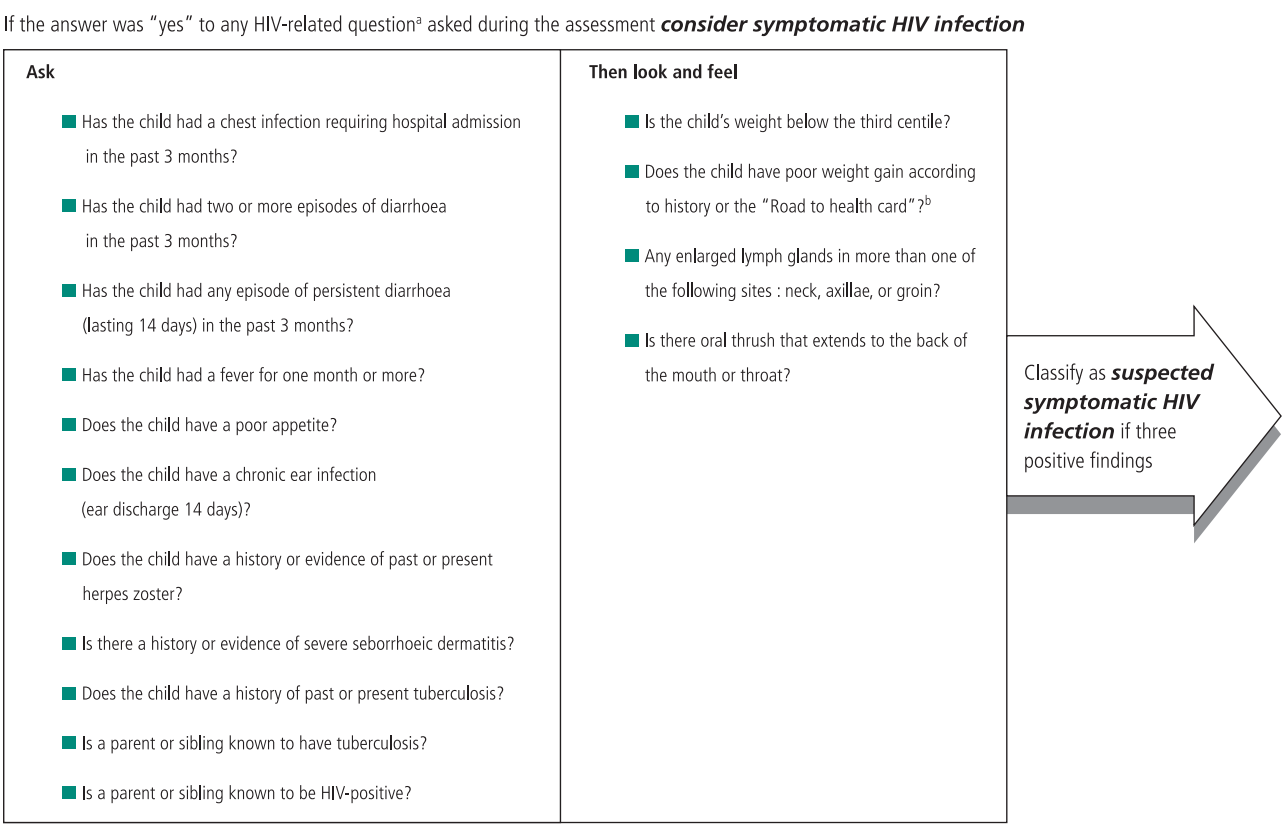
Before a child was enrolled, written consent was obtained with a detailed consent form for participation in the study and for anonymous HIV testing. Mothers were given the option to participate in the study without being given the HIV result, because we anticipated that if there was no clinical indication for testing, mothers might not wish to know the HIV status of their child. Consent was accepted from mothers, fathers, and grandparents, and the child was excluded if no appropriate family member was present. Consent was obtained in a confidential setting by a Zulu-speaking AIDS counsellor who was not involved in the care of the child. The advantages of knowing the HIV result were explained, and if the child was accompanied by the mother (or legal guardian, if the mother was dead), same day voluntary counselling and testing of the child were offered. If these were accepted, open HIV testing was done through routine hospital services, with the results and post-test counselling given by our study counsellor. Open testing was not offered to other family members to safeguard the mother's confidentiality. The paediatrician also advised mothers to have HIV counselling and testing wherever there was a clinical indication. All children who were identified as infected with HIV — either because the mother wished to know the HIV status of the child or because there was a clinical indication for testing — were offered all available treatments for HIV. Available treatments were prophylaxis for *Pneumocystis carinii* (recently renamed *Pneumocystis jiroveci)* pneumonia, treatment for concurrent illnesses, and regular follow-up. Children with clinical HIV infection where the mother refused open testing were offered the same treatment and follow-up. Carers of children who returned for HIV results were given post-test counselling before treatment was initiated by hospital staff and not the study staff. These results were not linked in any way to the study data.

