Vulvovaginal Candidiasis and its Relationship with Localized Provoked Vulvodynia (PVD)

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Candidiasis “Just thrush?”

- C. albicans is a common yeast producing symptomatic infections of the female genital tract during reproductive years, and at other times in the presence of risk factors
- 75% of healthy women affected at least once
- >5% without risk factors >3 times per year
- Similar symptoms to provoked vulvodynia
- Asymptomatic commensal status on culture, microscopy negative, point prevalence 20%, part of vaginal homeostasis

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Self Reporting of Candida

- Notoriously unreliable but “bias analysis” suggests a bidirectional relationship (Harlow et al 2017) with a doubling of PVD risk, and up to 5.5 OR if >10 episodes/year
- post-PVD diagnosis risk of new onset candida also doubled – dysfunctional immune responses?
- 25-50% of women with PVD had no reports of pre existing candida symptoms

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“Vulvodynia” is a descriptive term not implying causation

- Vulva + pain: described as raw, burning, dry, prickling, tearing or itching.
- 2015 ISSVD 1.vulvar pain caused by a specific disorder (such as infection or dermatitis) and 2.vulvodynia. Vulvodynia is defined as “vulvar pain of at least 3 months duration, without clear identifiable cause, which may have potential associated factors”.
- However category 1 can be associated with 2 and probably in a bidirectional mechanism.

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What is pain?

- “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or is described in terms of such damage” IASP
- Is designed to “protect the body by making the organism aware of damaging events and to promote healing by causing sensitivity to movement or other stimuli”
- PVD is “Dysfunctional” pain, is not associated with a lesion (ie not “neuropathic”)

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Characteristics of localized (to the vestibule) provoked vulvodynia

- Pain at the introitus at initial penetration, may then subside or persist during and afterwards = mechanical allodynia +- hyperpathia
- May have accompanying dysuria (MSU –ve)
- Heat and mechanoreceptors not “nociceptors”, as nociception occurs in CNS
- There are other triggers for nociception
- However, there is evidence for peripheral nerve growth in vestibule in PVD

