

Monitoring neurodevelopmental and neurocognitive outcomes in the UK paediatric HIV cohort

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Ethos of developmental care

Echoing the 'Every Child Matters' paper in 2004 the ethos in the care of HIV children is to enhance wellbeing and quality of life. To improve outcomes for these children, careful attention needs to be given to monitoring all aspects of progress (physical, cognitive, behavioural, learning, social and emotional). Monitoring should include addressing the changing demands of daily life e.g. self-care, independence, growth and appearance, routines, relationships and school achievements etc, as the child moves through childhood and adolescence.

Background

Neurodevelopmental

Children who acquire HIV in the perinatal period have been found to be more at risk of developmental weaknesses than children who acquire HIV later in life, as underlying structures and processes in the brain and central nervous system CNS are still forming when exposed to HIV.

Following the introduction of antiretroviral treatments there has been an increase in survival status and improved health, growth and wellbeing for children with HIV infection (Gibb et al 2003, Judd et al 2007). Also the prevalence of acute encephalopathy and progressive neurodevelopmental presentations have significantly reduced for children where appropriate HIV care and treatments have been available, both during pregnancy as well as in childhood (Willen 2006, Patel et al 2008). However there remains a significant number of HIV infected children with long term and chronic neurodevelopmental weaknesses. For example an audit from St Mary's Hospital Paediatric HIV service found 10-19% of children, across different age groups, with demonstrable neurological signs; these were of varying severity but non progressive. (Biggs & Melvin 2007).

The most common neurological presentation reported in children with HIV is hypertonia of the lower limbs (similar to that seen in cerebral palsy and usually presenting as a diplegia). This results in impaired mobility of varying degrees of severity, but is non-progressive, if health is well maintained. These neurological sequelae can exist alone but sometimes occur with other features, such as microcephaly, and sometimes other developmental weaknesses also occur, such as delayed early language (Foster et al 2006, Biggs & Melvin 2007).

Early co-factors such as prematurity, failure to thrive, maternal intravenous drug use and additional early infections, such as CMV, which may compromise the immature immune system, have been associated with an increased likelihood of such neurological sequelae in children with HIV (European Collaborative study 1994, Wachslar Fielder & Golden 2002, Willen 2006, Foster et al 2006). There are a small proportion of children with HIV who have severe general neuro-developmental delays affecting all areas of functioning and who are unlikely to be able to achieve independent living in adult life. These children will present extra challenges to service providers particularly during transition to adult HIV services. Whilst antiretroviral treatment (ART's) cannot reverse pre-existing neurological damage, they may minimize effects on functioning by improving health and wellbeing and possibly optimising the use of alternative neuronal pathways developing to support particular functions. ART treatments known to have good central nervous system penetration may be particularly effective in reducing the effects on functions of underlying neurological difficulties.

Cognitive, learning and behavioural weaknesses.

As the average age of children living with HIV increases, many more of the population in the UK are now of older school age. This has resulted in more focus on later developmental progress, including school achievements and behavioural adjustment. Increasing numbers of children are being reported with a profile of neurocognitive weaknesses which include poor concentration, forgetfulness, problems processing information or applying skills or effort in learning situations. (Koekkoek et al 2008, Patel et al 2008, Scopazzini 2011). At times these are found to occur with other difficulties in expressive skills, psychomotor organisation, and poor regulation of behaviour or mood. Difficulties can range in severity but can often be quite subtle and variable with tests of global development or cognition, especially at younger ages, not reflecting or detecting the complexity of difficulties. This

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pattern of neurocognitive and behavioural weaknesses suggests underlying difficulties in attention regulation and with executive functions. (These are processes governed by the midbrain and prefrontal structures in the brain). Some features of these difficulties may be noted at all ages but the effects on performance, school progress and behaviour appear to increase during secondary school years when learning and social demands become greater. It is unclear what the relative effects of early exposure to HIV, chronic effects of HIV and its treatments, and adverse or difficult psychosocial experiences may have on such later difficulties. Maintaining health and good viral control appear to help prevent further deterioration in performance but more has to be learnt about the nature of these kinds of neurocognitive difficulties.

