Dealing With Your Mental Health – Managing Hepatitis C, Symptoms And Treatment

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- **Brisbane 2009**

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Summary

- The psychiatric screening program prior to interferon treatment for Hepatitis C at the Princess Alexandra Hospital, Brisbane
- 1 liaison psychiatrist (funded)
- Background and evidence base
- What happens on the ground
- Disclaimer: Haemophilia and Hepatitis C co-morbidity tends not to be managed at this site

The Scale Of The Problem

- Up to 85-90% of patients with bleeding disorders treated with plasma derived clotting factors have been exposed to HCV prior to routine testing in 1990
- Many exposed as children or teenagers
- Sometimes multiple members of family affected
- Most keep their infection a secret because of stigma
- Those suffering alone found it helpful to read about others' experiences

Hepatitis C virus

- 6 genotypes (1a and 1b most common)
- Modes transmission: shared needles IV drug use (80%), reused tattooing needles, transfusions(prior to routine screening), sexual (less common – 3%)
- 278,000 antibody positive in Australia (10,000 new cases/ year)
- 75% develop chronic infection (235,000 in Australia)
- Of these, 60% develop chronic hepatitis
- Of these, 4-20% develop cirrhosis (20 years), 2-5% develop hepatocellular carcinoma (30 years) <*The Silent Killer*>
- Factors affecting disease progression: Age of acquisition, gender, host genetics/ethnicity, steatosis/insulin resistance, alcohol, cannabis, cigarettes, immunosuppression, coexisting hemochromatosis, HBV, HIV
- Interferon therapy produces sustained viral eradication in 45-95% (depending on genotype, viral load and drug adherence) Note: *Small Australian study(2009) Hemophilia/HCV/HIV 1/13: 8%**
- Pegylated interferon reduces frequency of injection to once/week. Cost: $1400/week: Commonwealth now funds re-treatment
- **Denholm et al(2009) Hemophilia, 15:538-543*

The Issue Of Public Stigma

- Pamela Anderson
- Steven Tyler
- Chopper Read
- Natalie Cole

Dave

- 40 y.o. casual labourer living with girlfriend
- HCV genotype 1 diagnosed 12 months ago, LFTs normal
- Adopted out at birth – biological mother suffered with depression and had several suicide attempts
- Poor relationship with adoptive parents – described father as physically abusive
- Ran away from home age 15, lived on the streets, forensic offences to support illicit drug use – heroin, amphetamines, cannabis
- Chronic affective instability – history of assaults on others, especially during a total of 2 years of incarceration in juvenile and adult prison facilities
- No history of homicide, no past suicide attempts
- Life stabilised 12 months ago in setting of 6 month inpatient rehab
- Last used drugs 12 months ago, steady job of 6 months, stable relationship of 3 months
- Current mood state euthymic

James

- Born in 1970 with genetically inherited haemophilia
- Teased by schoolmates for constant bruising
- Received plasma derived clotting factors as a child and adolescent (prior to introduction of recombinant factors)
- 1984 – Diagnosed with HIV (window 1981-1984)
- 1990 – Hepatitis C chronic infection picked up (testing introduced Australia 1990)
- Has had difficulty with sustained employment because of need to take time off for medical appointments
- Has noticed subtle discrimination by GPs and health workers
- Some failed relationships after revealing infection status prior to meeting current partner
- Unable to get life insurance

Psychological themes with IVDU acquired HCV sufferers

- Correlates with vulnerability factors associated with IV drug use, commonest mode of infection
- Developmental vulnerability psychologically
- Biological predisposition to depression (drug related or self mood modulation?)
- A period of life instability (often associated with drug use – existential life crisis, drug-using peer group)
- Some stabilisation of life situation promoting help-seeking (jail, internally motivated life change)

Psychological themes with transfusion acquired HCV sufferers

- “The double whammy”
- Haemophilia, HCV ± HIV (*poor treatment response, earlier disease progression)*
- “The quadruple whammy”
- The stigma of infection – community attitudes, prospective relationship partners, employers, life insurance.
- The anger and frustration of non-validation of fault by the health system

