

## **Management of dyslipidaemia in HIV infected children: rationale for treatment algorithm**

**Authors:** Julie Lanigan, Lisa Cooke and Clare Stradling  
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### **Background**

The introduction of highly active antiretroviral therapy (HAART) for treatment of paediatric HIV infection has markedly improved survival. However, both HIV and HAART are associated with metabolic complications and increased risk of cardiovascular disease (CVD).<sup>1, 2</sup> Lipid profiles in some infected children are similar to those with familial hyperlipidemia who usually develop premature atherosclerotic disease in adulthood.<sup>3</sup>

Observational studies have demonstrated a clear correlation between lipoprotein disorders and the onset and severity of atherosclerosis in children, adolescents, and young adults.<sup>4-6</sup> Over the same time period a steep rise in obesity prevalence has led to an increase in children with dyslipidemia. HIV is recognised as a disease that is associated with moderately increased CVD risk ref. HIV and obesity can therefore be considered concomitant epidemics that increase CVD risk in children.

### **Justification**

Evidence from observational studies suggest that Identification and treatment of dyslipidaemia in HIV infected children could reduce CVD risk. In the UK, screening recommendations for paediatric hyperlipidaemia are available for children with familial hyperlipidaemia only<sup>7</sup>. Recent guidelines from the American National Heart Lung and Blood Institute recommend the use of single cut-offs to identify children with abnormal lipid and lipoprotein concentrations (Table 1)<sup>8</sup>.

**Table 1**                      **Cut Offs for Total and LDL Cholesterol Concentration in Children and Adolescents**

<b>Category</b>	<b>Acceptable (mMol/l)</b>	<b>Borderline High (mMol/l)</b>	<b>Elevated (mMol/l)</b>
TC	<4.4	4.4 - 5.2	>5.2
LDL-C	<2.8	2.8 – 3.3	>3.3
TG			
0-9 years	<0.8	0.8 – 1.1	>1.1
TG			
10-19 years	<1.0	1.0– 1.5	>1.5
HDL-C	>1.2	1.0 – 1.2	<1.0
Non-HDL-C	<3.1	3.1-3.7	>3.8

Adapted from NHLIB guidelines for children and adolescents (2011)

### **Recommendations**

Lipid screening should be routinely carried out in HIV infected children in the UK to identify children at increased risk of premature CVD. In the absence of guidelines from the UK it is recommended that cut offs identified from the US NHANES study are used. A suggested pathway for screening, based on NHLBI guidelines ref (NHLBI 2011), is described in the attached algorithm (Fig 1). It is recommended that children undergo annual dietetic review (Appendix 1 for use by dietitians), and are referred for advice on diet and lifestyle for lipid modification (Appendix 2 for use by dietitians).

Pharmacologic intervention could be considered in children  $\geq 10$  years either with severe dyslipidaemia or borderline to raised lipids and additional risk factors (Appendix 3).