In summary, available evidence indicates that a significant proportion of children with perinatally acquired HIV have long term neuro-developmental or neurocognitive difficulties severe enough to interfere with everyday functioning including school performance (Biggs & Melvin 2007, Scopazzini 2011). It is becoming increasingly important to gather systematic longer term developmental and psychological data on the UK population to identify early who needs extra support to enhance coping and later achievements, to identify risk and protective influences from health, psychosocial and other experiences and to better understand the contribution of HIV and ART treatments on these developmental outcomes.

Aims of developmental monitoring

The primary aim is early detection of any developmental weaknesses in a child in order to facilitate interventions which prevent and/or reduce the impact of and weaknesses on functions and progress. Earlier access to interventions for those who are struggling with a developmental weakness may decrease the burden of coping on the child and family, which in turn may enhance HIV management and increases self esteem and achievement enabling more youngsters to achieve their potential.

Further aims of developmental monitoring:

- To provide general data about changing developmental needs of the UK paediatric HIV population to allow for planning for service provision and reduce variations across different centres.
- To help in understanding effects of treatments (particular combinations, length of treatments, timing of starting etc).

- To promote a greater understanding of the chronic influence of HIV infection on developmental processes and identify associations with risk and resilience factors.

Developmental monitoring in paediatric HIV clinics: A tiered approach

The recommendation is that all paediatric HIV services should adopt a developmental screening approach or interview carried out on all clinic attendee's and updated regularly (preferably annually). This would enable some basic developmental outcome data to be collected for the UK cohort as well as helping identify which children need more detailed assessment or referral. More detailed developmental, cognitive or functional assessments for all children are often difficult to obtain in clinics because of limited resources, time restraints or lack of experienced personnel to carry out assessments. Some developmental weaknesses may not meet the referral threshold for assessment or intervention by already stretched local child development services, but these weaknesses still require regular monitoring because demands and circumstances change as children get older.

The following describes such a graded approach.

Section 1. A standard core set of outcome markers around developmental information and associated psychosocial factors to be collected on all children attending clinics. AUDIT Data (appendix 1)

Section 2. A general screening interview to be carried out on all patients attending clinic (at baseline and annual review). SCREENING data (appendix 2 provides an example of a screening instrument)

Section 3. More detailed assessment. Paediatric HIV services with access to resources and personnel able to carry out more detailed and specific developmental and cognitive assessments, particularly at key times of change. ASSESSMENT data (appendix 3).

Suggestions for more specific assessments or tests are discussed in this section

Section 1. **Clinic Audit:**

Core developmental indices on all children attending HIV clinics in UK

The following is a template of basic developmental data which all clinics could collect annually as part of regular outcome data.

A. Numbers/proportion of total clinic attenders with:

- *demonstable neurological signs/diagnosis (and description of problems)*
- *numbers with head circumference falling below 5th centile*
- *motor or speech delays in early years (reported or observed to be below average range for age)*
- *significant sensory impairment: hearing & vision*
- *a developmental diagnoses (e.g. ADHD, ASD, dyslexia)*
- *a psychiatric diagnosis (and kind)*
- *numbers requiring extra support in school (Special Needs Code of Practice/Statement of special educational need OR, School action plus or school action)**
- *number attending special school or units (for learning, behaviour etc.)*

**This may need to rely on parental/carer report.*

B. Referrals *(number from total clinic attenders who are being seen by or been referred to)*

- *local developmental services e.g., physiotherapy, SALT, Child Development Centre*
- *specific psychology service (clinical, neuro-psychology, educational etc.)*
- *educational/learning support services*
- *CAMHS (Child and Adolescent Mental Health Services).*

Note: reason for referral, outcome of referral is also useful and date intervention completed.

An example of audit sheet developed by Biggs & Melvin (2007) is shown in Appendix 1

Section 2. **Screening:**

An interview or screening which gathers carers (and older children's) reports on aspects and concerns about development, behaviour and school progress. Screening would include an indepth baseline interview (at first engagement with clinic) and a 'change' or follow up sheet to be used for follow up reviews (annually). It covers significant psychosocial events likely to influence development and behaviour as well as health and other influences. (See appendix 2 for an example of a screening questionnaire covering aspects of progress and behaviour). The screening interview can be carried out by a non development specialist member of the paediatric HIV team as a means of identifying which children require further referral or assessment and collecting descriptors of common developmental concerns. It is recommended that a standardised quality of life measure, such as the PedsQL, be used with the screening interview.

