Anxiety, Depression & Delirium

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“if you wish to know the mind of man,
listen to his words…”

possibly a Chinese proverb

Case Study – Mr AS 68yr ♂ former taxi driver

- divorcee (nil contact with former partner & adult children; 2 sisters & other siblings & nephews & nieces closest supports)
- previously living alone independently, nil services, walking aid

Case Study - Mr AS known metastatic RCC

- admission with devastating neurological deficits 2^{o} to malignant thoracic spinal cord compression, past RT & laminectomy known met RCC Dx 2015
- admission under radiation oncology with progressive weakness & numbness of lower limbs & recent fall; on 2nd-line sorafenib

Mr AS's progress

unable to mobilise independently (ECOG 4)

- despite re-irradiation therapy, nil significant return in power lower limbs, remains continent for now
- good insight into neurological prognosis & dependency on others for care needs & terminal implications
- voicing desire for life to end – prefers 'pill' / medication way

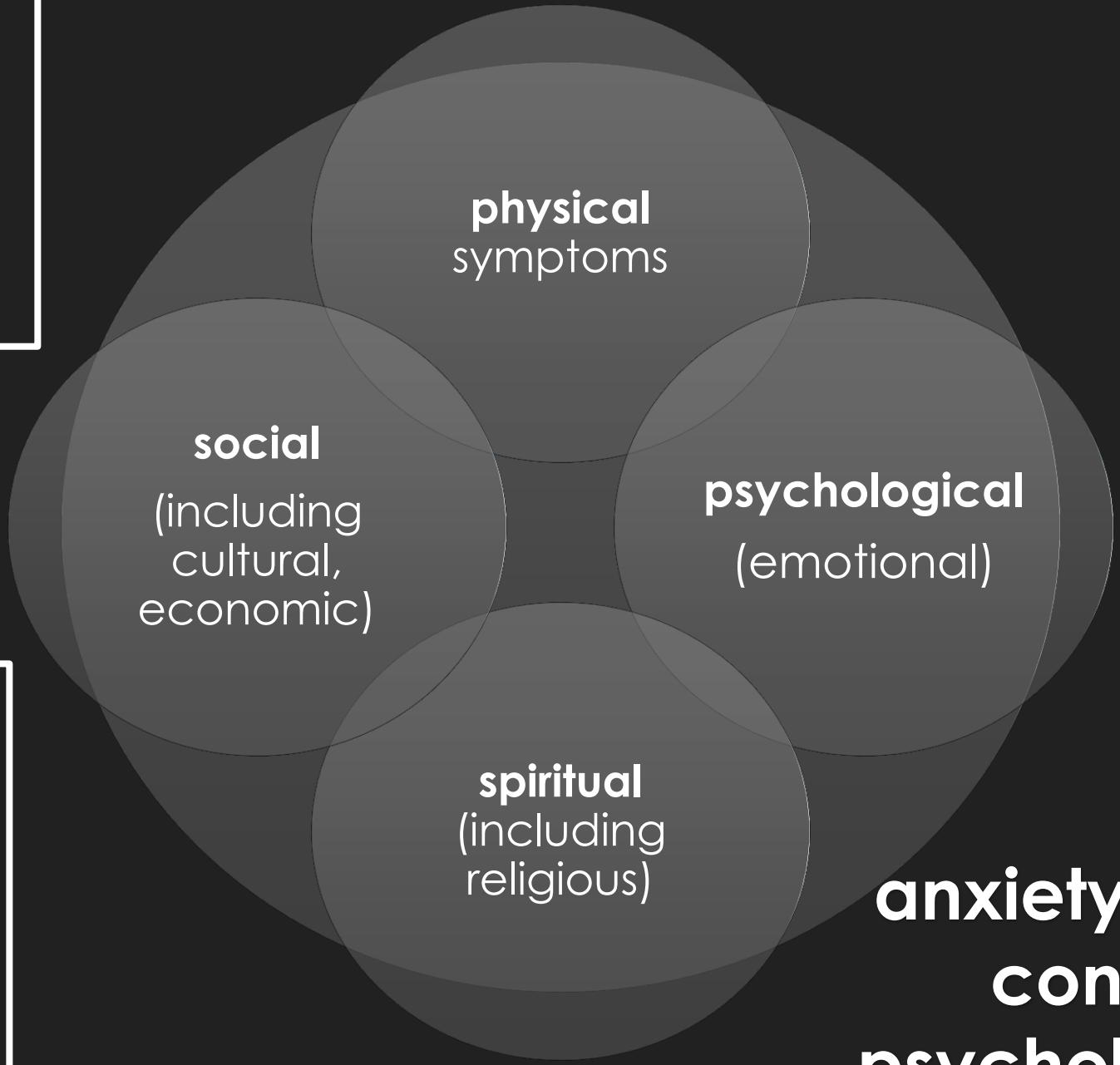
clinical depression?