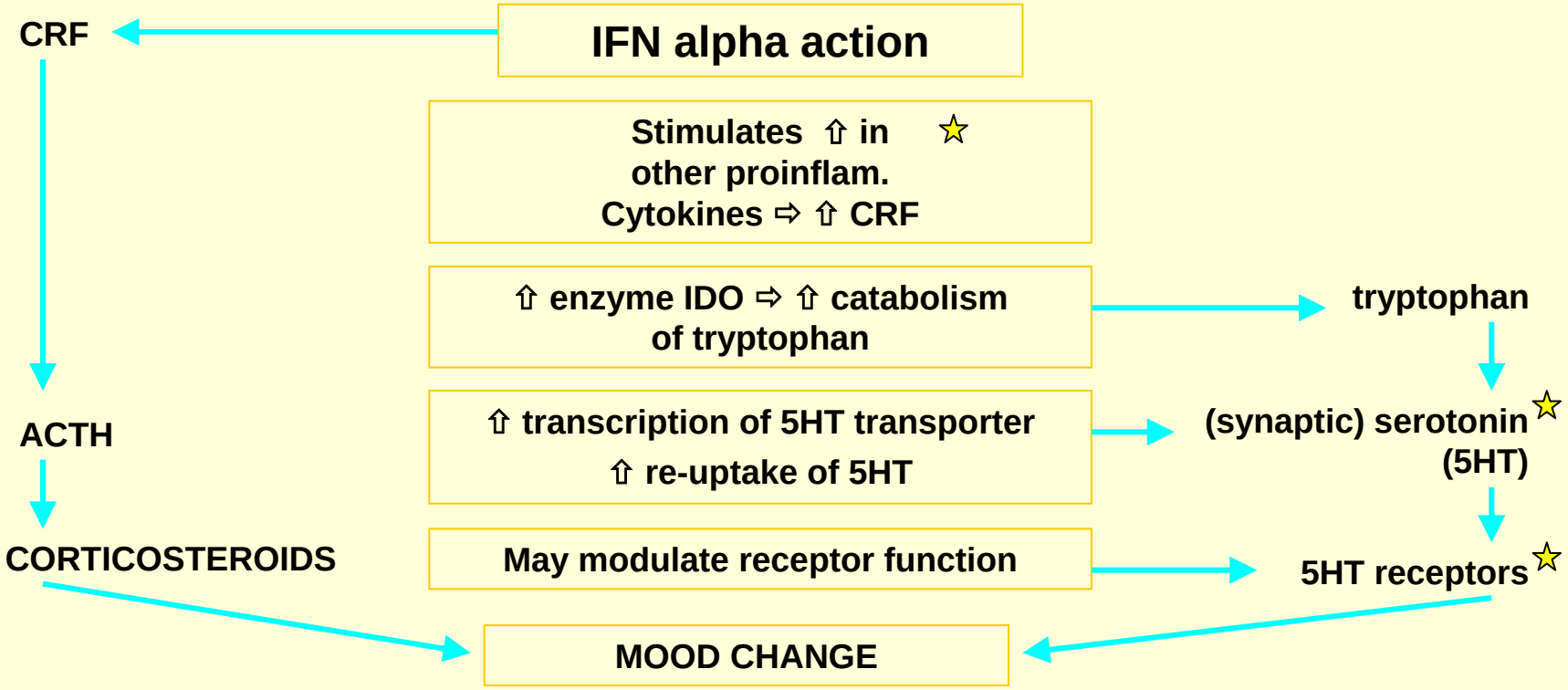
Neurocognitive deficits with HCV infection

- HCV – RNA virus that crosses blood-brain barrier in infected lymphocytes
- Infects macrophages and glial cells causing release of neurotoxic cytokines leading to neuronal death
- Clinical picture of subcortical cognitive impairment (problems with motivation, apathy, impaired executive functions and working memory) thought to be due prefrontal hypometabolism and damage to the hippocampus.

Cytokines and depression

- Interferon – class of pro-inflammatory cytokines, immunoregulatory
- Depression is thought to be due to:
- 1) induction of or amplification of other cytokines, interleukins (IL), IFN-gamma and tumour necrosis factor (TNF),
- 2) reduction in serotonin levels by inducing the enzyme responsible for metabolising tryptophan and 5HT and
- 3) altered HPA by the IFN altered activity of IL-6.
- Effects akin to major depressive disorder i.e. anhedonia, fatigue, listlessness, poor memory, sleep and appetite disturbance.