Each child was assigned a study number at the time of enrolment, and their name was not recorded in the database. Results of HIV tests were linked only to clinical data after completion of the study. Ethical approval was obtained from the Ethics Committee of the University of Natal Medical School and from WHO Secretarial Committee on Research involving Human Subjects (SCRIHS).

Evaluation of the HIV algorithm

Each child was assessed by an IMCI practitioner with the HIV algorithm (Fig. 1). Clinical findings and HIV classification were recorded. The child then had a clinical assessment by a paediatrician; this was standardized with a structured data collection tool that detailed the history and examination. The paediatrician recorded an opinion as to whether the child had HIV infection and the reasons for this decision, with reference to the Centres for Disease Control and Prevention (CDC) criteria for paediatric HIV (*24*). The paediatrician's assessment allowed the performance of the HIV algorithm to be compared with the best possible clinical assessment. The HIV test provided an objective standard for both clinical assessments. The principal outcome measure from

Fig. 1. **Original HIV algorithm**



[a] " Screening questions" asked during the routine assessment of every child.
[b] "Road to health card" showing weight for age.

WHO 03.203

each assessment was whether the child had suspected symptomatic HIV infection. The IMCI and the paediatrician's assessments were made separately, without any contact between the IMCI practitioner and the paediatrician.

Two IMCI practitioners and two paediatricians made the assessments. The IMCI practitioners were a professional nurse and a primary care doctor, who both were experienced IMCI trainers. Both the study paediatricians had worked for more than three years in a setting with a high prevalence of HIV. The paediatricians and IMCI practitioners assessed the same patients from a sample of one in 20 enrolled patients to allow measurement of interobserver variation.

HIV testing

HIV testing was done after completion of both clinical assessments. Blood spots were collected from all children with a capillary blood sample, dried on filter paper, and labelled with the study number and age of the child. Initial HIV-1 testing was performed on dried blood spots with two different serological assays: a broad-based HIV-1/HIV-2 enzyme-linked immunosorbent assay (ELISA) (Vironstika HIV-1 IMPVD; Organon Teknika, Durham (NC), USA) and then a confirmatory ELISA (Murex Wellcozyme HIV 1+2 GACELISA; Murex Corporation, Dartford, England). To differentiate between infants who were infected with HIV-1 and those who carried maternal HIV-1 antibodies, we tested all antibody-positive dried blood spots for the presence of virus with the NucliSens HIV-1 RNA QT kit (Organon Teknika, Durham (NC), USA) adapted for use with dried blood spot samples. These techniques have been shown to be reliable for the study of subtype C viruses in Africa (*25–27*).

Analysis

Results were precoded and double entered into EpiInfo software (version 6.04). The data were validated and analysed in EpiInfo and SPSS software (version 10.0). The sensitivity, specificity, positive and negative predictive values, and likelihood ratios were calculated for the paediatrician and IMCI assessments. We calculated 95% confidence intervals for proportions with the exact binomial method and compared results by means of a χ^2 test. Confidence intervals for likelihood ratios were calculated with the method of Simel et al. (*23*). Diagnostic odds ratios were calculated to identify variables significantly associated with HIV infection. Stepwise logistic regression was used to identify the most useful independently significant predictors of HIV infection.

A model developed in Microsoft Excel was used to calculate the validity of alternative algorithms on the study population with these independent predictors of HIV. Different combinations of screening and scoring variables were entered into the model, which then calculated the validity for each. In this way, possible improvements to the HIV algorithm were evaluated. We calculated weighted kappa statistics, which measure the agreement between observers beyond random agreement and take the degree of disagreement into account, for the comparison between the two observers (*28*).

Results

Study participants and HIV prevalence

Overall, 690 children were enrolled into the study. Only 22 (3.2%) of carers of the children who were asked to participate refused permission. We noted a very high uptake of voluntary

counselling and testing: of 555 children accompanied by the mother, 353 (63.6%) asked to know the result of their child's HIV test. In total, 198 children were found to be infected with HIV, which shows a 28.7% prevalence of HIV in the overall study sample. Table 1 shows the age of the participants and age-related seroprevalence.

Evaluation of the HIV algorithm

Table 2 shows a comparison of the validity of the HIV algorithm and the paediatrician in identifying HIV infection. The paediatrician performed better in all aspects; however, the IMCI practitioner and paediatrician made the same decision about the child's HIV status in 561 (81.3%) children ($\kappa = 0.52$, $P < 0.001$) (*28*). Of the 46 children correctly identified by the paediatrician but not by the IMCI practitioner, 30 had splenomegaly, hepatomegaly, or parotid enlargement (signs not included in the initial HIV algorithm), whereas the others had a variety of features. The validity of the algorithm did not change significantly when analysed for different age categories. When the IMCI/HIV algorithm was used, of 111 children identified as HIV-infected by the IMCI practitioner, 71 (64%) would have been referred according to the IMCI guideline without inclusion of the HIV component.

Interobserver agreement

In total, 42 children were assessed by both IMCI practitioners. In seven children, a difference in the HIV classification was noted, which gave an agreement of 83.3% ($\kappa = 0.51$, $P < 0.001$) (*28*). All differences were in the interpretation of a history of poor weight gain from the carer.

