Lipoprotein Apheresis

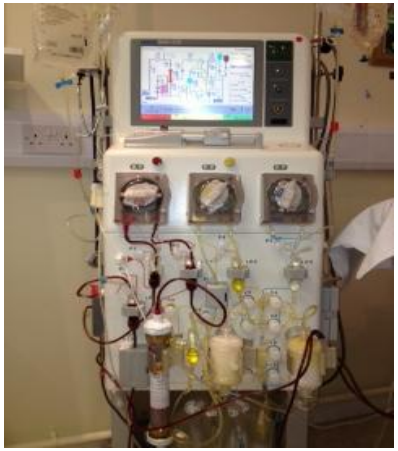
Dev Datta
Consultant in Biochemistry& Metabolic Medicine
Clinical Lead, Cardiff Lipid Unit
Medical Advisor, FH Wales Cascade Testing Service

FH WALES
Familial Hypercholesterolaemia

NHS WALES GIG CYMRU

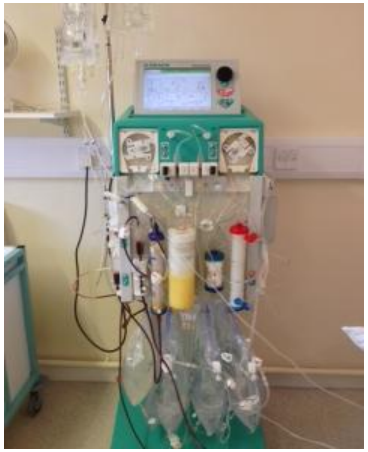
What is lipoprotein apheresis?