anxiety & depression

introduction

- among cancer pts, most commonly major depressive disorder, adjustment disorder, reactive depression
- prevalence rates for depression in cancer as high as 25-35%*
- cancer pts higher risk of depression than general population
- pre-existing depression / anxiety prior to cancer diagnosis OR develop anxiety disorder / depression after cancer diagnosis

multiple dimensions of suffering



based on the late Dame Cicely Saunders's concept of total pain

anxiety / depression contributes to psychological distress

WHY IMPORTANT?

↓ QUALITY OF LIFE

↓ SURVIVAL

patient experiences & perspectives

themes in multiple concurrent symptoms in advanced cancer :

- imminence of death and deterioration (impending death, anticipatory fear)
- overwhelming loss of control (symptom volatility, debilitating exhaustion, demoralisation, isolation)
- impinging on autonomy, identity (losing independence, refusal to a diminished self, self-advocacy, reluctance to burden others)

Dong, S. T., et al. (2016). "Patients' experiences and perspectives of multiple concurrent symptoms in advanced cancer: a semi-structured interview study." Support Care Cancer **24**(3): 1373-1386.

patient experiences, perspectives

- psychological adaptation (accept recovery impossibility, maintain hope, mindfulness, seek distractions, accommodate self-limitations)
- burden of self-Mx responsibility (perpetual self-monitoring, ambiguity in self-report, urgency decision making, optimising Mx)
- valuing security & empowerment (safety in coordinated, compassionate care, medical abandonment fear, social support dependence)

Dong, S. T., et al. (2016). "Patients' experiences and perspectives of multiple concurrent symptoms in advanced cancer: a semi-structured interview study." Support Care Cancer **24**(3): 1373-1386.

possible factors for / sources of distress

- uncertainty (anti-cancer Tx, response, prognosis)
- loss & impending loss
- physical symptom(s)
- changing roles and/or relationships
- finances, external conflicts, guilt
- fears of decline & dying & death, planning for future
  - life after death (unknown, family left behind)

normal to be anxious…

especially heightened at time of diagnosis, when therapy ceases, for management goals change to palliative

question is when does anxiety become abnormal?

generalized anxiety disorder DSM-V

- difficult to control excessive & persistent worrying, associated with :

restlessness or feeling keyed up or on edge	difficulty concentrating or mind going blank
easily fatigued	irritability
muscle tension	sleep disturbances

diagnosing anxiety disorder

- **and causes significant distress or impairment in social, occupational, other important areas of functioning**
- which occurs more days than not for at least 6 months
- and not caused by physiological effects of substance (including medications) or medical condition

Diagnosis of Major Depressive Disorder DSM-V

- minimum 5 symptomatic criteria (duration of at least 2 weeks) :

depressed mood	loss of energy
loss of interest or pleasure	weight loss (or weight gain)
excessive guilt	insomnia / hypersomnia
trouble concentrating	psychomotor agitation or retardation
thoughts of death	