PROPOSED MECHANISMS OF AETIOLOGY

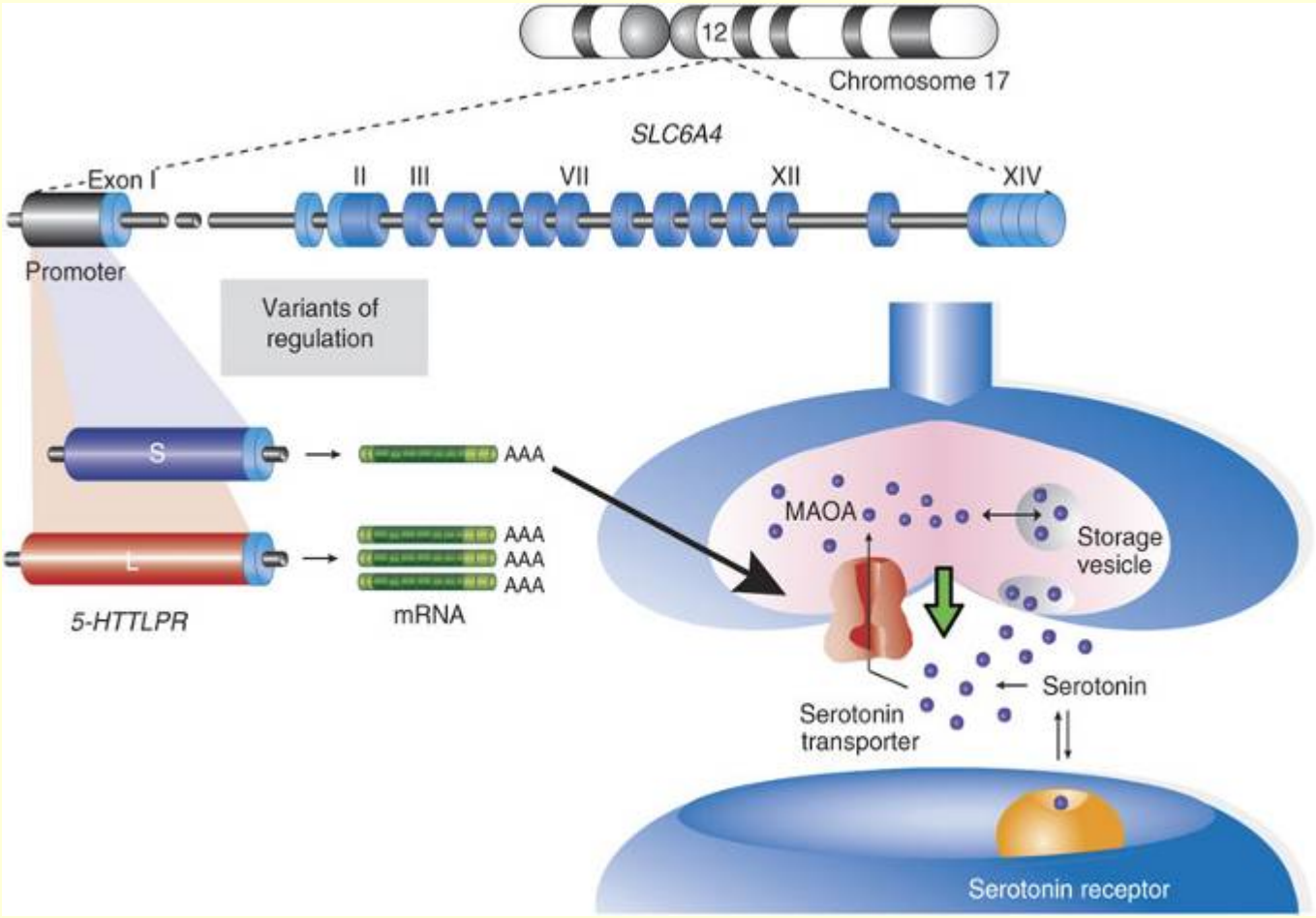


☆ points of action of antidepressants