Both paediatricians also assessed 42 children; in only three was a difference in the diagnosis of HIV infection noted, which gave a 92.9% agreement ($\kappa = 0.73$, $P < 0.001$).

Development of an improved HIV algorithm

Signs and symptoms used to develop the improved algorithm were chosen from those identified as significant independent predictors of HIV infection. The signs considered for inclusion were those that were clinically relevant, widely applicable, and practical to teach during IMCI training (Table 3). For this reason, the design of the improved algorithm may not have been the most statistically sensitive or specific.

Oral thrush in children was associated strongly with HIV infection. Any severity of thrush was a more sensitive predictor than severe thrush alone (25.8% vs 8.1%), with little difference in specificity or positive predictive value. Lymph nodes in two or more sites, as used in IMCI, had a similar association with HIV (odds ratio (OR) = 4.6, 95% confidence interval (CI) = 3.2–6.5) compared with WHO's definition of three sites (OR = 3.6, 95% CI = 2.5–5.1) (*21*), but the former was a more sensitive predictor of HIV infection (60.1% vs 42.9%).

Table 1. **Prevalence of HIV infection in children enrolled in the study, by age group**

Age group (months)	Children	Children infected with HIV
2–11	226	85 (37.6)[a]
12–23	169	48 (28.4)
24–35	106	28 (26.4)
36–47	117	23 (19.7)
48–59	72	14 (19.4)
All ages	690	198 (28.7)

[a] Values in parentheses are percentages.

Various combinations of screening questions and clinical features were tested with the model to maximise the sensitivity and specificity of the improved algorithm. Although the sensitivity could be improved by doing the full assessment for HIV on every child, this would be time consuming and might be unacceptable to health workers. We therefore included a screening step that comprised four simple and sensitive screening questions to be asked for every child (Fig. 2). With this combination of screening questions, 92.4% of HIV-infected children in our study population would have had the full assessment for symptomatic HIV infection (Table 4).

By using these screening questions and additional clinical features of HIV, we developed an improved algorithm (Fig. 2) that would identify symptomatic HIV infection in our study population with a sensitivity of 67.2% and a specificity of 81.5% (Table 4). When the screening questions were omitted and every child was assessed, the performance of the algorithm in our population did not improve significantly. Similarly, hepatomegaly and splenomegaly were not independent predictors of infection with HIV in this population, so their inclusion in the algorithm did not improve its performance (Table 4). Application of WHO's case definition for paediatric AIDS to our population was very specific but not sensitive in identifying HIV-positive children (Table 4) (*21*).

Discussion

This is the first study to evaluate a tool for primary level health care workers to identify symptomatic HIV infection in children. The algorithm performed with reasonable sensitivity and specificity compared with a paediatrician. The paediatricians provided the best performance that can be expected of a clinical assessment, as not all children with a positive laboratory HIV test are symptomatic. We also used the clinical data collected on

Table 2. **Validity of paediatrician and original IMCI/HIV algorithm in identification of HIV-infected children**

Variable	Method of identification		Comparison	
	Paediatrician	HIV algorithm	χ^2 test	*P*-value
Sensitivity (%)	71.7 (64.9–77.9)[a]	56.1 (48.8–63.1)	10.5	0.001
Specificity (%)	90.4 (87.5–92.9)	85.0 (81.5–88.0)	6.9	0.009
Positive predictive value (%)	75.1 (68.3–81.1)	60.0 (52.6–67.1)	9.8	0.002
Negative predictive value (%)	88.8 (85.7–91.4)	82.8 (79.2–86.0)	7.5	0.006
Likelihood ratio positive	7.47 (4.83–11.55)	3.74 (2.63–5.33)		

[a] Values in parentheses are 95% confidence intervals.

these children to develop an improved HIV algorithm with a higher sensitivity and specificity when applied to our population. This improved algorithm is simpler than the initial algorithm, and its performance is close to that of an experienced paediatrician (Fig. 2). We also described the clinical features that, if found in children who present to a health facility in an area of high prevalence of HIV, are most strongly predictive of HIV infection.

This algorithm is a critical step towards provision of adequate services for HIV-infected children in South Africa and settings where HIV/AIDS is a public health problem. Primary health workers in clinics could provide the continuing care and support needed for these children and their families. As most countries in sub-Saharan Africa are currently implementing IMCI, this HIV algorithm and accompanying management guidelines are an important step towards giving health workers the skills they need (*12*). Although many of the children identified as infected with HIV would have been referred to hospital according to IMCI guidelines that do not take HIV status into account, most children in our sample had been referred already. Even in this hospital-based sample, 36% of children identified as possibly being infected with HIV would not have been referred, and this is likely to be higher in a primary care setting. Referral does not ensure that a diagnosis is made at the hospital and, more importantly, is unlikely to be communicated to primary care level. Implementation of the HIV algorithm by primary health workers will raise awareness and allow follow-up to be provided at this level.