Diagnosis of Major Depressive Disorder DSM-V

- AND **requires at least "loss of interest / pleasure" (anhedonia) OR "depressed mood"**
- ALSO **represents change from previous functioning**
  - clinically significant distress or impairment in social, occupational, or other important areas of functioning
- not attributable to physiological effects of substance

Diagnosis of Major Depressive Disorder

potential limitations in applying DSM-V criteria to diagnose major depression in palliative care patients?

screening tools – multiple available

- **Hospital Anxiety & Depression Scale (HADS)**
  - most extensively validated scale for screening emotional distress in cancer, focus on psychological aspects of depression rather than somatic symptoms
- Beck Depression Inventory (BDI-II)
- Edmonton Symptom Assessment Scale
- others eg. Center for Epidemiological Studies Depression (CES-D)

Hospital Anxiety Depression Scale (HADS)

- 14-item screening tool for anxiety & depression
  - self-reported, each item rated on 4-point scale (scores 0-3)
  - scores range from 0-21 for each subscale – HAD-A & HAD-D
- score cut-off points assist to classify anxiety & depression levels as within normal range, borderline or clinical

reality of clinical practice

- allow time required for adequate assessment of critical issues
  - reality of ‘time-poor’ clinical practice
- studies looking at usefulness of a screening question :
  - “*Are you depressed?*”
  - initially promising results

single screening question?

- variation in question :
  - *"Have you felt depressed, most of the day, nearly every day for 2 or more weeks?“*
- **variable levels of sensitivity & specificity**
- variation in answers :
  - *"Yes, I am depressed“, "No, I am not depressed“, "Neither“*

relevant screening question?

- diverse cultural / ethnic backgrounds & multi-faith society
- when translated, evidence that usefulness (sensitivity, specificity) not always transferable to different communities, cultural groups

- **additionally culturally appropriate to ask?**
- **potential for "lost in translation"?**

eliciting history

- symptomatology (psychological & physical symptoms)
  - pre-morbid personality & past or present psychiatry disorders
- for patients with depressed mood, risk of suicide & self-harm
- psychosocial context – stressors, supports, financial, relationships
- medications & substance use – including alcohol, illicit drugs & withdrawal)

Examples of questions….

How are you coping mentally?

What do you enjoy doing?

How long have you been feeling that way?

What gives you joy or happiness?

You seem a little down. Do you think that you are depressed?

Are there times when you wanted your life to end?

Please tell me more.

What have you tried for this?

What worries you the most?

What seems to bring it on?

Have you thought about harming or killing yourself?

risk factors for suicide

- underlying psychiatric disorder
- past suicide attempt, family Hx of suicide
- ambivalence towards survived suicide attempt
- definite plan for suicide attempt, ready access to suicide means with high potential lethality (eg drugs, firearms)

risk factors for suicide

- history of dangerous behaviour / impulsive
- social isolation/absence of social supports
- recent major loss
- chronic medical illness, especially chronic pain
- feeling of hopelessness

Who feels uncomfortable asking about suicide?

Psychological Medicine

December 2014, pp. 3361-3363

Does asking about suicide and related behaviours induce suicidal ideation? What is the evidence?

T. Dazzi [a1], R. Gribble [a2], S. Wessely [a2] and N. T. Fear [a2]

a review of published literature in adults, adolescents, general & at-risk populations – **no statistically significant increase in suicidal ideation among participants asked about suicidal thoughts**

general approach to anxiety & depression

- modify stressors (acute & chronic) whenever possible
  - exclude contributing factors, esp. uncontrolled pain
- involve general practitioner, family, friends +/- volunteers, social work, support groups
- referral to clinical psycho-oncology and/or psychiatry (psychotherapy programs, cognitive behavioural therapy, other)

anxiety & depression

- important to exclude contributing underlying medical conditions
  - anaemia, infection
  - other inflammatory / autoimmune conditions, advanced organ failure
  - endocrine (thyroid disorders, hypocortisolism, hypogonadism)
  - medications, other

when to treat pharmacologically?