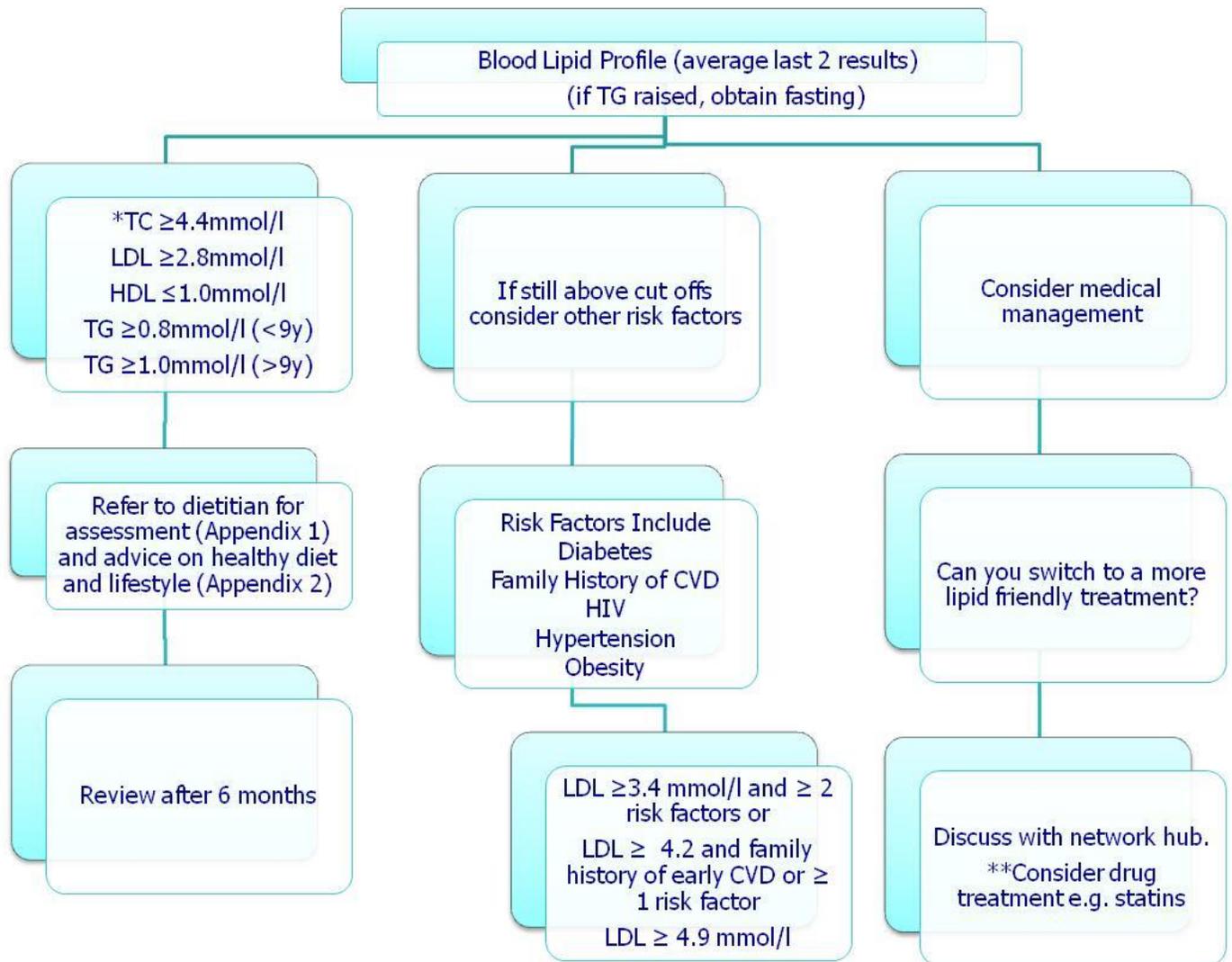
### **Dietary Advice**

Within appropriate age- and gender-based requirements for growth and nutrition, in normal children and in children with hypercholesterolemia intake of total fat can be safely limited to 30% of total calories, saturated fat intake limited to 7% to 10% of calories.

The remaining 20% of fat intake should comprise a combination of monounsaturated and polyunsaturated fats. Intake of trans fats should be limited as much as possible (AAP, 2011).

Figure 1

**Algorithm for management of HIV associated dyslipidaemia in children aged more than 2 years**



Dietetic Annual Assessment Form

<b>Name:</b>		<b>DOB:</b>		<b>Date:</b>			
<b>Age:</b>							
<b>Hospital No</b>				<b>Current Treatment:</b>			
<b>Ht (cm)</b>	<b>Wt (kg)</b>	<b>BMI</b>	<b>MUAC(cm )</b>	<b>Waist (cm)</b>	<b>Hip (cm)</b>	<b>Calf (cm)</b>	<b>Thigh (cm)</b>
<b>Centile</b>	<b>Centile</b>	<b>Centile</b>	<b>Centile</b>	<b>Centile</b>	<b>Centile</b>	<b>Centile</b>	<b>Centile</b>
<b>Skinfold (mm)</b>		<b>Triceps</b>	<b>Biceps</b>	<b>Subscapular</b>		<b>Suprailiac</b>	
1							
2							
3							
<b>Mean</b>							
<b>Lipids (mmol/l) (1 = latest; 2 = previous)</b>		<b>Date</b>	<b>Result</b>	<b>Blood Results</b>	<b>Date</b>	<b>Result</b>	
TC 1				Hb			
TC 2							
Ref: <4.4 >4.4 refer to Figure 1							
HDL 1							
HDL 2							
Ref: > 1.0 <1.0 refer to Figure 1							
LDL 1							
LDL 2							
				Hb			
				Vit D			
				Calcium			
				Alk Phosphate			
				PTH			
				CD <sub>4</sub> No. (%)			
				Viral load			
				<b>Goals and Action</b>			