The limited interventions available to HIV-infected children in resource-poor settings like South Africa, where antiretroviral drugs are not available, has been used to argue against early identification of these children. Effective interventions, including treatment of intercurrent infections, cotrimoxazole prophylaxis for *Pneumocystis jiroveci* pneumonia, and support for families isolated by the stigma of HIV are available. These can only be implemented if health workers identify children infected with HIV. As additional treatments become available for these children and their families, these can be integrated into the IMCI management guidelines. Increased identification of children infected with HIV may increase awareness of the extent of the problem at all levels of the health system and encourage policy changes towards improving the availability of treatment.

Identification of HIV-infected people and promotion of behaviour change are the major challenges of any HIV prevention programme. Early diagnosis and implementation of care for children of HIV-infected mothers may be a way of positively engaging these mothers to promote wider education messages about AIDS. The level of uptake of voluntary counselling and testing by mothers of children enrolled in our study was very high (63.6%), which suggests that, with appropriate counselling, mothers do want to know their own and their children's HIV status. During our study, the increase in HIV testing resulted in many mothers being identified as infected with HIV, and a mothers' support group has now been set up. Health workers are reluctant to talk about HIV with patients and have a perception that it is not acceptable to do so, but our study suggests that in a confidential setting, discussion of HIV may be well received and can result in mobilisation of communities. All health workers need skills to discuss and manage HIV/AIDS-related problems on a day-to-day basis in areas with a high prevalence of HIV.

Our study had a number of strengths. When we evaluated the algorithm, we were able to recruit a large sample size and to determine reliably the HIV status of all enrolled children. Viral loads were determined in all children to confirm HIV infection. The IMCI practitioners who collected data in the study were very experienced and highly motivated, so the data was accurate and complete. Considerable experience has been gained in the use of the initial HIV algorithm, which was introduced in KwaZulu-Natal Province in 1998.

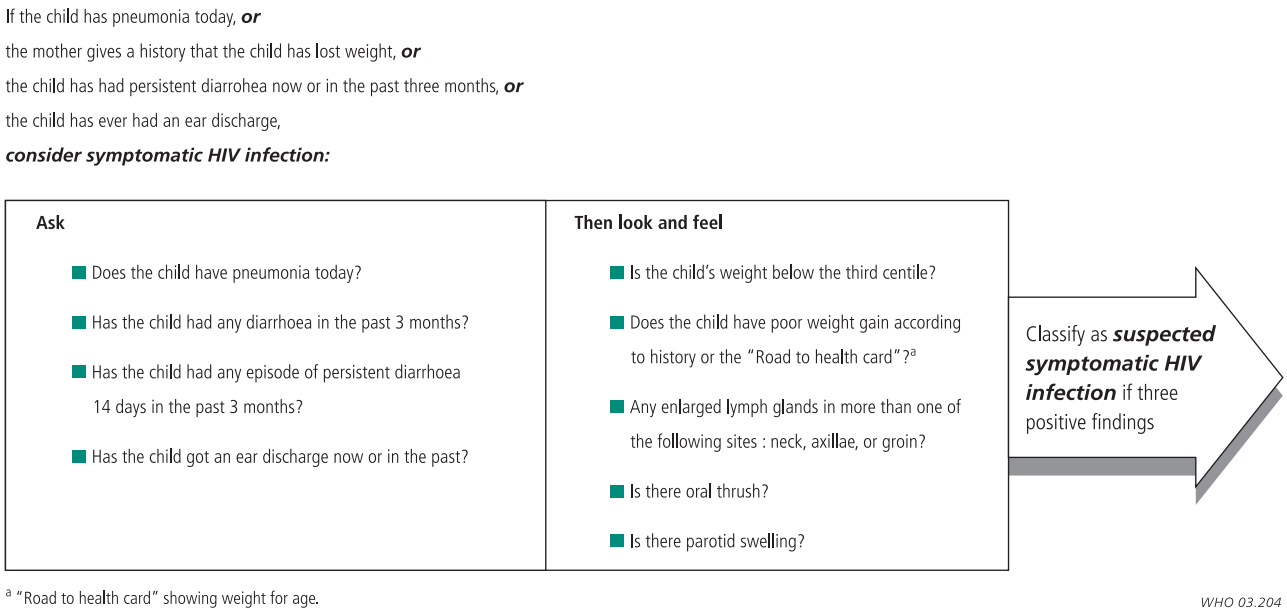
Our findings also have some limitations. The HIV algorithm may perform differently in a primary level facility, in which there will be fewer cases of HIV/AIDS. This evaluation was made in a hospital setting in an area of high prevalence of HIV, because resources were not available to obtain the large sample that would have been needed at the primary care level. Similarly, the performance of the algorithm will be different in countries with lower prevalences of HIV. Our practitioners were experienced

Table 3. **Validity of single clinical features in predicting HIV infection in children aged 2–59 months**