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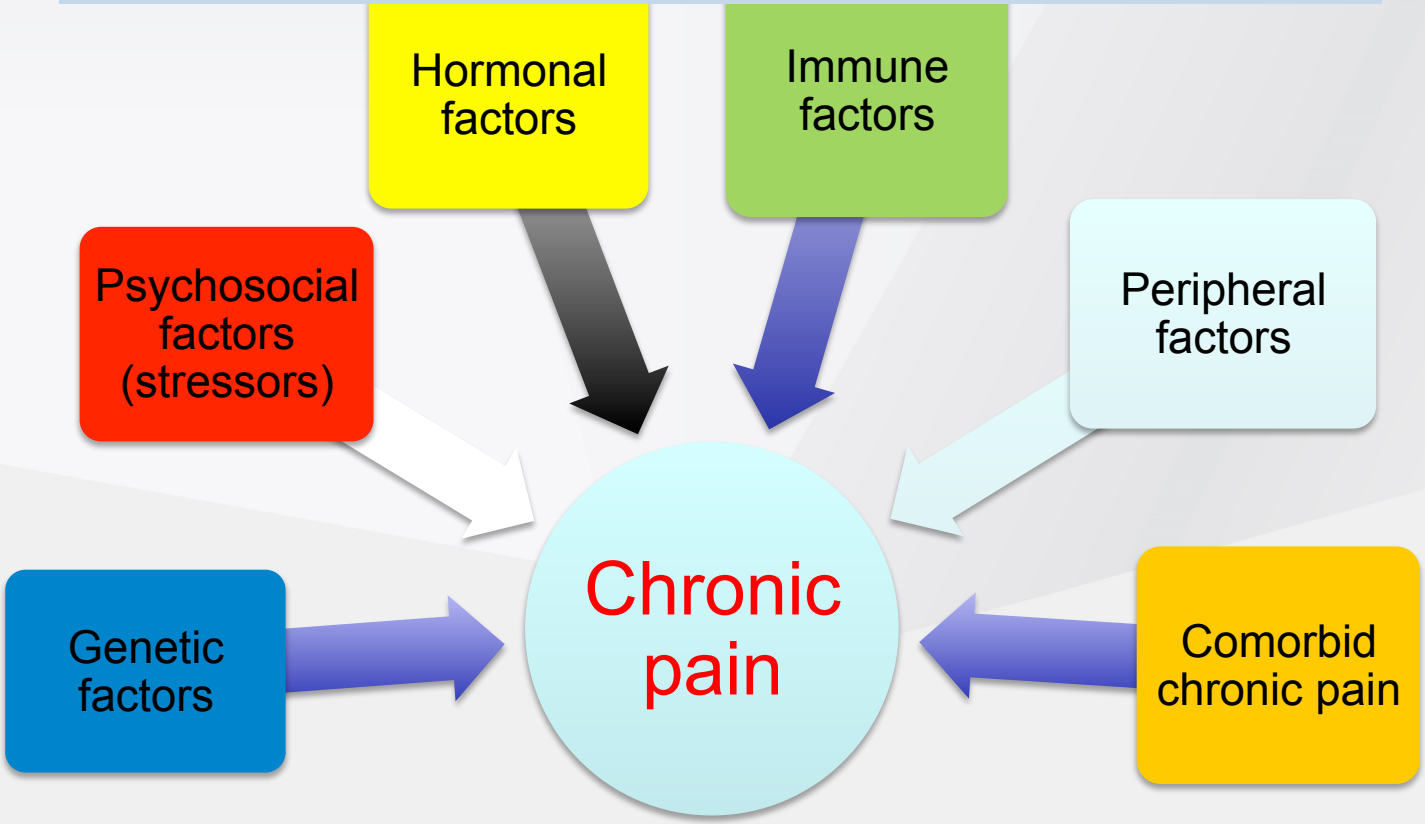
Pathophysiology in chronic pain is likely complex and multifactorial, and differs from person to person



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Spontaneous and/or provoked? Generalized and/or localized?

- The commonest type is localized and provoked +- some spontaneous component
- Health seeking is not common < 50% of whom only 20% might get a diagnosis
- Stigma, fear of not being taken seriously
- Often falls into “medically unexplained symptoms” with poor outcomes
- Women want to be asked about sexual symptoms, but there are clinician barriers

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PVD as “Chronic Pain”

- The ISSVD definition is “3 months” and includes associated features
- IASP/WHO 2019 new pain definitions:
  1. chronic primary - pain in one or more anatomical regions that persists or recurs for longer than 3 months and is associated with significant emotional distress or functional disability (and cannot be better accounted for by another chronic pain condition) .
  2. chronic secondary pain eg due to chronic inflammation such as RA, even after successful treatment of the initial cause

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PVD associated increased vulval innervation

- Biopsy studies in PVD patients compared with controls show increased nerve fibres
- Mouse study N=15 (Farmer 2011)
- 40% induction of mechanical allodynia with live C. albicans, treated with fluconazole after 7 days, resolving by 4 weeks, x4 density innervation
- 3rd infection or single prolonged infection can lead to 7-11 weeks of painful allodynia

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Conclusion?

- Highly likely and biologically plausible that untreated, prolonged or repeated candidiasis is strongly associated with PVD in many women
- 25-50% women with PVD do not report antecedent candida
- Is candida causative? Studies are small and heterogenous. Difficult to draw conclusions
- Chicken or the egg? Or both?

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What happens when pain is chronic?