Section 3. **Detailed assessment at key times:**

It is known that key times of change or adjustment i.e. significant developmental stages such as starting school or end of primary school and times of significant psychosocial change e.g. child in care, child newly arrived in UK, may exacerbate any underlying developmental vulnerabilities. These would be key times to carry out more detailed assessments in order to identify which children need referral or access to more support. The kind of assessment possible may depend on the expertise of the professional carrying out the assessment, availability of tests and amount of time available to carry out such assessments. It is recommended that the above screening information and quality of life measure (appendix 2) should be considered the minimum to collect at these times of change and added to by collecting some other information about progress such as viewing the child's school report (if parents/carers are able to bring these).

Where there is access to services or professionals qualified to assess more detailed aspects of progress or development. Appendix 3 documents which functions, skills or behaviours are most useful to assess at key ages or times as well as the kinds of interventions which may be appropriate should difficulties be identified. Examples of tests in this table have an emphasis on tests with UK norms.

More specific or detailed assessment

Some clinics have access to psychology, physiotherapy or other child development professionals and can provide more in-depth assessments for individual patients with clinical concerns about progress or can research aspects of developmental or cognitive outcomes. More detailed assessments are time consuming and require access to specific tests and staff trained in their administration and interpretation. Further, this is a culturally diverse population, with a wide age range, and careful selection and interpretation of results is needed to provide a reliable picture of children's functioning. Also the timing of assessment for children newly arrived into the country can be particularly challenging and requires careful interpretation.

A standardized test of global cognitive ability, such as the WPPSI or WISC IV, should be part of the initial assessment, but it is also becoming increasingly clear that global tests of development or cognition such as IQ are not always sensitive in picking up more subtle effects on function or performance. More specific neuro-cognitive tests, particularly those monitoring attention, working memory and information processing as in executive functions

may provide more useful data. Items from tests such as the Test of everyday attention (TEACH), Working memory scales, NEPSY, Kaufman Assessment Battery etc, can be useful. Non-verbal items from these tests may also be more reliable.

There are also some computer based tests such as the CANTAB or Cogstate which are useful for executive functions and which are free from cultural or linguistic bias. Furthermore assessing speed of performance such as pegboard or tapping speed can also be useful e.g. Movement Assessment Battery for Children (Movement ABC). At present few paediatric HIV services have access to services or test resources which can carry out such in depth neuro-psychology and neuro-cognitive assessments.

In future, support for a multicentre resource with a specialist and multidisciplinary neurodevelopmental/neurocognitive assessment team, may enable such neurocognitive and performance assessments to be available more widely to local HIV centres. This resource could also be a focus for interventions and research, e.g. monitoring effects of treatments, and could link with other services such as neuroimaging. Such a resource could be shared across other chronic or paediatric specialties.

Onward referral

The importance of referral for early intervention for developmental difficulties is recognised by parents as well as services. However because HIV remains a stigmatizing condition and there is often a lack of up to date information about Paediatric HIV within general paediatric, educational and community services, there can be anxiety about a referral to a developmental or educational service. Conversations about the benefits for sharing the HIV diagnosis for the child's future care can be helpful, together with a discussion about confidentiality which includes to whom and how the information will be shared, and can help reduce parental concerns. Parental consent for referral is essential and the information being shared needs to be clearly agreed and communicated. Sometimes several discussions will be needed with parents or carers as there may be considerable anxiety about the sharing of sensitive information. Explaining how services work in the UK and what they can provide can also be very helpful for families newly arrived who may have experienced different provision in their country of origin.

Whilst it is generally better to share full knowledge about a child's diagnosis when referring to new services, it may not always be possible or appropriate to do so, especially when making an initial enquiry about what services are available and what the referral pathway entails. Sometimes an initial referral describing the child's difficulties i.e. that they have mobility problems, are slow in talking, are struggling with work at school etc, can be used to make the first engagement with a new service. This can help parents and carers have time to build up trust and form a relationship with new providers and services before a full discussion about the diagnosis occurs. Sometimes identifying a key person within the service where a referral is to be made can be helpful, and that staff at the clinic have checked out how sensitive information is stored. It can often be difficult for anxious parents or carers to negotiate this by themselves.

There is no legal obligation to share children's HIV diagnosis with schools, nurseries or colleges and doing so should always be led on the premise that there is a need and benefit for the child (Conway 2005). It helps to remember that there are many children in schools who may have some difficulties without there being a known cause. Sometimes it can help to discuss that a child's difficulties with development or with school progress may have arisen because of early illnesses; a partial explanation. However in some circumstances, sharing the HIV diagnosis may be essential and will need to be explained to parents e.g. if the HIV service is asked to contribute to a Statement of Special Educational Needs for a child.