clinically significant distress or impairment in social, occupational, or other important areas of functioning

pharmacological Mx

identify & discuss options, balance potential benefit & adverse effects

anxiety management

- **psychological therapy generally 1st line treatment**, likely better at improving long-term outcome
  - barriers - low patient motivation and/or acceptance of psychological therapies (typically time-consuming nature), availability of psychologists
- **pharmacological** : consider SNRI, SSRI, possible benzodiazepine

Pharmacological therapy for depression

concurrent non-pharmacological measures essential

Mother Goose & Grimm, Wed Mar 24th 2004, source :http://www.grimmy.com/comics.php

antidepressants – "1st line options"

- **Selective Serotonin-Reuptake Inhibitor (SSRI)**
  - citalopram (Cipramil™), sertraline (Zoloft™)
- Serotonin-Noradrenaline Reuptake Inhibitor (SNRI)
  - venlafaxine
- mirtazapine (tetracyclic antidepressant)

antidepressants – “later line agents”

- tricyclic antidepressants (TCA) eg. amitriptylline, nortriptyline
- reboxetine (noradrenaline reuptake inhibitor)
- moclobemide (reversible MAO-A inhibitor)
- others

- **avoid combining antidepressants*, ’wash period’ when changing**

antidepressant considerations

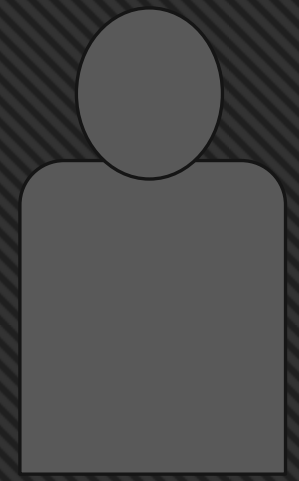
- individual responses vary, differ between various antidepressants
- typically slow onset action (2-3 weeks) for mood improvement
- often longer for full therapeutic effect (6-8 weeks)
  - mindful of individual patient prognosis & appropriateness
  - assessment of ‘response’ in progressive cancer

antidepressant caveats

- generally “go low, titrate slow”
  - ↓ reserves, ↑ adverse effects in advanced cancer patients
- ↑ suicidal thoughts & behaviour can occur soon after starting antidepressants
- consider potential lethality in overdose situation (risk of suicide)
  - SSRI relatively safer, usually avoid TCAs, MAO-I

medication	ANTIDEPRESSANTS class	starting dose & maximum dose	considerations	when changing to another antidepressant
sertraline	selective serotonin reuptake inhibitor	25-50mg po daily / mane, (MAX 200mg/day)	favourable risk-benefit ratio*, risk ↑ QTc, 'activating', hyponatraemia risk	wait 2-4 days
citalopram	selective serotonin reuptake inhibitor	10-20mg po daily / mane (MAX 40mg/day)	favourable risk-benefit ratio, risk ↑ QTc, 'activating', hyponatraemia risk	wait 2-4 days
velanfaxine	serotonin noradrenaline reuptake inhibitor	37.5-75mg po daily (MAX 225mg/day)	may increase BP*, caution in renal / hepatic impairment, hyponatraemia risk	wait 1-2 days
mirtazapine	tetracyclic antidepressant	15mg po nocte (MAX dose 60mg/day)	benefit with increasing appetite, potentially weight gain, sedating	wait 2-4 days

avoid combination of antidepressant medications



case study continued : Mr AS

what needs to be asked? main questions?

- What is the reason(s) he wishes for life to be over?
- Why does he wish to die?
- How well controlled are his physical symptoms?
- How well supported by social circle? (collateral Hx helpful?)
- Any active plans to harm himself & access / ability to medication?
- Any other symptoms of depression?

further assessment

- objectively reactive, easy to engage, smiling at times appropriately
- comfortable, pain well controlled, sleeping & eating well
- feels comfortable with being cared for by nurses - provides ‘good care’
- enjoys watching TV, reading newspapers & engaging in sporting news

further assessment

- feeling current quality of life poor, does not want to live remaining life bedbound and "staring at ceiling" most of the time
- spiritual but not religious
- insightful require ongoing high level care & unable to return home, possibly nursing home
- previously very active; "made peace" with life & dying & 'happy' to die any time now

clinically depression?