Ref: <2.8  
>2.8 refer to  
**Figure 1**

**TG 1**

**TG 2**

Ref: <0.8 <9 y  
>0.8 refer to  
**Figure 1**

Ref: <1.0 >9 y  
>1.0 refer to **Figure 1**

Diet history	Diet Summary
	<b>Meat/ Fish/Pulses:</b>
	<b>Milk/dairy:</b>
	<b>Fruit/vegetables:</b>
	<b>Butter/margarine/oil:</b>
	<b>Drinks:</b>
	<b>Checklist:</b> Snacks Nuts Crisps Cakes Sweets Choc Biscuits Sweet drinks
	<b>Out of home e.g. friends/relatives/school:</b>  <b>Weekends/holidays:</b>
	<b>Exercise and physical activity:</b>
	<b>Omega 3:</b>
	<b>Nutritional supplements:</b>

## Appendix 2

### **Dietary and lifestyle recommendations for targeting lipid abnormalities.**

#### **Reducing LDL and non-HDL cholesterol levels**

Restrict proportion of total calories to:

25% to 30% from fat

≤7% from saturated fat

Replace saturated with unsaturated fats where possible

Avoid trans fats. Trans fatty acids are found mainly in processed foods including pies, pastries and meat products. Diets high in fat, and particularly those high in saturated and/or trans fats, are considered a risk factor for the development of atherosclerosis<sup>9</sup>

Consideration use of foods enriched with plant sterol/stanol esters.

Increased consumption of soluble dietary fibre (present in fruits, vegetables and pulses (peas, bean and lentils)).

#### **Reducing triglyceride levels**

- Restrict proportion of total calories to:

25% to 30% from fat

≤7% from saturated fat

Preferred use of mono and polyunsaturated fats

Avoidance of trans fats

Increased consumption of soluble dietary fibre

Decrease sugar intake, particularly sugar sweetened drinks

Include foods high in n-3 (omega 3) fatty acids. Long chain n-3 fatty acids, in particular docosahexaenoic and eicosapentanoic acids found in high concentrations in fish have been shown to reduce triglyceride concentrations in many studies. Fish oils have repeatedly been shown to reduce plasma TG in a dose-dependent manner<sup>10</sup>.

#### **Increasing HDL-C**

Increase soluble fibre intake (fruits, vegetables, pulses (peas/beans/lentils))

Assess and advise on appropriate exercise and physical activity levels

For age specific guidance see link below

[http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_127931](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_127931)

For further information see table 9.8 NLHBI 2011

[http://www.nhlbi.nih.gov/guidelines/cvd\\_ped/](http://www.nhlbi.nih.gov/guidelines/cvd_ped/)

## Appendix 3

### Recommendations Regarding Drug Therapy for Children and Adolescents.

1. Measure and average values from the 2 most recent lipid profiles.
2. Consider changing to a more lipid friendly antiretroviral therapy if above cut offs.
3. Consider medical management under the following circumstances:

- Clinical CVD.
  - LDL-C  $\geq 4.90$  mmol/L (non-HDL-C  $\geq 5.30$  mmol/L)
  - LDL-C 4.15-4.89 mmol/L (non-HDL-C 4.50-5.29 mmol/L) and either positive family history of early CVD, or  $\geq 1$  CVD risk factors
  - LDL-C 3.35-4.14 mmol/L (non-HDL-C 3.75-4.49 mmol/L) and  $\geq 2$  risk factors
- (NB if triglycerides  $> 2.25$  mmol/L, may use non-HDL-C cut offs)

#### Risk factors include:

Hypertension requiring drug therapy (BP  $> 99^{\text{th}}$  percentile + 5mm Hg)

Passive smoke exposure or current smoker

BMI  $> 95^{\text{th}}$  percentile

Diabetes (Type I or II).

HIV, CKD, nephrotic syndrome, postorthotopic heart transplant, Kawasaki disease

The choice of statin is a matter of preference. Start with the lowest dose, monitor for adverse effects, and titrate the dose upwards if therapeutic targets are not achieved.

#### Therapeutic target:

Minimal: LDL-C  $< 3.35$  mmol/L (non-HDL-C  $< 3.75$  mmol/L)

Ideal: LDL-C  $< 2.85$  mmol/L (non-HDL-C  $< 3.25$  mmol/L)

If LDL-C remains  $\geq 3.35$  mmol/L after a sufficient trial of a statin, and TG  $< 2.25$  mmol/L, consideration may be given to adding a bile acid sequestrant or cholesterol absorption inhibitor.

In high LDL-C patients, if non-HDL-C remains  $\geq 3.75$  mmol/L after effective LDL-C treatment then target therapy towards reducing triglycerides, by adding a fibrate or nicotinic acid. This should be done in consultation with a lipid specialist.

**Abbreviations:** CVD, cardiovascular disease; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; RF/RC, risk factor/risk condition

## Reference List

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