Local child development, educational and community services in the UK may have little up to date knowledge about children and HIV and often welcome some extra general information and support about the condition from the HIV clinic. Staff from the HIV clinic helping support the initial contact a family has to an educational or community referral, by a visit or telephone call, can be reassuring for both parents and the receiving service.

Summary

To ensure the best developmental and psychological outcomes and wellbeing of the child, developmental monitoring should be a core part of the management of paediatric HIV at all centres.

Regular screening, especially at key stages for all children, should become part of clinical practice. It is suggested that a multi-centre resource is one way of making specialist multidisciplinary developmental and neuro-cognitive assessments available for those with more complex problems.

References

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Appendix 1

Clinic Audit (Case notes): Neurodevelopmental problems in HIV infected children

Centre:

Date:

Total number of infected children attending clinic:

Present age <i>Years of birth</i>	Early years 0–4 yrs <i>2012-2008</i>	Primary school-infant 5–7 yrs <i>2007-2005</i>	Primary school-junior 8-11yrs <i>2004-2001</i>	Early Secondary school 12-14 yrs <i>2000-1998</i>	Later secondary 15-17yrs <i>1997 & earlier</i>	TOTALS
Number included in audit	Males= ()	Males= ()	Males= ()	Males= ()	Males= ()	Males= ()
New diagnosis in previous year ()	Females= ()	Females= ()	Females= ()	Females= ()	Females= ()	Females= ()
No. with abnormal neurological signs: increased muscle tone abnormal reflexes microcephaly epilepsy other						
No. with significant sensory impairment of neural origin - hearing - vision						
No. with other developmental diagnosis ADHD/ADD ASD Dyslexia/ other						
Known to child dev. service or CDS professional in last year e.g. SALT/ PT						
No. with significant delay on assessment. i.e. score > - 2 standard deviations below mean for age on test of Speech/language Cognitive Learning Motor/psychomotor						
Receiving extra help in school <i>- no. with statement or on school action plus - (parent report)</i> <i>- no. referred to education/ school support service</i>						
Referred to CAMHS, psychology or psychiatric service						
Total with NO identified developmental problem						

Neuro-developmental Audit sheet St Mary's Family Clinic. Biggs & Melvin

Appendix 2 Example of baseline and annual screening interview for development

Screening for school aged children (PHP group 2009)

2A Baseline screening form

Clinic:..... Date of Completion:.....

Full name (as on medical file):..... Hospital no:.....

Known as:..... DOB:.....

Address:.....

.....

Tel No:(H)..... (M):.....

Date of diagnosis:..... Date of contact with present clinic:.....

Child's main carer (at present):

Other members of household (current):.....

Significant others in family (not living at home)

Child born in UK: Yes/No: If No record country of birth:

Number of years living in UK: Ethnicity:.....

Maternal Country of Origin:..... Paternal Country of Origin:.....

Languages spoken in home (underline child's main language):.....

Significant events in child's history (note changes in carer, family circumstances, deaths in family, traumas etc) Note date

Other services/agencies involved in child's care at present:

Developmental history summary (from medical notes and carer report)

Age achieved early milestones (walking, first words):

Note any reported delays/concerns:.....

Feeding/growth difficulties:.....

Hearing:..... Vision:.....

Abnormal tone:..... Epilepsy:.....

Other Developmental or behavioural difficulties/problems noted:.....

Record co-existing diagnoses – physical, neurodevelopmental, psychiatric (date confirmed):.....

P2

Educational history

School attended at present: Age started school:.....

No of previous schools:

Any concerns noted about progress at school at present or earlier:

Any other concerns (attendance, behaviour, friendships etc.)