- If it hurts enough women might seek help but by then pain patterns risk becoming entrenched (<50% see a clinician and only 20% diagnosed, 25% lifetime, 8%/year)
- Acute pain maps to sensory areas in the brain and serves to protect the organism eg injury “nociceptive” and “inflammatory” pain (peripheral receptors detect sensation , and “nociception” is a brain function)
- Chronic pain transition involves processing in areas involved in emotion and evaluation

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“Catastrophization” has derogatory potential – language is important

- Defined as an experience of helplessness and loss of personal control over the pain
- Anxiety about the future
- Loss of sexual function “not a real woman”
- Fear of loss of relationships
- Fear of loss of probability of pregnancy
- Fear of childbirth
- Fear the pain will never go
- Partners have fears and sexual dysfunction

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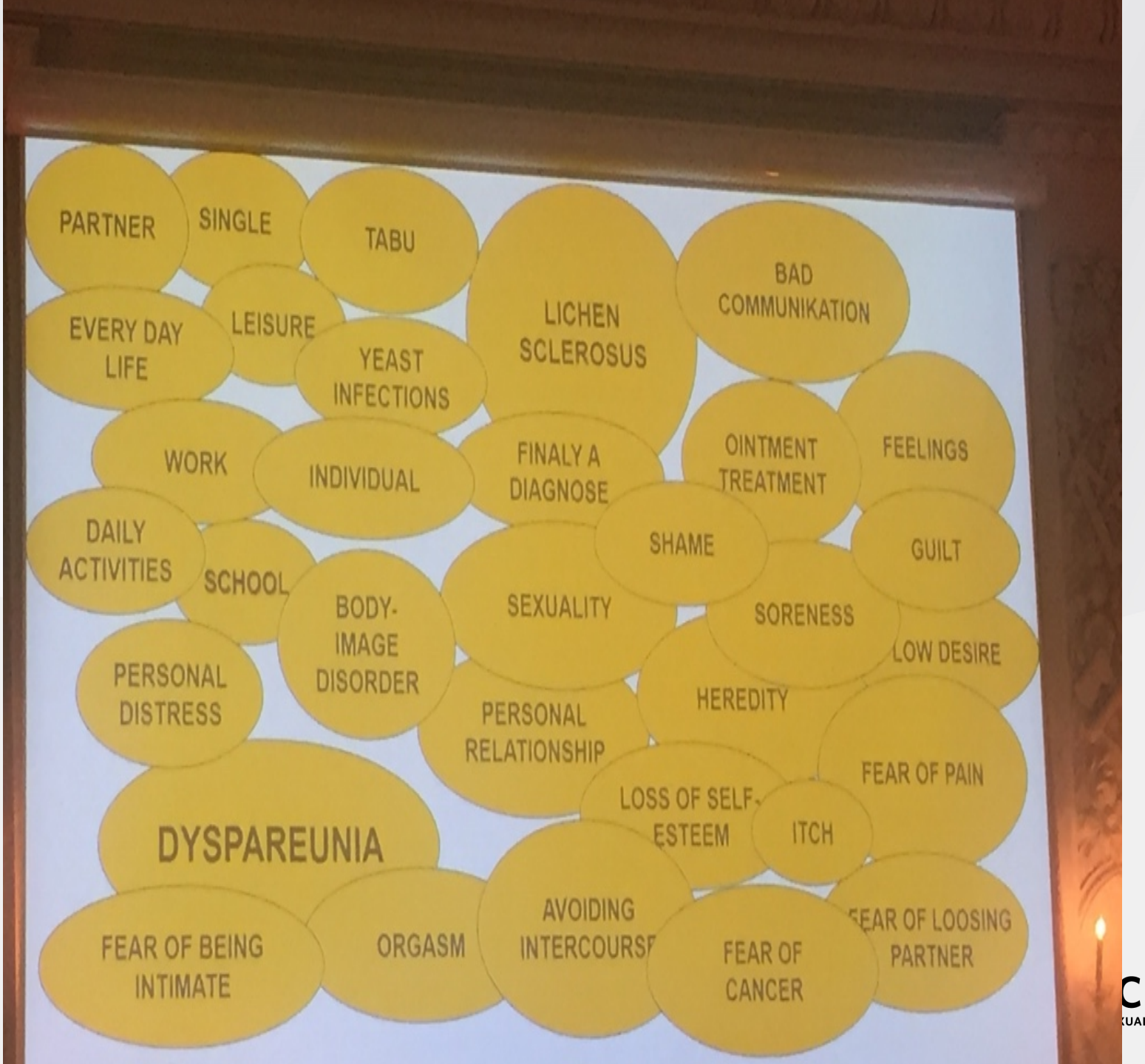
PARTNER
SINGLE
TABU
LICHEN SCLEROSUS
BAD COMMUNIKATION
EVERY DAY LIFE
LEISURE
YEAST INFECTIONS
WORK
INDIVIDUAL
FINALY A DIAGNOSE
OINTMENT TREATMENT
FEELINGS
DAILY ACTIVITIES
SCHOOL
SHAME
GUILT
BODY-IMAGE DISORDER
SEXUALITY
SORENESS
LOW DESIRE
PERSONAL DISTRESS
HEREDITY
PERSONAL RELATIONSHIP
FEAR OF PAIN
LOSS OF SELF-ESTEEM
ITCH
DYSPAREUNIA
AVOIDING INTERCOURSE
FEAR OF LOOSING PARTNER
FEAR OF BEING INTIMATE
ORGASM
FEAR OF CANCER