Sign[a]	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Likelihood ratio positive	Bivariate diagnostic odds ratio[b]
History of weight loss	72.2	51.4	37.4	1.49	2.8 (1.9–3.9)
Lymphadenopathy (any palpable nodes in two sites)	60.1	74.8	49.0	2.39	4.5 (3.2–6.3)
Weight below third percentile	53.0	83.5	56.5	3.22	5.7 (4.0– 8.3)
Pneumonia this visit[c]	47.4	71.3	40.0	1.66	2.3 (1.6–3.2)
Any diarrhoea in past three months	47.0	72.2	40.4	1.69	2.3 (1.6–3.2)
Any persistent diarrhoea in past three months	13.1	97.0	63.4	4.30	4.8 (2.5–9.3)
Ear discharge (ever)	33.3	86.6	50.0	2.49	3.2 (2.2– 4.8)
Splenomegaly	27.3	98.6	88.5	19.20	26.0 (11.6–58.3)
Hepatomegaly	26.3	96.8	76.5	8.08	10.6 (5.9–19.1)
Oral thrush (any)	25.8	97.8	82.3	11.50	15.2 (7.7–29.9)
Parotid enlargement	7.6	99.0	75.0	7.43	8.0 (2.9–22.3)

[a] Presence of signs are based on the findings of the paediatrician.
[b] Values in parentheses are 95% confidence intervals.
[c] Pneumonia as defined in IMCI guidelines and identified by IMCI practitioner.

Fig. 2. **Improved HIV algorithm**



[a] "Road to health card" showing weight for age.

WHO 03.204

Table 4. **Validity of improved HIV algorithm and WHO clinical criteria for paediatric AIDS applied to study population**

Variable	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Likelihood ratio positive
Screening questions only	92.4	31.5	35.2	1.35
Improved HIV algorithm with screening questions[a]	67.2	81.5	59.4	3.63
Improved HIV algorithm applied to all children[b]	70.1	80.1	58.6	3.52
Improved HIV algorithm with hepatomegaly and splenomegaly included[a]	71.5	80.5	59.5	3.65
Improved HIV algorithm with four points used to classify WHO clinical criteria for paediatric AIDS[c]	35.4	94.3	71.4	6.21
	8.5	98.7	68.0	6.54

[a] Classification on basis of three positive findings.
[b] Full assessment applied to all children; no screening questions used.
[c] Major signs: weight loss or abnormally slow growth, chronic diarrhoea >1 month, and prolonged fever >1 month; minor signs: generalized lymphadenopathy, oropharyngeal candidiasis, repeated common infections, persistent cough, generalized dermatitis, and confirmed maternal HIV infection (*22*).

and highly motivated and therefore were likely to perform better than those working in routine clinical practice.

These findings relate to a particular population and may not all be generalizable to other settings in Africa. The validity of the HIV algorithm may be affected if it is implemented in areas in which the clinical features we identified as predictive of HIV infection are more prevalent in the general population. For example, rates of malnutrition are lower in South Africa than in other African countries, and this may reduce the predictive value of signs related to malnutrition. Hepatomegaly and splenomegaly may not be useful predictors of HIV infection in a population in which malaria is prevalent. In recognition that disease profiles vary, generic IMCI guidelines are intended to be adapted for local conditions, so our HIV algorithm will be used differently in other settings. At a workshop in Harare in June 2001, WHO adopted a generic HIV algorithm based on our data, which can be adapted and incorporated into IMCI in countries with prevalence of HIV >2% (*29*).

Adaptations to the HIV algorithm also may be made according to availability of resources in countries that intend to implement the algorithm. In South Africa, if a child has suspected HIV infection, an HIV test would be recommended to confirm the diagnosis. In many countries, HIV testing is not available at the primary care level, so management decisions may need to be based on the algorithm alone. To make the improved HIV algorithm more specific for use in this setting, the number of clinical features used to classify a child suspected as being infected with HIV could be increased from three to four. In this way, the specificity and positive predictive value of the algorithm can be increased and, although this results in a lower sensitivity (Table 4), children missed by a more specific algorithm may be identified later, as the disease progresses. A significant rate of false positives still exists, and this cannot be avoided entirely with a clinical diagnosis. Children may be exposed to unnecessary stigma and follow-up, but all children with these clinical features are vulnerable and could benefit from extra care. Countries that intend to use the algorithm in this way, without the support of HIV tests, would need to develop training materials to give health workers the counselling skills needed to explain this to mothers. The HIV algorithm is only the first step towards ongoing management of paediatric HIV infection. Health workers need to use the algorithm and facilities for diagnosis and follow-up of

identified children must be available at primary level. This may severely limit implementation in many resource-poor settings.

Conclusion

Health workers at the primary care level can identify children with symptomatic HIV infection through the identification of simple signs taught within IMCI. We developed an improved HIV algorithm that is evidence based and can be recommended for use in settings with a high prevalence of HIV. Further research is being undertaken to validate the algorithm in other clinical settings and to assess its use and acceptability among primary care practitioners. WHO's current clinical definitions of paediatric AIDS (*21*) have not been evaluated formally, and these may be reviewed as a result of this data. As implementation of this algorithm will result in earlier diagnosis of children infected with HIV, we also suggest further evaluation of the interventions recommended for these children. ■

Acknowledgements

We thank the staff and patients at Ngwelezane Hospital; Elizabeth Muruthi and Gugu Qwabe for help with data collection; Lulu Muhe, Nigel Rollins, and Stephen Knight for help with developing the proposal; and Elizabeth Mason and Olivier Fontaine from WHO for their support and encouragement.