- important to avoid medicalizing ‘normal’ emotions including sadness in oncology
- at same time, need to recognize clinical depression in patients who require further intervention

FINAL WORDS - depression

- assessment / diagnosis of depression often more difficult in advanced life-limiting diseases such as cancer with progressive constitutional symptoms
- attempt to mitigate any contributing factors whenever possible
- assessment of self-harm / suicide risk in depression is essential
- ongoing evaluation for depression & anxiety - periodic screening

FINAL WORDS - depression

- multi-disciplinary approach, combined modalities (social work, diversional therapy, psycho-oncology
- psychological interventions / support +/- antidepressant
- individualise decision on appropriateness of antidepressant, considering prognosis, potential benefit & harm for that patient
- psychiatry input (severe / persistent depression, suicide ideation)

delirium

Mr AS – 68yr metastatic renal cell cancer

- 3 weeks onwards, progressive malignant thoracic cord compression, developed dual incontinence
- fallen out of bed in the morning, appears confused, disorientated, otherwise nil pain & settled
- yesterday lucid, unclear if confusion occurring prior of after fall

Delirium? Sisters distressed…

- Mr AS usually lucid, sharp, witty
- easily distracted, disorientated, seeing little kangaroos at times
- occasionally referring to sisters as their deceased mother
- sleeping more, uninterested, at times hard to rouse
- sister asking whether Mr AS is dying?

Delirium

- acute complex neuropsychiatric syndrome
- acute, fluctuating change in mental status characterised by inattention, disorganised thinking & altered levels of consciousness, potentially reversible

- **distinguish from dementia** (a risk factor for delirium)

delirium diagnosis key features - DSM-V

essence of delirium diagnosis

A. disturbance in **a**ttention & **a**wareness
B. develops over a short time period, change from **b**aseline, & tends to fluctuate
C. additional disturbance in **c**ognition
D. not better explained by another pre-existing, evolving or established neurocognitive **d**isorder (eg. dementia) or coma
E. **e**vidence disturbance is caused by a medical condition, substance intoxication or withdrawal, or medication side effect

Prevalence in Palliative Care

- prevalence of delirium varies, ~1/3 of patients positive on screening, ~20% diagnosed on DSM-V

Risk factors for delirium in palliative care

- pre-existing cognitive impairment (dementia)
- elderly
- advanced disease
- multiple comorbidities
- sensory impairment

Significance of delirium

- affects ability to elicit reliable history, potential for suboptimal examination, assessment of pain, other symptoms as well as response to therapy
- potentially affects diagnosis & optimal management
- characterised by high morbidity & mortality, associated with more prolonged hospitalisation, institutionalisation

Impact of delirium

- higher mortality rates for inpatients with delirium with similar medical conditions as inpatients without delirium
- ↑ mortality with protracted delirium in elderly inpatients

Psychological impact

- distressing for patients & families
- importance for patients & families – maintaining lucidity
- especially for patient whose delirium settles & can remember*

- distressing for staff

delirium subtypes

clinical subtypes

- **hyperactive**
  - heightened arousal, restlessness, agitation, hallucinations, inappropriate behaviour
- **hypoactive**
  - display lethargy, reduced motor activity, incoherent speech & lack of interest
  - can mimic dying / terminal phase

clinical subtypes

- **mixed hyperactive & hypoactive**
  - combination of hyperactive & hypoactive signs and symptoms

hypokinetic delirium mimic dying

- cognitive impairment common in terminal phase
- understanding where patient is on their disease trajectory useful as may predict reversibility of delirium & guide appropriateness of therapy to attempt to reverse delirium

