# Guidelines for Management of Hyperlipidaemia in Children with Renal Disease

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*DISCLAIMER: These guidelines were produced in good faith by the author(s) in conjunction with the paediatric nephrology team at the University Hospital of Wales, Cardiff reviewing available evidence/opinion. They were designed for use by paediatric nephrologists at the University Hospital of Wales, Cardiff for children under their care. They are neither policies nor protocols but are intended to serve only as guidelines. They are not intended to replace clinical judgment or dictate care of individual patients. Responsibility and decision-making (including checking drug doses) for a specific patient lie with the physician and staff caring for that particular patient.*

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**Summary**
These guidelines are aimed at providing the doctors presented with a child with hyperlipidaemia in association with renal disease with information to help identify the underlying problem and to guide treatment.

## Introduction

Dyslipidaemia is a feature of a number of the renal diseases with which children can present and this can be exacerbated by other factors such as obesity. Dyslipidaemia in turn has a role in the development of atherosclerotic vascular disease which can have its origins in childhood. Unfortunately there is little evidence in the paediatric population on which to base guidelines on the management of dyslipidaemia and extrapolations have to be made from adult data. The American Academy of Pediatrics (AAP) have released a clinical report in July 2008 that replaces the 1998 AAP policy statement on cholesterol in childhood, which focuses on improving childhood and adolescent lipid and lipoprotein concentrations to lower the lifetime risk of cardiovascular disease (Daniels 2008).

The components of lipid metabolism which we are interested in are:

- Low-density lipoprotein (LDL) is one of the lipoproteins which enable transport of lipids like cholesterol and triglycerides within the water-based bloodstream. Blood tests typically report LDL-C, the amount of cholesterol contained in LDL. In practise the terms LDL & LDL-C are used interchangeably.
- High-density lipoprotein (HDL) which is the smallest of the lipoproteins and in healthy individuals carries about thirty percent of blood cholesterol. It has become known as "good cholesterol", as those with higher levels of HDL-C seem to have fewer problems with cardiovascular diseases.
- Triglycerides (TG) are esters derived from glycerol and three fatty acids. They are the main constituent of vegetable oil and animal fats. Triglycerides, as major components of very-low-density lipoprotein (VLDL) and chylomicrons, play an important role in metabolism as energy sources and transporters of dietary fat. High levels of triglycerides in the bloodstream have been linked to atherosclerosis and, by extension, the risk of heart disease and stroke. However, the relative negative impact of raised levels of triglycerides compared to that of LDL:HDL ratios is as yet unknown. The risk can be partly accounted for by a strong inverse relationship between triglyceride level and HDL-cholesterol level.

## Conditions carrying a risk of dyslipidaemia:

- Chronic renal failure
- Nephrotic syndrome
- Renal transplants

## Monitoring

LDL can be measured in random blood sample while TGs should be measured with a fasting blood specimen (at least 6 hours). However, problems in LDL results occur when TG levels are high as the result we get for LDL is a calculated one using the equation:

LDL = Total Chol – HDL – (Triglyceride/2.2)

Therefore if TG level > 2 mmol/l, the LDL assessment should also be carried out on a fasting blood sample.
Therefore, in the first instance, measure LDL and TG on non-fasting specimen and repeat at next visit, fasting, if TG > 2 mmol/l. If TG ≤ 2 mmol/l on non-fasting blood then you can accept this result.

**Recommended frequency of measurement:**

| **Disease state** | **LDL** | **TGs** |
|---|---|---|
| CKD Stage 2 & 3 | Annually | Annually |
| CKD Stage 4 & 5 | 6 monthly | 6 monthly |
| Steroid resistant nephrotic syndrome | 6 monthly | 6 monthly |
| Renal transplants on ciclosporin | 6 monthly | 6 monthly |
| Renal transplants on tacrolimus | Annually | Annually |

## Management

Regarding raised LDL levels:

- Check thyroid function particularly in nephrotics as hypothyroidism can cause hyperlipidaemia.
- If LDL > 3.4 mmol/l then request dietary assessment to ensure that lipid intake not excessive.
- If LDL > 4.1 mmol/l start a statin, with 4.1 mmol/l the target level. If 10y or over use Atorvastatin; if under 10y use Simvastatin.

Neither Atorvastatin nor Simvastatin are licensed for use in children under 10 years.

**Dosing according to BNF for Children:**

Simvastatin
Child 1-5 years: Initially 5 mg at night, increased if necessary, at intervals of at least 4 weeks to max. 10 mg at night.
Child 5–10 years: Initially 10 mg at night increased, if necessary, at intervals of at least 4 weeks to max. 20 mg at night.
Reduced dose required with concomitant ciclosporin, danazol, fibrates (except fenofibrate), amiodarone, diltiazem, or verapamil.

Atorvastatin
Child 10–18 years: Initially 10 mg once daily, increased if necessary at intervals of at least 4 weeks to usual max. 20 mg once daily (max. 80 mg once daily in homozygous familial hypercholesterolaemia)
Reduced dose required with concomitant ciclosporin, clarithromycin, or itraconazole

**Monitoring**

NICE guidelines suggest that liver enzymes should be measured before treatment with simvastatin or atorvastatin, and repeated within 3 months and at 12 months of starting treatment, unless indicated at other times by signs or symptoms suggestive of hepatotoxicity. CPK should be checked at the same time or if muscle symptoms occur.
There are particular concerns about the risk of myositis when statins are used alongside ciclosporin. Myositis can develop years after starting statins. Patients /families should be asked to seek advice if symptoms develop.

Ezetimibe can be added if target level of 4.1 mmol/l not reached after 6 months of maximum statin therapy. If ezetimibe is used in combination with a statin, there is an increased risk of rhabdomyolysis and liver dysfunction.
Ezetimibe dosing according to BNF for Children:
Child 10–18 years: 10 mg once daily

**Regarding raised triglyceride levels:**

- If fasting TG level > 10 mmol/l firstly ensure any acidosis corrected (Mak 1999). If it remains > 10 mmol/l then start Maxepa.

If can take tablets:
Omacor® (Abbott Healthcare)
Capsules, 1 g of omega-3-acid ethyl esters 90 containing eicosapentaenoic acid 460 mg and docosahexaenoic acid 380 mg.
Adult Dose 2 capsules daily with food, increased if necessary to 4 capsules daily
Suggest if child under 10 years can take a capsule, then administer 1 capsule daily.

If require liquid preparation:
Maxepa® (Seven Seas)
Liquid, golden-coloured, concentrated fish oils containing eicosapentaenoic acid 170 mg, docosahexaenoic acid 115 mg/g (1.1 mL). Vitamin A content less than 100 units/g, vitamin D content less than 10 units/g.
Adult Dose 5 mL twice daily with food
Due to unpleasant taste, only really able to give if child receiving tube feeds.

Suggested dosing regime:

| | |
|---|---|
| Under 10 kg | 2 mls in feed |
| 10-20 kgs | 4 mls in feed |
| 20-30 kg | 6 mls in feed |
| 30-50 kg | 8 mls in feed |
| > 50 kg | 10 mls in feed |

**References**

Daniels SR, Greer FR and the Committee on Nutrition. Lipid Screening and Cardiovascular Health in Childhood. Pediatrics 2008; 122: 198–208.

Mak RHK. Effect of metabolic acidosis on hyperlipidemia in uremia. Pediatr Nephrol (1999) 13: 891–893.

**Flow chart for management of hyperlipidaemia.**