Funding: Department of Child and Adolescent Health and Development, World Health Organization, Geneva.

Competing interests: none declared.

Résumé

Algorithme clinique pour le diagnostic de l'infection à VIH chez l'enfant dans les services de soins de santé primaires

Objectif Déterminer la validité d'un algorithme utilisé par les agents des soins de santé primaires pour repérer les enfants présentant une infection à VIH symptomatique. Cet algorithme est appliqué en Afrique du Sud dans le cadre de la prise en charge intégrée des maladies de l'enfant (PCIME), stratégie visant à réduire la morbidité et la mortalité infantiles en améliorant les soins de santé primaires. Le SIDA étant l'une des principales causes de mortalité chez l'enfant en Afrique australe, le diagnostic et la prise en charge des infections à VIH symptomatiques ont été ajoutés à l'algorithme actuel de la PCIME.

Méthodes Au total 690 enfants de la consultation externe d'un hôpital de district d'Afrique du Sud ont été vus par un praticien appliquant l'algorithme pour le VIH, puis par un pédiatre. La charge virale du VIH a ensuite été déterminée pour chaque enfant. La validité de l'algorithme pour la détection de l'infection à VIH symptomatique a été comparée avec celle du diagnostic clinique par le pédiatre et avec les résultats du test de dépistage. L'algorithme a été amélioré par le recueil minutieux des données cliniques.

Résultats Au total, 198 enfants (28,7 %) étaient infectés par le VIH. Le pédiatre en a identifié correctement 142 (71,7 %) et l'algorithme VIH/PCIME a permis d'en trouver 111 (56,1 %). Les odds ratios ont été calculés pour déterminer les facteurs prédictifs de l'infection à VIH et utilisés pour améliorer l'algorithme et atteindre, pour le dépistage clinique, une sensibilité de 67,2 % et une spécificité de 81,5 %.

Conclusion L'utilisation d'un algorithme permet aux agents des soins de santé primaire de repérer efficacement les enfants présentant une infection à VIH symptomatique. L'algorithme amélioré mis au point dans cette étude pourrait être utile dans les pays à forte prévalence du VIH et permettre aux praticiens appliquant la PCIME de repérer et de soigner les enfants infectés.

Resumen

Diagnóstico de la infección infantil por VIH con un algoritmo clínico en un entorno de atención primaria

Objetivo Determinar la validez de un algoritmo usado por los trabajadores de salud del nivel de atención primaria para identificar a los niños con infección por VIH sintomática. Este algoritmo de detección del VIH se está aplicando en Sudáfrica como parte de la Atención Integrada a las Enfermedades Prevalentes de la Infancia (AIEPI), estrategia que aspira a mejorar la morbilidad y la mortalidad en la niñez mejorando la atención en el nivel de atención primaria. Dado que el SIDA es una importante causa de muerte en la niñez en el África meridional, se decidió añadir el diagnóstico y el manejo de la infección sintomática por VIH al algoritmo de AIEPI que se venía empleando.

Métodos En total, 690 niños que acudieron al departamento de pacientes ambulatorios de un hospital de distrito de Sudáfrica fueron evaluados mediante el algoritmo VIH y por un pediatra. Todos los niños fueron sometidos luego a la prueba de carga viral del VIH. La validez del algoritmo como medio de detección de la infección sintomática por VIH se contrastó con el diagnóstico clínico realizado por un pediatra y con el resultado de una prueba del VIH. El algoritmo fue mejorado utilizando diversos datos clínicos más detallados.

Resultados De todos los niños incluidos en el estudio, 198 (28,7%) estaban infectados por el VIH. El pediatra identificó correctamente a 142 niños (71,7%) infectados, mientras que el algoritmo AIEPI/VIH identificó a 111 (56,1%). Las razones de posibilidades calculadas para identificar los factores predictivos de la infección por VIH se utilizaron para desarrollar un algoritmo mejorado del VIH, que detecta la infección clínica mediante una sensibilidad del 67,2% y una especificidad del 81,5%.

Conclusión El personal de salud del nivel primario puede identificar eficazmente a los niños con infección sintomática por VIH utilizando un algoritmo desarrollado al efecto. El algoritmo mejorado puesto a punto en este estudio podría ser utilizado por los países con alta prevalencia del virus, donde los especialistas de AIEPI podrían así identificar y atender a los niños infectados por el VIH.