FRESENIUS MEDICAL CARE
DALI



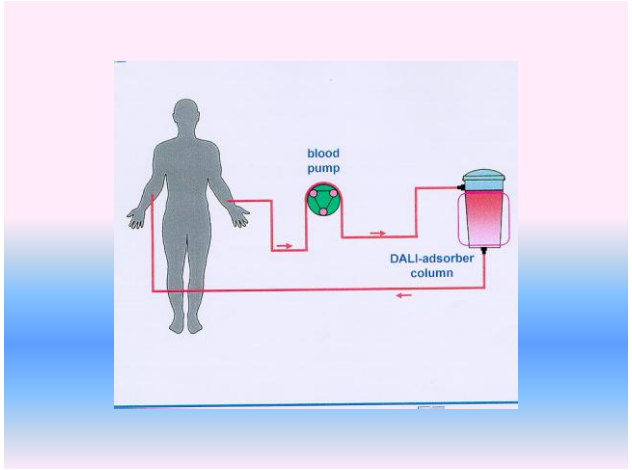
KANEKA PHARMA
CELL SEPERATOR LA 15

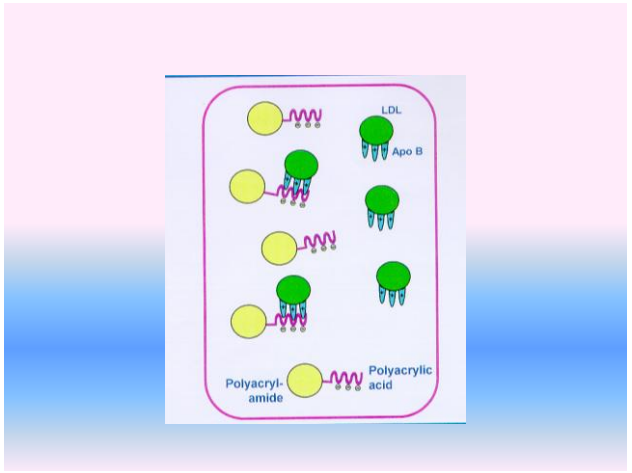
KANEKA PHARMA
WHOLE BLOOD DLP 100



B BRAUN AVITUM
HELP

LINC MEDCIAL HF440



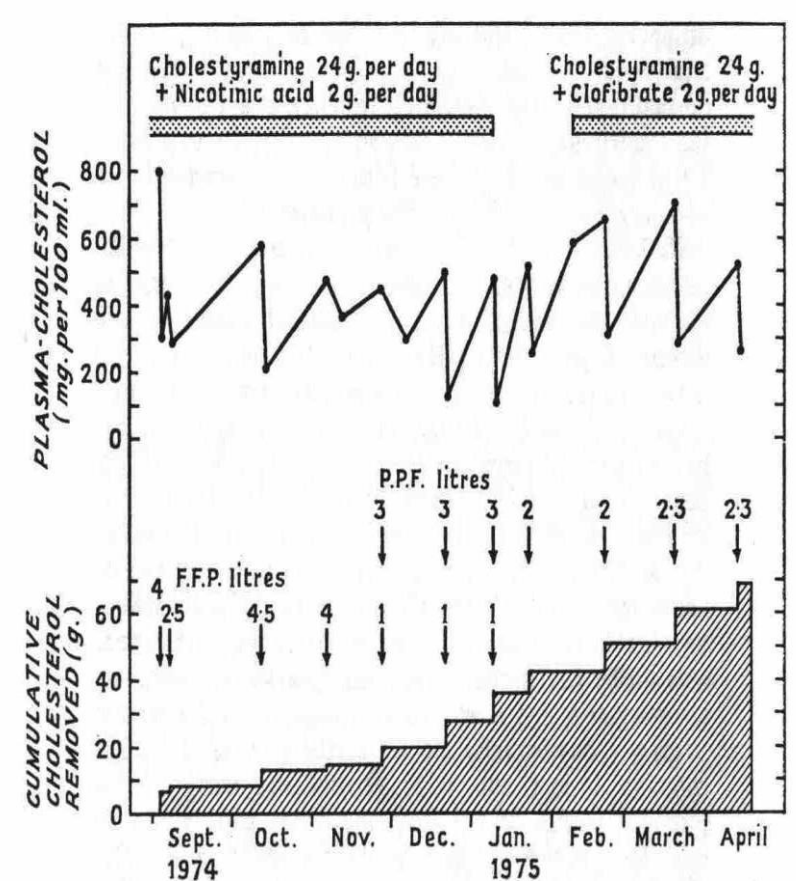


PLASMA EXCHANGE IN THE MANAGEMENT OF HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLÆMIA

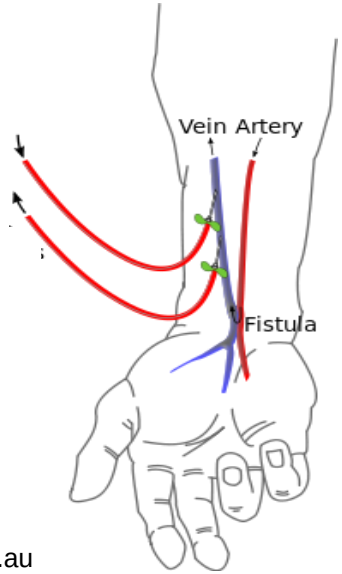
G. R. THOMPSON R. LOWENTHAL
N. B. MYANT

Departments of Medicine and Hæmatology, Royal Postgraduate Medical School, and Medical Research Council Lipid Metabolism Unit, Hammersmith Hospital, London W12 0HS

