Management of steroid resistant nephrotic syndrome remains a clinical challenge. The clinician has to balance toxicity of medications and unknown long term prognosis. The patients’ response to initial steroid treatment appears to be the best predictor of disease progression. In long term cohort studies of children and adults with primary FSGS renal survival has been directly associated with degree of proteinuria control. Focal segmental glomerulosclerosis (FSGS) is a histologic finding that may result from a variety of insults. The Malaysian Registry of Renal Biopsy reported that FSGS is the histological finding in 25% of renal biopsies in our children over the period 1998 – 2008. FSGS contributed 8% of Malaysian children on dialysis. The lecture focuses on current therapeutic approach toward children with primary FSGS. Therapy of FSGS incorporates conservative and immunosuppressive protocols to control proteinuria.

Corticosteroids
Corticosteroids have been the mainstay of treatment for childhood nephrotic syndrome regardless of its aetiology. A response to corticosteroid is generally consistent with a more favourable response. Corticosteroids remain a key component of many therapeutic regimens for FSGS usually in various combinations with other drugs. A few paediatric protocols have advocated high doses of intravenous methylprednisolone with varying degree of success.

Cyclosporine A
Cyclosporine A and Tacrolimus are both potent calcineurin inhibitors. Activated T cells produce lymphokines such as interleukin 2 that mediate glomerular basement damage. Cyclosporin A acts by preventing full activation of T helper cells. A major concern is the potential for nephrotoxicity. A second concern is the high relapse rate after drug withdrawal.

Tacrolimus
The newer and more potent tacrolimus have been shown in anecdotal reports to have favourable responses in the treatment of children with FSGS. One retrospective study of 16 patients including 13 children with biopsy proven FSGS documented reduction in protein excretion. There were two small prospective studies that also showed a positive response.

Mycophenolate mofetil
Mycophenolate mofetil (MMF) was initially introduced in the 1990s as an immunosuppressive agent for organ transplantation. MMF blocks de novo synthesis of both T and B cell lymphocytes through non-competitive reversible inhibition of the enzyme inosine monophosphate dehydrogenase. Choi et al reported 18 children with FSGS with statistically significant decrease in proteinuria in patients receiving MMF. Catran et al reported an open label 6 month trial of MMF in 18 patients with FSGS. All had received various combination of therapy previously. Four out of 18 maintained complete remission. MMF is showing early promise as a steroid sparing therapy but questions remained about length of therapy and long term malignancy risk. MMF is also potentially teratogenic.

Plasmapheresis
Plasmapheresis has been considered as a rescue option. The rationale for its use is for the removal of circulating factor from the plasma that alters glomerular barrier function. It is an invasive procedure with significant risks of hypocalcaemia, infection and bleeding.
Rituximab
Current concepts indicate that not only T cells but B cells are actively involved in the pathogenesis of FSGS. A number of case reports on the use of rituximab on a selected group of children with complicated nephrotic syndrome. Rituximab is a chimeric monoclonal antibody inhibiting CD 20 mediated B cell proliferation and differentiation. All children remained on concomitant treatment with prednisolone and or calcineurin inhibitors. The overall report is rather promising but one must be aware of publication bias as only positive outcome would be reported.
Progress in this therapeutic field remains a priority in an attempt to normalize protein excretion so as to prevent renal failure. The search continues for successful regimens with minimal toxicity.