ملخص

تشخيص العدوى بفيروس العَوَز المناعي البشري لدى الأطفال في مواقع الرعاية الصحية الأولية باستخدام خوارزمية سريرية

الهدف: تقييم صلاحية خوارزمية استخدمها العاملون في مستوى الرعاية الصحية الأولية لكشف العدوى بفيروس العَوَز المناعي البشري المصحوبة بأعراض. وقد استخدمت هذه الخوارزمية في جنوب أفريقيا كجزء من مبادرة التدبير العلاجي المتكامل لأمراض الأطفال، وهي استراتيجية تهدف لتحسين معدلات المراضة والوفيات لدى الأطفال عن طريق تحسين الرعاية على مستوى الرعاية الصحية الأولية. ولما كان الإيدز هو السبب الأول لوفيات الأطفال في جنوب أفريقيا، فإن تشخيص ومعالجة العدوى بفيروس العَوَز المناعي البشري المصحوبة بأعراض قد أضيفتا إلى مبادرة التدبير العلاجي المتكامل لأمراض الأطفال.

الطريقة: لقد تم تقييم ٦٩٠ طفلاً ممن راجعو القسم الخارجي في إحدى مستشفيات مناطق جنوب أفريقيا باستخدام خوارزمية العدوى بفيروس العَوَز المناعي البشري من قِبَل طبيب أطفال. ثم أجري لهؤلاء الأطفال معايرة للحمل الدموي من فيروس العَوَز المناعي البشري، وتمت مقارنة صلاحيته في كشف العدوى بفيروس العَوَز المناعي البشري المصحوبة بأعراض بكلٍّ من التشخيص السريري لطبيب الأطفال ونتائج اختبار فيروس العَوَز المناعي البشري. وقد استعملت المعطيات السريرية المفصلة في تحسين الخوارزمية.

الموجودات: وجد أن ١٩٨ طفلاً يشكلون (٢٨,٧٪) من بين الأطفال المدروسين مصابون بالعدوى بفيروس العَوَز المناعي البشري وقد استطاع طبيب الأطفال كشف ١٤٢ حالة تشكل (٧١,٧٪) من بين الأطفال المصابين بالعدوى بفيروس العَوَز المناعي البشري، فيما أمكن باستعمال خوارزمية كشف العدوى بفيروس العَوَز المناعي البشري في مبادرة التدبير العلاجي المتكامل لأمراض الطفولة كشف ١١١ حالة تشكل (٥٦,١٪) من بين الأطفال المصابين بفيروس العَوَز المناعي البشري. وكانت نسب الأرجحية قد حسبت لكشف عوامل التنبؤ بعدوى فيروس العَوَز المناعي البشري، وقد استخدمت لإعداد خوارزمية كشف العدوى بفيروس العَوَز المناعي البشري ذات حساسية تعادل ٦٧,٢٪ وذات نوعية في ٨١,٥٪ من الحالات التي تم كشفها سريرياً لإصابتها بعدوى فيروس العَوَز المناعي البشري.

الاستنتاج: يمكن كشف عدوى الأطفال بفيروس العَوَز المناعي البشري المصحوبة بالأعراض بشكل فعَّال من قِبَل العاملين في الرعاية الصحية الأولية إذا استخدموا خوارزمية. والخوارزمية المحسَّنة المعدَّة في هذه الدراسة لكشف العدوى بفيروس العَوَز المناعي البشري يمكن أن تستخدم في بلدان أخرى تعاني من معدلات انتشار عالية للعدوى بفيروس العَوَز المناعي البشري، وهذا ما يمكن للممارسين في مبادرة التدبير العلاجي المتكامل لأمراض الطفولة من كشف الأطفال المصابين بالعدوى بفيروس العَوَز المناعي البشري وتقديم الرعاية لهم.