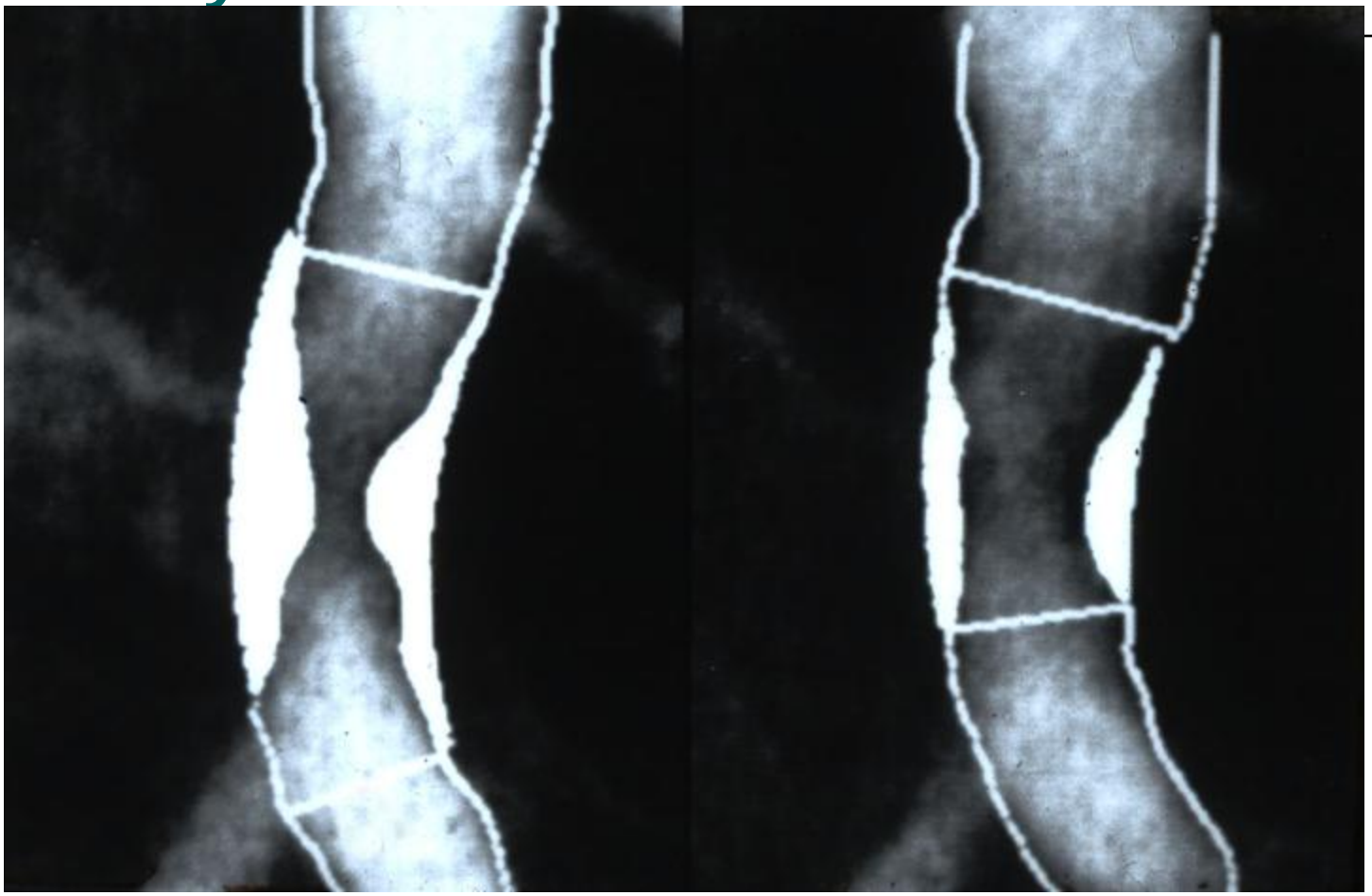
THE LANCET, MAY 31, 1975



How to treat

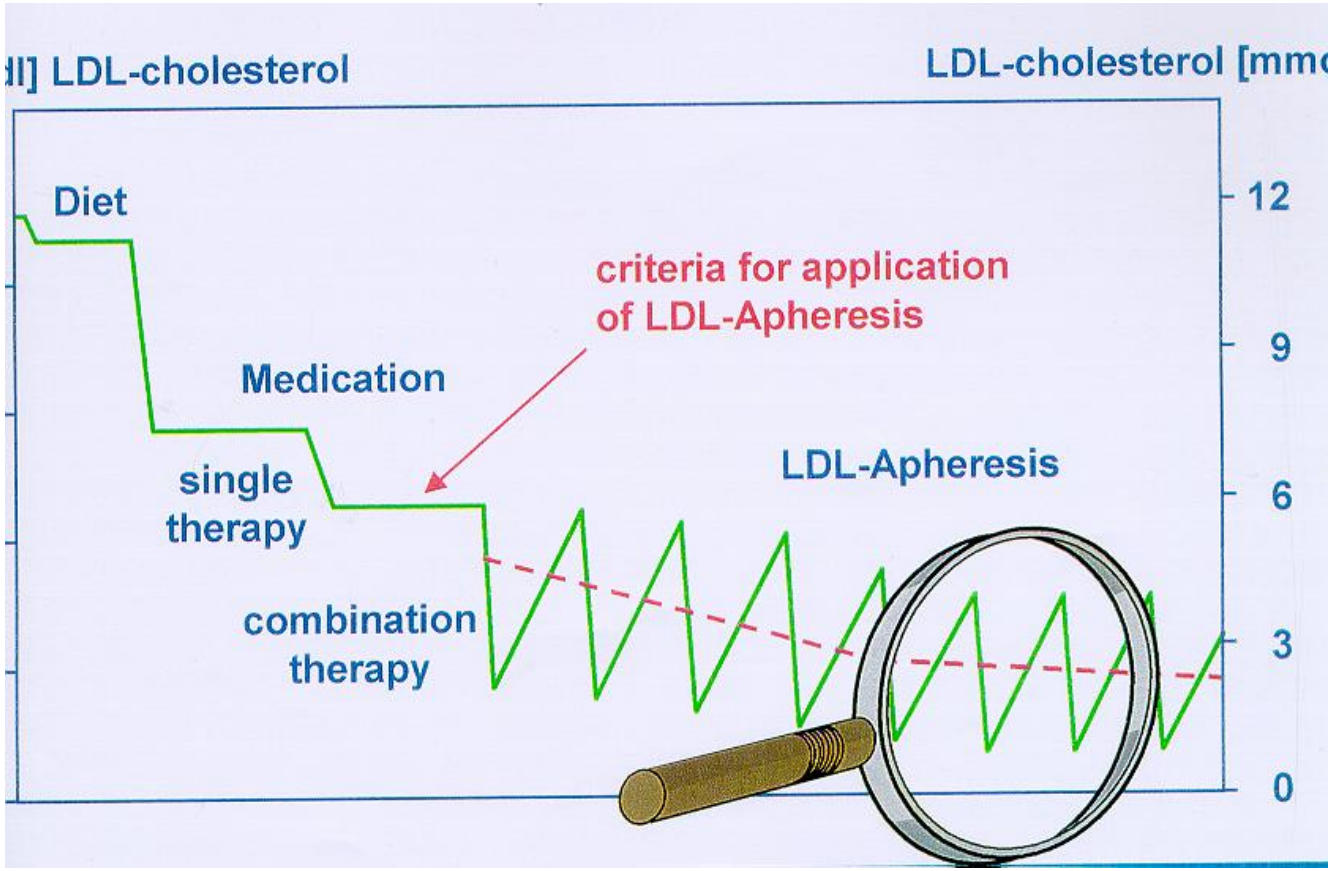


Why to treat



Quantitative coronary angiograms pre- and post- apheresis plus lovastatin for 18 months (Barbir et al, 1989) Courtesy of Prof. Gil Thompson