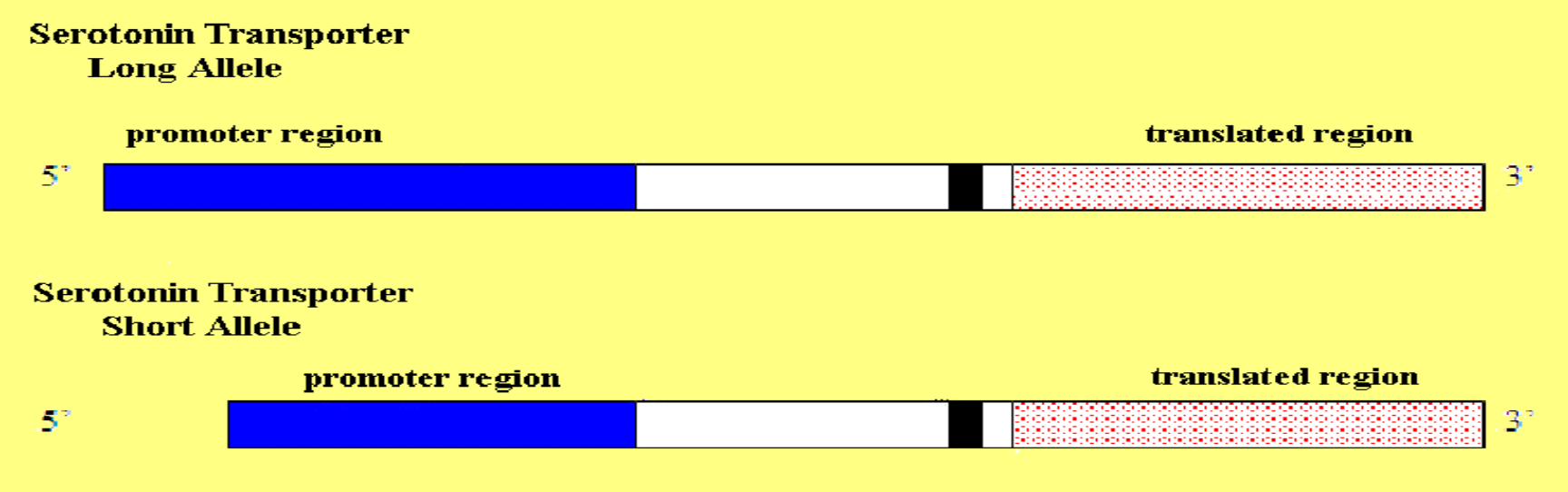
Wichers and Maes. Mechanisms of IFN alpha induced depressive symptoms.