Years to a diagnosis – why?

- Inadequate clinician training and specialized services ?who owns the vulva in a multidisciplinary setting
- Inadequate community knowledge
- Cultural sexual taboos and judgements
- Not life and death but high functional and mental health morbidity including for partners
- Sexual function often left out of management of other chronic conditions eg. cardiac, cancers, inflammatory, autoimmune, mental health – QUALITY OF LIFE

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Is it vulvodynia?

- Sometimes this is a straightforward diagnosis
- History gives the diagnosis and examination confirms it (expect to see “normal” skin and anatomy)
- Usually there is localized introital tenderness, some evidence of allodynia at the labia minora, and observable pelvic floor overactivity
- Burning/awareness persists after examination

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What mimics vulvodynia?

- Burning/tearing with penetration = allodynia BUT exclude focal dermatitis/splits

(often improves after initial penetration as the pelvic floor releases and fear reduces)

- Afterburn = hyperpathia BUT exclude candida
- Dysuria = hyperpathia BUT exclude STI and UTI

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Are laboratory tests helpful?

- What are we looking for – things that burn or irritate - candida mostly, sometimes HSV if fissures/erosions, BV or trichomonas
- Biopsies are generally unhelpful unless a lesion or dermatitis is present (can sometimes see swab negative candida in keratin layer) – “chronic inflammation” also in controls
- M + C from vaginal discharge and patches of vulval dermatitis (hopefully no antifungal used for a month - ASK). Vaginal pH helpful.

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Candidiasis – acute and recurrent

- M + C from vaginal discharge and patches of vulval dermatitis
- Acute candida often has obvious clinical signs
- Recurrent or chronic can be subtle
- Check trigger factors esp antibiotics, atopy postmenopausally - diabetes/A-I/oestrogen
- RVVC is thought of as a host immune mechanism “allergy model”
- PVD also has altered immunity ?bidirectional

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Candidiasis and Vulvodynia

- 2015 ISSVD 1.vulvar pain caused by a specific disorder (such as infection or dermatitis) and 2.vulvodynia. Vulvodynia is defined as “vulvar pain of at least 3 months duration, without clear identifiable cause, which may have potential associated factors”
- This fits with the IASP/WHO chronic primary and chronic secondary pain, where there is persistence even with successful treatment

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Does diagnosis get easier with experience?