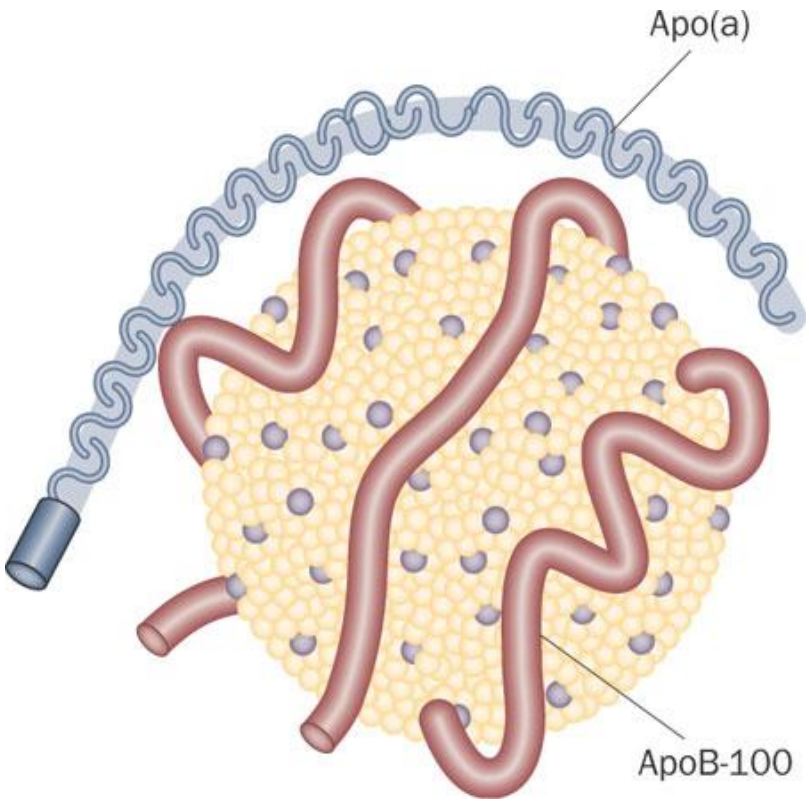
Treatment efficacy- lipids



Other Efficacy Data

- *Improved regional myocardial perfusion* Aengevaeren et al (1996)
- *72% reduction in coronary events* Mabuchi et al (1998)
- *MACE reduction from 7.02% per patient p.a. to 1.17%* Koziolek et al (2009)

Lp(a)