DIAGNOSIS >>> Time >>> DEATH

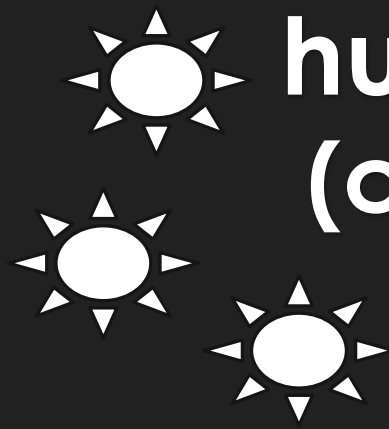
pathophysiology - complex, unclear

multiple theories of pathogenesis of cerebral dysfunction

- neurotransmitter imbalances
  - acetylcholine, serotonin, dopamine, gamma-aminobutyric acid
- inflammatory processes
  - disruption blood-brain barrier, pro-inflammatory cytokines
- other : humoral factors (cortisol), oxidative impairment

neurotransmitter imbalances

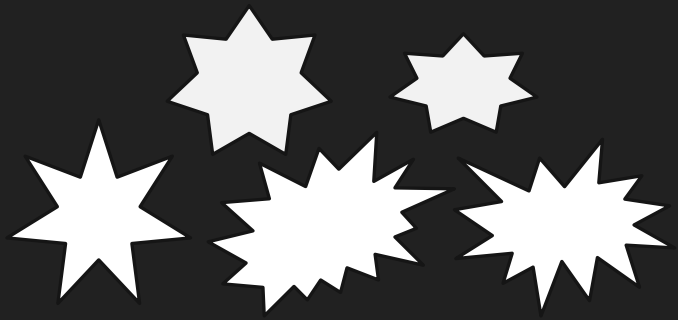
eg. acetylcholine



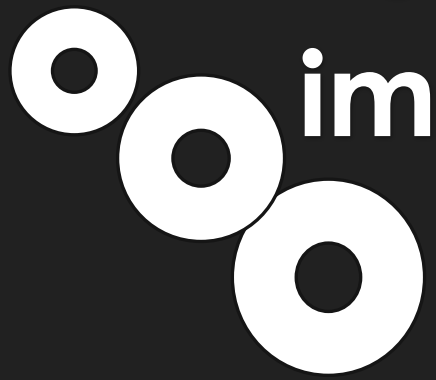
humoral

(cortisol)

theories / mechanisms for delirium



inflammatory process



oxidative

impairment

aetiologies / contributing factors

- CNS / neurological pathology
  - neoplasm (primary / secondary), stroke, bleeding, CNS infection, hypertensive crisis, ↑ intracranial pressure, seizure
- systemic infection
- organ failure
- autoimmune / immunological / inflammatory conditions

aetiologies / contributing factors

- electrolyte / metabolic (eg. hypercalcaemia)
- endocrine disorders (severe hypothyroidism)
- medications +/- iilicit drugs
  - including withdrawal
- **uncontrolled symptoms :** severe pain, anxiety, others

Assessment with tools – eg. NuDESC

- Nursing Delirium Screening Scale (NuDESC)
- 5 items, each rated on score of 0-2, usually assessed 3x/day :
  - disorientation, inappropriate behaviour, inappropriate communication, illusions / hallucinations, psychomotor retardation
- score >2 identifies delirium in 86% of cases