References

1. Murray CJL, Lopez AD Mathers CD, Stein C. The global burden of disease 2000 project: aims, methods and data sources. Evidence and information for Policy (EIP). Geneva: World Health Organization; 2001. Available from: URL: http://www3.who.int/whosis/discussion_papers/discussion_papers.cfm (accessed on 14 October 2003).
2. World Health Organization Division of Diarrhoeal and Acute Respiratory Disease Control. Integrated management of the sick child. *Bulletin of the World Health Organization* 1995;73:735-40.
3. World Bank. *World development report 1993: investing in health.* New York: Oxford University Press; 1993.
4. Gove S. Integrated management of childhood illness by outpatient health workers: technical basis and overview. *Bulletin of the World Health Organization* 1997;75 Suppl 1:7-24.
5. Bern C, Zucker JR, Perkins J, Otieno J, Oloo AJ, Yip R. Assessment of potential indicators for protein–energy malnutrition in the algorithm for integrated management of childhood illness. *Bulletin of the World Health Organization* 1996;75 Suppl 1:87-96.
6. Kalter HD, Burnham G, Kolstad PR, Hossain M, Shillinger JA, Khan NZ, et al. Evaluation of clinical signs to diagnose anaemia in Uganda and Bangladesh, in areas with and without malaria. *Bulletin of the World Health Organization* 1996;75 Suppl 1:103-11.
7. Weber MW, Kellingray SD, Palmer A, Jaffar S, Mulholland EK, Greenwood BM. Pallor as a clinical sign of anaemia in children: an investigation in the Gambia. *Bulletin of the World Health Organization* 1996;75 Suppl 1:113-8.
8. Kalter HD, Shillinger JA, Hossain M, Burnham G, Saha S, de Wit V, et al. Identifying sick children requiring referral to hospital in Bangladesh. *Bulletin of the World Health Organization* 1997;75 Suppl 1:65-75.
9. Simoes EAF, Desta T, Gerbresellassie T, Dagnew M, Gove S. Performance of healthworkers after training in the integrated management of childhood illnesses in Gondar, Ethiopia. *Bulletin of the World Health Organization* 1997;75 Suppl 1:43-53.
10. Kolstad PR, Burnham G, Kenya-Mugisha N, Black RE. The integrated management of childhood illness in western Uganda. *Bulletin of the World Health Organization* 1996;75 Suppl 1:77-85.
11. Weber MW, Mulholland EK, Jaffar S, Troedsson H, Gove S, Greenwood BM. Evaluation of the algorithm for the integrated management of childhood illnesses in an area with seasonal malaria in the Gambia. *Bulletin of the World Health Organization* 1996;75 Suppl 1:25-32.
12. World Health Organization Department of Child and Adolescent Health and Development. *Annual report 2000*. Geneva: World Health Organization; 2000. Available from: URL: http://www.who.int/child-adolescent-health/ (accessed on 11 September 2002).
13. Medical Research Council of South Africa. *South African demographic and health survey 1998. Preliminary report*. Pretoria: Medical Research Council of South Africa; 1999. Available from: URL: http://www.mrc.ac.za/researchreports/demographicsurvey.htm (accessed on 14 October 2003).
14. Zwi KJ, Pettifor JM, Soderlund N. Paediatric hospital admissions at a South African urban regional hospital: the impact of HIV, 1992-1997. *Annals of Tropical Paediatrics* 1999;19:135-42.
15. Oluwole D, Mason E, Costello A. Management of childhood illness in Africa. *BMJ* 2000;320:594-5
16. Health Systems Research and Epidemiology, Department of Health. *National HIV and syphilis sero-prevalence survey of women attending public antenatal clinics in South Africa 2000*. Pretoria: Department of Health; 2001. Available from: URL: http://www.doh.gov.za/facts/index.html (accessed on 1 September 2002).
17. Bobat R, Moodley D, Coutsoudis A, Coovadia H, Gouws E. The early natural history of vertically transmitted HIV-1 infection in African children from Durban, South Africa. *Annals of Tropical Paediatrics* 1998;18:187-96.
18. Jeena PM, Coovadia HM, Thula SA, Blythe D, Buckels NJ, Chetty R. Persistent and chronic lung disease in HIV-1 infected and uninfected African children. *AIDS* 1998;12:1185-93.
19. Bobat R, Coovadia H, Moodley D, Coutsoudis A. Mortality in a cohort of children born to HIV-1 infected women from Durban, South Africa. *South African Medical Journal* 1999;89:646-8.
20. Spira R, Lepage P, Msellati P, Van de Perre P, Leroy V, Simonon A, et al. Natural history of human immunodeficiency virus type 1 infection in children: a five-year prospective study in Rwanda. *Pediatrics* 1999;104:e56.
21. World Health Organization. Acquired immunodeficiency syndrome (AIDS). *Weekly Epidemiology Record* 1986;61:69-73.
22. Arkin CF, Wachtel MS. How many patients are necessary to assess test performance? *JAMA* 1990;263:275-8.
23. Simel DL, Samsa GP, Matchar DB. Likelihood ratios with confidence: sample size estimation for diagnostic test studies. *Journal of Clinical Epidemiology* 1991;44:763-70.

24. Centers for Disease Control. 1994 revised classification system for human immunodeficiency virus infection in children less than 13 years of age. *Morbidity and Mortality Weekly Report* 1994;(No. RR-12):1-10.
25. Biggar RJ, Janes M, Pilon R, Miotti P, Taha ET, Broadhead R, et al. Viral levels and CD4/CD8 counts in untreated African infants infected with human immunodeficiency virus type 1. *Journal of Infectious Disease* 1999;180:1838-43.
26. Taha ET, Hoover DR, Broadhead RL, van der Hoven L, Liomba GN, Kumwenda NK, et al. Association of HIV-1 load and CD4+ lymphocyte with mortality in untreated African children older than one year. *AIDS* 2000;14:453-9.
27. Broadbent R, Biggar RM, Janes M, Kumwenda N, Taha ET, Cassol S. Viral levels in newborn African infants undergoing primary HIV-1. *AIDS* 2001;15:1311-3.
28. Cohen J. A coefficient of agreement for nominal scales. *Educational and Psychological Measurement* 1960;20:37-46.
29. World Health Organization, Regional Office for Africa. *Report on the Workshop on Adaptation of IMCI Guidelines to include HIV/AIDS. Harare 18 to 23 June 2001.* Available from: URL:// http:/www.who.int/child-adolescent-health/New_Publications/HIV/report_HIV_Harare.htm (accessed 9 October 2003).