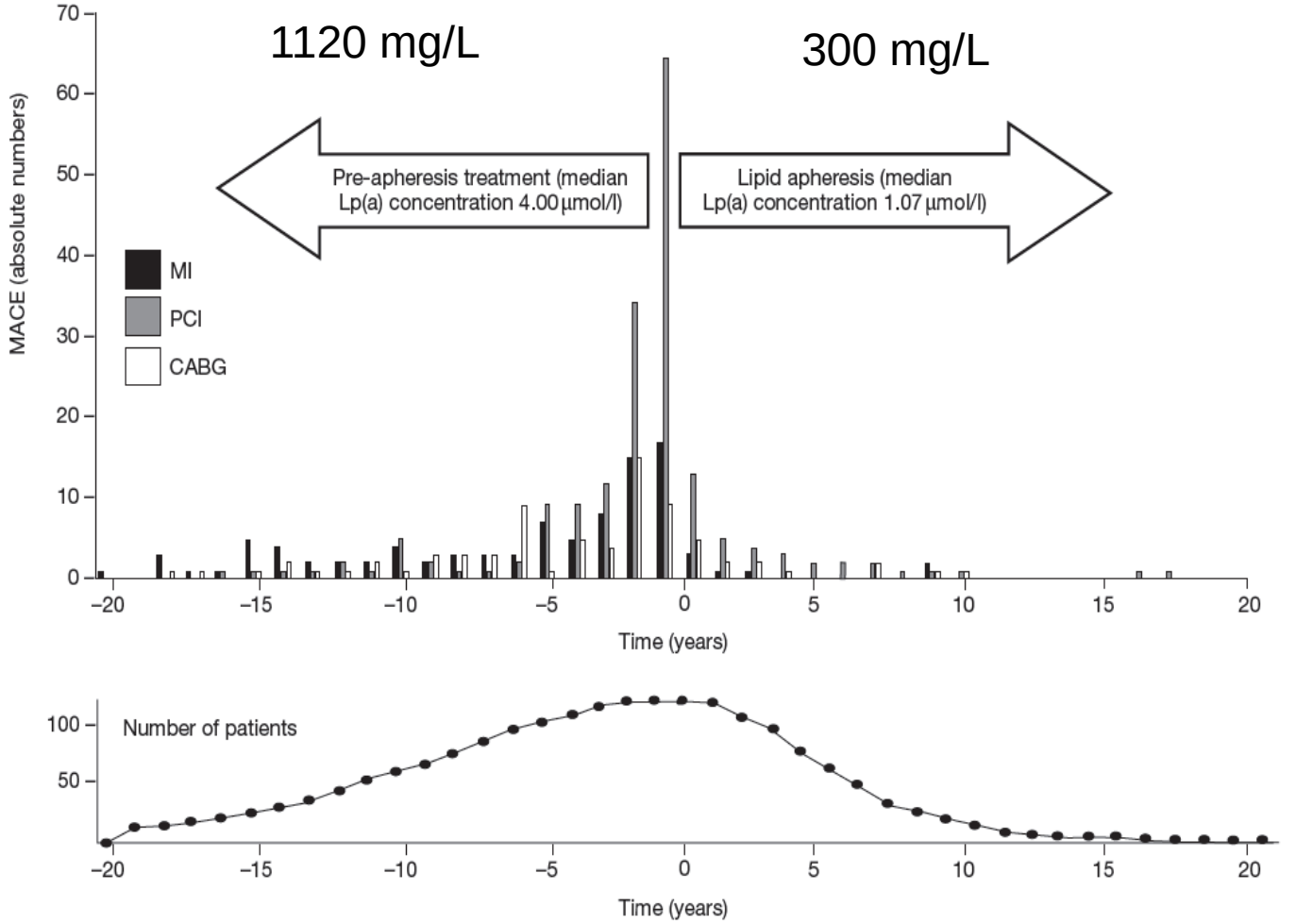


Figure 1 Absolute numbers of major adverse coronary events during lipid-lowering medication alone and during combined lipid-lowering medication and lipid apheresis. Timepoint zero corresponds with the beginning of apheresis treatment for each patient. Since individual observation times varied, the number of patients studied for each year is shown in the lower panel. Abbreviations: CAD, coronary artery disease; Lp(a), lipoprotein(a); MACE, major adverse coronary events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Jaeger BR et al, 2008, Nature Clinical Practice Cardiovascular Medicine

Who to treat

- ** currently aged 50
- HeFH (LDL R c.2042G>C)
- CABG aged 34
- L femoral angioplasty aged 37
- Referred for apheresis aged 45
- Atorvastatin 80mg
- Ezetimibe 10mg
- Fenofibrate 160mg