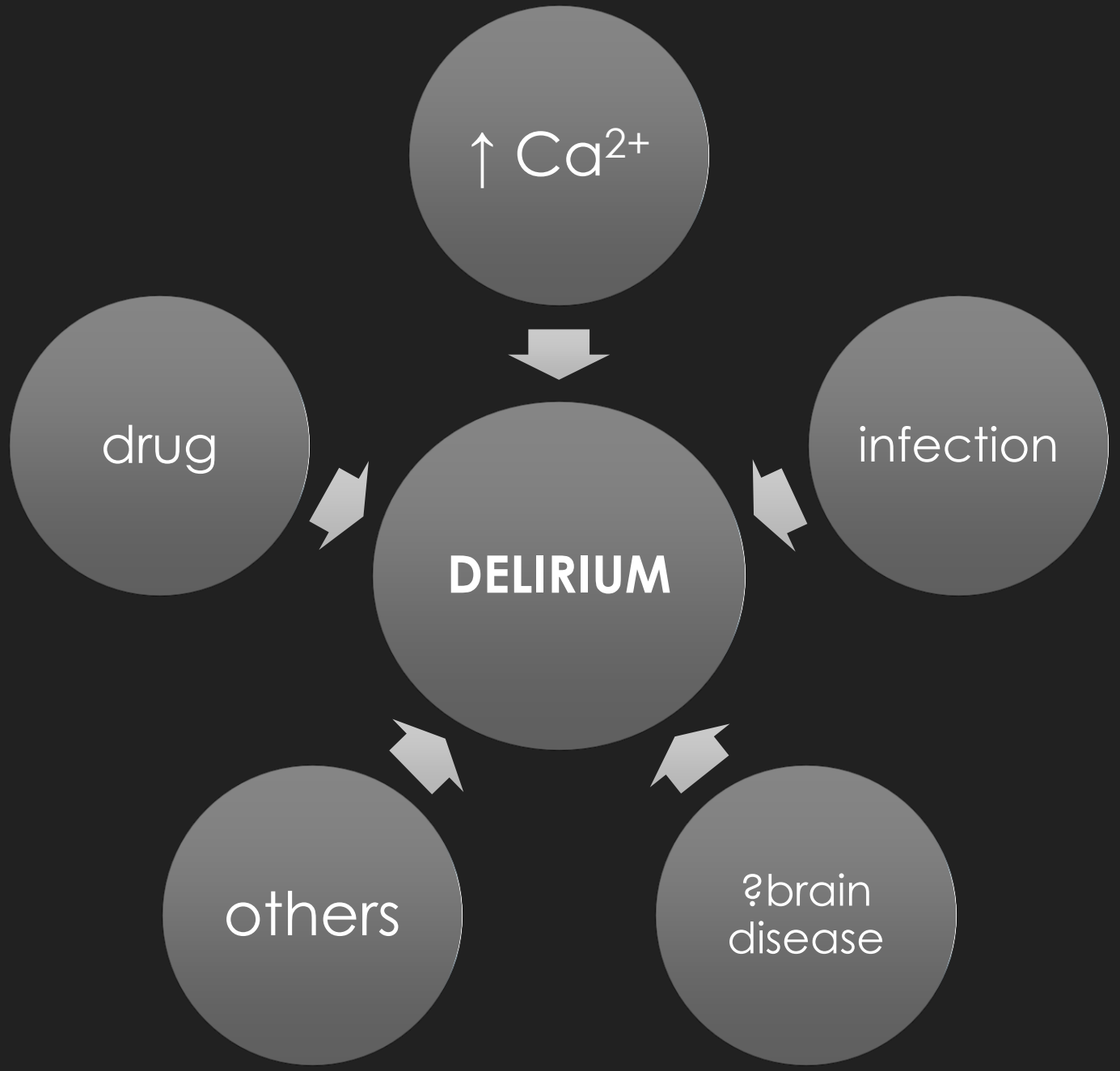
Mr AS's NuDESC consistent with delirium

management principles

- safety & symptom control :
  - patient - risk of falls, injury
  - others (healthcare professionals, family) - if aggression present
- reversibility :
  - investigate and/or treat reversible conditions if appropriate
- distress of patient, family (aim to ↓ distress including ↓ agitation)

possible causes for delirium in Mr AS

commonly multiple factors concurrently



respecting Mr AS's preferences

- patient's wishes when cognitively clear previously was not for further investigations, not for life-prolonging therapy & family supportive :
  - no investigations done, medications reviewed
  - support for family
  - management focusing on comfort & preserving dignity as much as possible

simple measures

- exclude urinary retention
- exclude severe constipation
- optimise pain & symptom Mx
- pressure area care, mouth care
- consider medications as last resort :
  - neuroleptics, steroids