Acta Neuropsychiatrica, 2002: 12: 103 - 105

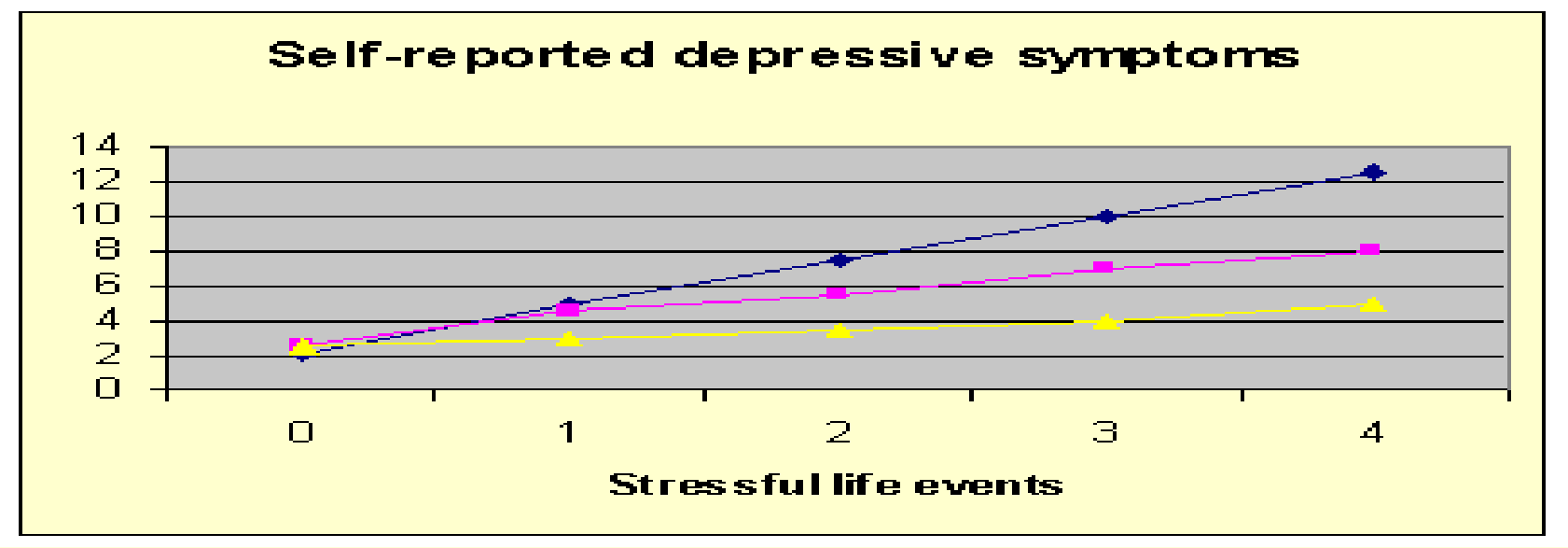
Amount of serotonin transporter protein depends on promoter



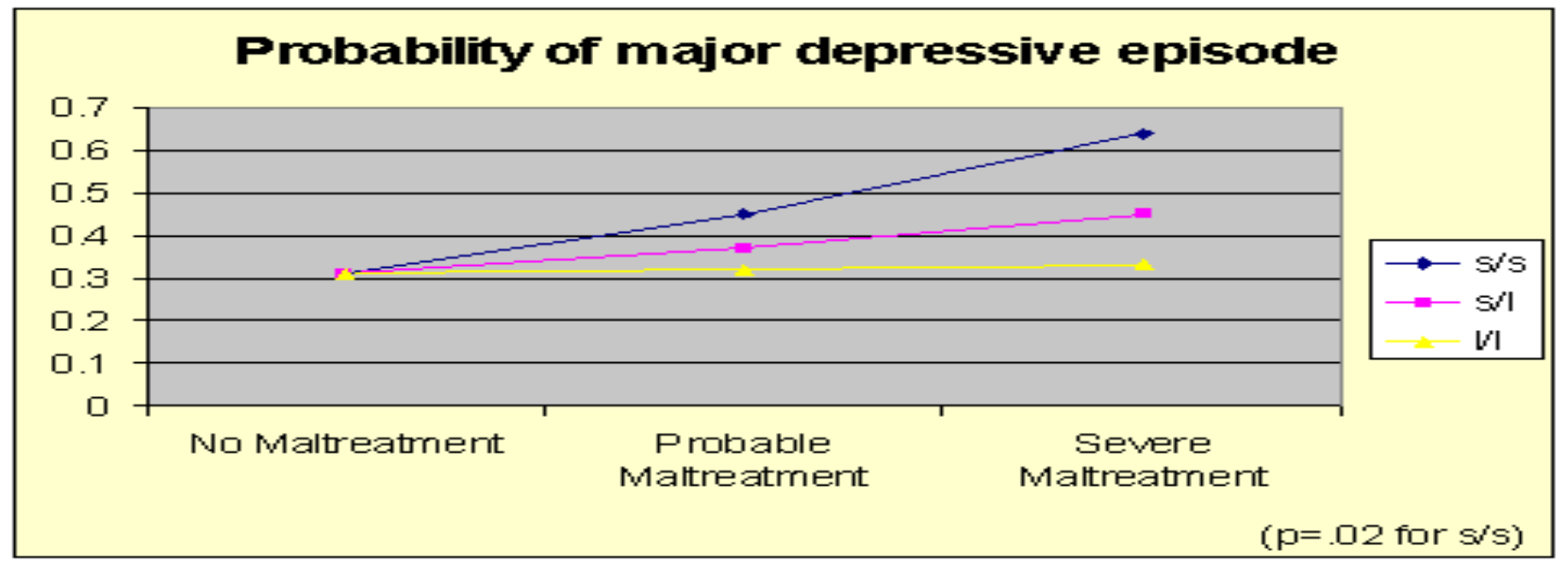
Vulnerable patients have a shorter promoter region



Having 2 short allelles increases ones vulnerability to life events



Childhood abuse interacts with biology – vulnerable vs resilient kids



How common is interferon depression?