Any additional help child receives in school:

None / school action / school action plus / statement

Describe

Results from last key stage assessments (SATS) if available School report available Yes/No

	Very poor		OK		Very good
Carer rating of child's progress at school	1	2	3	4	5
Child rating of school progress	1	2	3	4	5

P4 Carer ratings (example)

Carer ratings

Child's name & H/N:..... Date completed:.....
Completed by:
Relationship to child:

As the parent/carer of a child attending this clinic are you worried about your child in any of the following

	No concerns	A few concerns	A lot of concerns
How your child is growing	_____	_____	_____
Their appetite	_____	_____	_____
How they move (runs, jumps, climbs etc)	_____	_____	_____
Having too much energy/activity	_____	_____	_____
Having too little energy/not active enough	_____	_____	_____
How child talks or expresses themselves	_____	_____	_____
Their routines e.g. sleeping, toileting	_____	_____	_____
Feelings or mood	_____	_____	_____
Missing school because unwell	_____	_____	_____
How they're learning/keeping up with school work	_____	_____	_____
Concentration	_____	_____	_____
Their memory	_____	_____	_____
Any difficult behaviours (specify)	_____	_____	_____
How they get on with other children	_____	_____	_____

Note any other concerns you have over your child's progress:

P5 Child ratings (example)

Your name & H/N:..... Date completed:.....

Age:

As the child/young person attending this clinic are you worried / concerned about any of the following:

	No concerns	A few concerns	A lot of concerns
My health	_____	_____	_____
My medicines	_____	_____	_____
How I am growing	_____	_____	_____
My appetite/eating	_____	_____	_____
Sleeping at night	_____	_____	_____
Having energy to join in all activities	_____	_____	_____
How I am managing with school work	_____	_____	_____
Concentrating in class	_____	_____	_____
Remembering	_____	_____	_____
My feelings	_____	_____	_____
Getting on at home	_____	_____	_____
Having someone to talk to	_____	_____	_____
Getting on with friends	_____	_____	_____

Please tell us about anything else you might be worried or concerned about:

Appendix 2 B: Follow up review Form

Review sheet

- a. Check details on initial sheet (2A) are still correct
- b. Carer to rate school progress and health (see 2A)c. Completion of carer and child ratings
- d. Results from any new tests or quality of life measure carried out
- e. Feedback from previous action plan/referrals

f. **NEW events or changes since previous review:** (date of previous review:.....)

(Completed by staff and carer and child if appropriate)

- 1. *Change of child's main carer:*

- 2. *Change of home or place living:*

- 3. *Any prolonged hospital admission (details):*

- 4. *Serious Illness/Loss/Death of family member*

- 5. *Date started or changed medicine/treatment.....*

- 6. *Adherence concerns:*

- 7. *New problems and diagnoses (development or learning, physical, emotional, behaviour):*

- 8. *New referrals or services involved in care e.g. physiotherapy, dietetics, social worker, speech and language, psychologist, support group etc.*

- 9. *Changes in child's knowledge about their health & diagnosis*

- 10. *Other significant events*

Quality of life measure completed

New action plan agreed (Date:)
Action agreed Referral More detailed assessment Intervention
Date for review

Appendix 3.

Specific Assessment Tools & Interventions appropriate for different key stages

Key Stage	Functions to be screened	Examples of appropriate developmental or cognitive tests	Examples of intervention
Infancy (Less than 3 years)	Neurological Signs Sensory Functions Milestones – Motor & speech Growth & feeding	Bayley scales of Infant development (screener or full) Griffiths Mental Development scales	Referral to local services -Health Visitor -Child Development Services -SALT, Physiotherapy -Home learning e.g.Portage -Dietetic/feeding team
Pre-school (Early Years)	Neurological & Sensory Mobility Language & communication Behaviour checklist Activity & attention Self care & routines including appetite & sleep	Bayley Griffiths Specific language tests e.g. Reynell WPPSI Draw a Person Connors scale (ADD)	Referral to local services (as above) Opportunity playgroup Nursery placement Speech and Language Therapy
Primary School age	Cognitive screen Psychomotor Concentration & sustainability Attainments e.g. screen or via School Report	WASI (screener) or WISC IV WIAT or other UK Attainment tests. Draw a person Movement ABC Pedsqol or other health related quality of life measure	Referral for detailed assessment SENCO Educational Psychologist Child Development Services Disability services
Adolescent	Self report scales: quality of life, coping, mood School Report – learning & behaviour Exam results Growth & Puberty Independence Competency & understanding Mood/behaviour scale e.g. PE-ID: Paediatric Index of Emotional stress	WASI or WISC Specific tests of executive functions, memory and information processing. Pedsqol	Detailed Neuro-psychology assessment Peer group opportunities Access to CAMHS Adolescent counselling services e.g. Connexions at school/college