simple interventions

- **safe, familiar, quiet, calm environment**
- music, lighting level, family
- re-orientation strategies
- hearing & visual adaptation strategies
- simple communication, interpreter*

simple interventions

- avoid conflict / confrontation, no restraints
- remove hazardous objects (potential ‘weapons’)
- preferably single room
- minimise change(s) in environment
  - avoid room changes if possible

reorientation strategies & others

Thursday

10th NOVEMBER 2016

harm minimization esp. ‘mobile’ patients

- **if high risk of falls :**
- **constant supervision**

AND / OR

- high visibility room / bed
- low mattress
- bedrails down

Bedrails

- inappropriate use of bedrails common in patients with cognitive impairment or agitation in acute hospital setting
- predictors of bedrail use : electric profiling beds, confusion, reduced alertness, difficulty with transferring from bed
- commonest reported indication : 'to prevent rolling out of bed‘, 'to prevent getting out of bed'

Avoid physical restraints*

- bedrails form of restraint
- physical & psychological harm
- potentially worse agitation, fear, delirium
- impact on dignity

dealing with aggression

if patient not in danger, step / stand back, allow to settle down :

- healthcare providers to avoid placing themselves in danger
- avoid shouting (or touching* patient)
- communicate in a calm, non-confronting way
- “redirect and/or distract” strategies

essentially…

core principles of
non-pharmacological
approach

"tolerate, anticipate, and don't agitate"

(the T-A-DA method)

pharmacological approach

- when non-pharmacological measures are insufficient
- antipsychotics :
  - conventional (eg. haloperidol)
  - atypical (eg. olanzapine, risperidone)
- benzodiazepines :
  - eg. midazolam, clonazepam

Antipsychotic - haloperidol

- haloperidol typical antipsychotic / neuroleptic agent
- potent dopamine antagonist centrally
  - start 0.5mg-1mg subut bd, usually limit at about 5mg / day
  - avoid Parkinson disease
  - extrapyramidal effects risk
  - potential for QTc prolongation

alternatives - atypical antipsychotics

antipsychotic	starting dose* & route	frequency	maximum dose*
risperidone	0.25mg – 0.5mg po (including oral disintegrating, liquid)	nocte-bd	4mg*
olanzapine	2.5mg – 5mg po (including oral disintegrating)	nocte – bd	20mg*

Benzodiazepine

- includes lorazepam, midazolam, clonazepam, others
- helpful in calming down, reducing anxiety, ‘settling’
- different benzodiazepine, different duration of action
- sedating, midazolam potentially amnestic properties
- commonly use fasting-acting benzodiazepine for severe acute agitation

evidence for antipsychotics

- delirium in HIV pts : antipsychotic preferred, less side-effects (drowsiness) than benzodiazepines
- medical non-palliative care setting : suggest benefit of haloperidol, olanzapine over usual care in ↓ delirium severity
- medical non-palliative care setting : similar efficacy risperidone, haloperidol, olanzapine

evidence in palliative care setting

- randomized controlled trial : risperidone v. haloperidol v. placebo with subcutaneous midazolam ('rescue') PRN allowed
- 165 patients with symptomatic delirium, composite of several delirium symptoms assessed using Nursing Delirium Screening Scale at 72hrs
- **risperidone, haloperidol - worse delirium symptoms, required more midazolam rescue, poorer overall survival**

FINAL WORDS - delirium

- delirium associated with poorer prognosis
- much remains unclear – differences pathophysiology for hypoactive versus hyperactive
- generally more pharmacological interventions used for hyperkinetic delirium & need for pharmacological therapy often related to degree of agitation & response to treatment
- **focus should be non-pharmacological measures** essentially

FINAL WORDS - delirium

- prevention & ideally early identification of delirium risk factors
- degree of investigations, therapy of reversible causes depends on patient's phase, other medical issues, goals of care
- hypoactive delirium may mimic dying phase
- delirium common in dying patients, terminal agitation*
- recognise distress esp. for families, potential loss of dignity

Any questions?

- Thank you
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