- 15-60% in various studies (Note: 2009 Dutch study documented rate of 60% in hemophilia HCV comorbidity)
- Variance across studies may reflect different dosing schedules, different compositions of study cohorts, and different instruments measuring depression
- Ribavirin may confer increased risk (especially irritable depression)
- Predictive factor 1: Baseline high depressive scores
- Casera et al (2002) n=33 *Hepatology,35(4):978-979.*
- Baseline MADRS score <3, no depressive symptoms
- Baseline MADRS score >15, 42% depressive symptoms. Significantly higher MADRS
- Predictive factor 2: Baseline sleep disturbance
- Lotrich et al (2008) Biological Psychiatry

Interferon-related depression- The case for a unique depressive subtype

- Standard risk factors not seen e.g. equal incidence male:female
- 75% of these depressions occur in the first 8 weeks of interferon treatment
- Serotonergic deficit? (SSRIs)
- More treatment responsive (80%)
- More rapidly responsive (1-2 weeks)

What are SSRIs

- Selective Serotonin Reuptake Inhibitors
- Most commonly prescribed antidepressant class
- Fluoxetine, Paroxetine, Sertraline, Citalopram, Fluvoxamine.
- Citalopram’s safety demonstrated in liver disease (transaminases < 2.5X normal)
- Caution re antiplatelet effect SSRIs (relatively mild)

The psychiatric literature

- Interferon-related depression first described by Musselman(1979)
- Initially managed by withdrawal of interferon
- First case report of successful antidepressant treatment of interferon-related depression: Goldman(1994)
- Initial contraindication: psychiatric history
- More recent studies: Pre-existing psychiatric disorders no longer a contraindication, provided treatment occurs in an interdisciplinary setting with hepatologists, speacialized nurses and psychiatrists

- Pariante et al(1999) Lancet(354):131-132
- Musselman et al (2001) New England Journal of Medicine (13):961-966
- Schaefer et al (2005) Journal Hepatology (42):793-798

The psychiatric assessment prior to interferon

- ***Current Mood State, any sleep disturbance***
- ***Stability of Current*** ***(next 6-12 months)*** ***Living Situation (Interpersonal, Vocational, Housing, Supports)***
- Gradient of past depression/psychosis – occurrence outside periods of drug use, family history
- Includes risk suicide/homicide/parenting
- Psychological resilience to tolerate physical effects of interferon – implications for depression and compliance
  (Note non-prescribed mood-modulating agents)
- Proven track record of compliance with treatment services
- Note somatically focused expressions of distress – pain disorder, analgesic dependence
- Psychological resilience to cope with failure of interferon

Psychiatric interventions

- Treat baseline depression, even sub-syndromal baseline depression, ideally deferring commencement interferon until remission of depressive symptoms
- Continue SSRI through interferon course
- Adjustment of dosing during course
- Address insomnia: Exercise, sleep hygiene, hypnotic
- Defer interferon if significant life events are occurring eg separation, loss, housing issues.
- Positive activity scheduling, recruit supports
- Baseline pain disorder: cognitive-behavioural approach to optimising non-pharmacological pain control strategies
- Keep an eye on TFTs (interferon side-effect) which can exacerbate depression
- Regular follow-up mood monitoring during interferon treatment
- Few patients need to stop treatment because of mood change

The “failed” interferon patient

- The depressive meaning of failure and anticipated loss – sense of foreshortened future
- The post-interferon “lingering physical symptoms” – element of somatic manifestations of anxiety and depression associated with failure? Or continuing neuropsychological effects of HCV? Or neuro-modulation of serotonergic activity?

Thank you for your attention

- Questions and Discussion