DALI apheresis

- At referral 2008

- TC 7.3 mmol/L
- cLDL 5.9 mmol/L
- HDL 0.7 mmol/L
- Lp(a) 2219 mg/L

- Mean values pre treatment 2013

- TC 5.8 mmol/L
- cLDL 4.2 mmol/L
- HDL 0.9 mmol/L
- Lp(a) 1485 mg/L

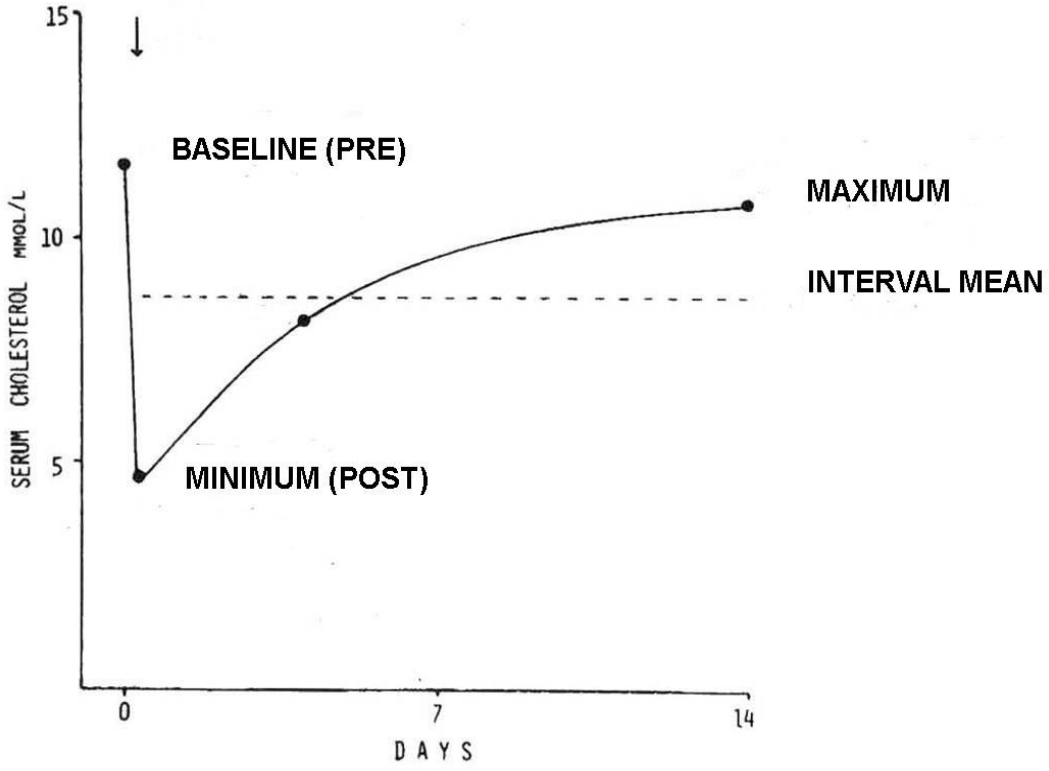
- Mean values post treatment 2013

- TC 2.7 mmol/L (55%)
- cLDL 1.5 mmol/L (63%)
- HDL 0.7 mmol/L
- Lp(a) 827 mg/L (44%)

- Interval mean values 2013

- TC 4.7 mmol/L
- LDL 3.3 mmol/L

Interval mean



Who to treat- 2

- 60 year old lady
- Genotype proven FH
- CABG 2011
- Long history of intolerance to statin based lipid lowering regimes
- Trial of Evolucumab

- Atorvastatin 10 mg once per fortnight
- Colesevalam 1.25g TDS
- Bezafibrate MR 400 mg OD

- Cholesterol 9.7 mmol/L
- Apo B 1.82 g/L
- Apol A1 1.14 g/L
- Lp(a) 94 mg/L

Current Guidance

- All FH homozygotes from the age of seven onwards unless their serum cholesterol can be reduced by >50% and/or decreased to ≤9 mmol/l by drug therapy
- Individual patients with either heterozygous FH or a bad family history of premature cardiac death whose coronary disease progresses and where LDL cholesterol remains >5.0 mmol/l or is decreased by <40% with maximal drug therapy. Apheresis may also occasionally be indicated on a case-by-case basis for patients with lower levels of LDL
- LDL apheresis should also be considered for patients with aggressive progressing coronary disease and Lp(a) > 600 mg/l whose LDL cholesterol remains >3.2 mmol/l despite maximal drug therapy.

Thompson, GR et al, Recommendations for the use of LDL apheresis Atherosclerosis 198 (2008): 247-255

NICE guidance for apheresis in HeFH

- " In exceptional instances (such as when there is progressive, symptomatic coronary heart disease, despite maximal tolerated lipid-modifying drug therapy and optimal medical and surgical therapy), healthcare professionals should consider offering LDL apheresis for the treatment of people with heterozygous FH. This should take place in a specialist centre on a case-by-case basis and data recorded in an appropriate registry."

Current Challenges

- Knowledge of apheresis in lipid clinics
- Access to treatment in UK & geographical variation
- Germany 1.2 per 100 000
- North America 0.13 per 100 000
- UK 0.06 per 100 000
- Establishing new patients on treatment
- Justifying ongoing funding

Problems and Costs

- Time and travel
- Nausea, hypotension, bradykinin, angina
- Iron deficiency, electrolyte problems
- Venous access problems
- Cost


The Future
NEXT EXIT

Summary

- Lipoprotein apheresis is an established, effective and well-tolerated treatment for HoFH and HeFH refractory to standard treatment
- Logistical and cost constraints are the main barriers
- Newer drug therapies may reduce the requirement for apheresis in the future

Acknowledgements

- Prof Gil Thompson
- Suzanne Watkins

www.cardiffandvaleuhb.wales.nhs.uk/lipidunit
www.fhwales.co.uk

dev.datta@wales.nhs.uk

FH WALES
Familial Hypercholesterolaemia

NHS WALES GIG CYMRU