- It always takes time “paradigm shift”
- It always takes multiple consultations, availability with symptoms flares
- Individually tailored management
- Evidence is poor – small numbers in trials, heterogenous designs and outcome measures, few trials compared with those for general medical conditions, few include partners, but most women IMPROVE
- The process of health seeking helps

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Studies

- “Pain” has been the commonest outcome measure but function, emotional and sexual satisfaction might be better
- No single treatment has been found to be superior to another
- Aim of treatment is self management and “self efficacy” as opposed to helplessness
- Placebo studies offer mechanisms from trials that can be used clinically

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Placebo as Trial Participation Effects “Contextual Factors”

- Multiple studies in chronic pain (IBS), nausea and Parkinson’s Disease support openly disclosed use of inert tablets (not deception)
- Researchers are enthusiastic, encourage and provide followup, take the symptoms seriously and document them (Hawthorne Effect)
- Essential are clinician and patient expectation of improvement, and warm empathic manner
- Nocebo is similarly potent

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Pain is Dynamic

- Newer psychological “dyadic” studies involve partners, symptoms occur in intimate setting
- Recognizes that all chronic pain (primary and secondary) is multifactorial and biopsychosocial, and >1 factors contribute to onset, maintenance and exacerbations
- Women’s daily diaries for 2 months revealed less pain and anxiety if higher “sexual communal strength”, ie meeting partner’s needs without neglecting their own (Muise, Bergeron et al 2018)

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So Candida ….

- Highly plausible that it can contribute to chronic pain as it is common (75% once, >5% recurrent),often poorly diagnosed if no tests or recent antifungal used
- Skin and RVVC are often undertreated
- Symptoms can mimic provoked vulvodynia – burning with and after sex (burning after sex may precede PVD by a year – Harlow and Haefner) so are self reports accurate?
- Women often resume sex whilst symptomatic – can trigger more pain anticipation (central) and skin fragility (peripheral)

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PVD Clinical Subtypes Henzell et al 2017

Uncomplicated PVD on history

- Shorter-duration PVD
- Milder pain severity
- 0–1 comorbid pain condition
- None or mild current depression and/or anxiety, good social supports
- “facilitative” partner relationships,
- No trauma history
- Good sleep

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Uncomplicated PVD = predominantly peripheral factors

- Predominantly overactive pelvic floor muscles
- Well treated candida, dermatitis, MSU confirmed cystitis, STI
- Limited psychosocial factors – always explore IMPACT of symptoms
- “facilitative” partner relationships – curious to explore the pain rather than avoid, both have a “voice”, strong “communal sexual motivation”

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Complicated PVD on history

- Longer-duration PVD
- Greater pain severity >5/10
- Two or more co-occurring pain conditions, pelvic or distant
- Psychosocial factors present and past – anxiety, depression, PTSD/abuse/neglect, fear–avoidance, catastrophizing, poor social supports, intimate relationship problems
- Associated conditions not responding to treatment - Candidiasis or skin conditions difficult to control (eg lichen planus)

Complicated PVD = Central Sensitization = Multidisciplinary

- Significant psychosocial and emotional factors – anxiety/PTSD/abuse, depression, FEAR
- Overlapping chronic pain conditions (COPCs) suggestive of genetic vulnerability, migraine, fibromyalgia, IBS, TMJ, dysmenorrhoea. Uncommonly POTS, Ehrler's Danlos Syndromes (connective tissue disorders with autonomic dysfunction and chronic pain)
- Brain fog, sensitivities to food, chemicals, sensory, poor sleep, memory

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Pelvic Floor Physiotherapy – mindful focus “regain” the body

- Education including limited neuroscience information “Sore but Safe”, “Hurt not Harm”
- Posture and breathing techniques
- Bladder and bowel training
  Voiding and defecation dynamics
  Good bladder and bowel habits
- Treatment of musculoskeletal dysfunction
- Stress reduction strategies using the body
- “Safe” Guided exercise and reconditioning – hands on and personalized, validation

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Treat what can be treated

- Reviews over time – empathic and upskilled general practitioner is vital
- Recognize that candida is likely a potent sensitizer in some women for chronic secondary pain
- If recurrent candida is suspected, suppressive treatment for 6 months or more is SAFE
- If the diagnosis of candida is uncertain, consider PVD but suppress candida for about 2 months

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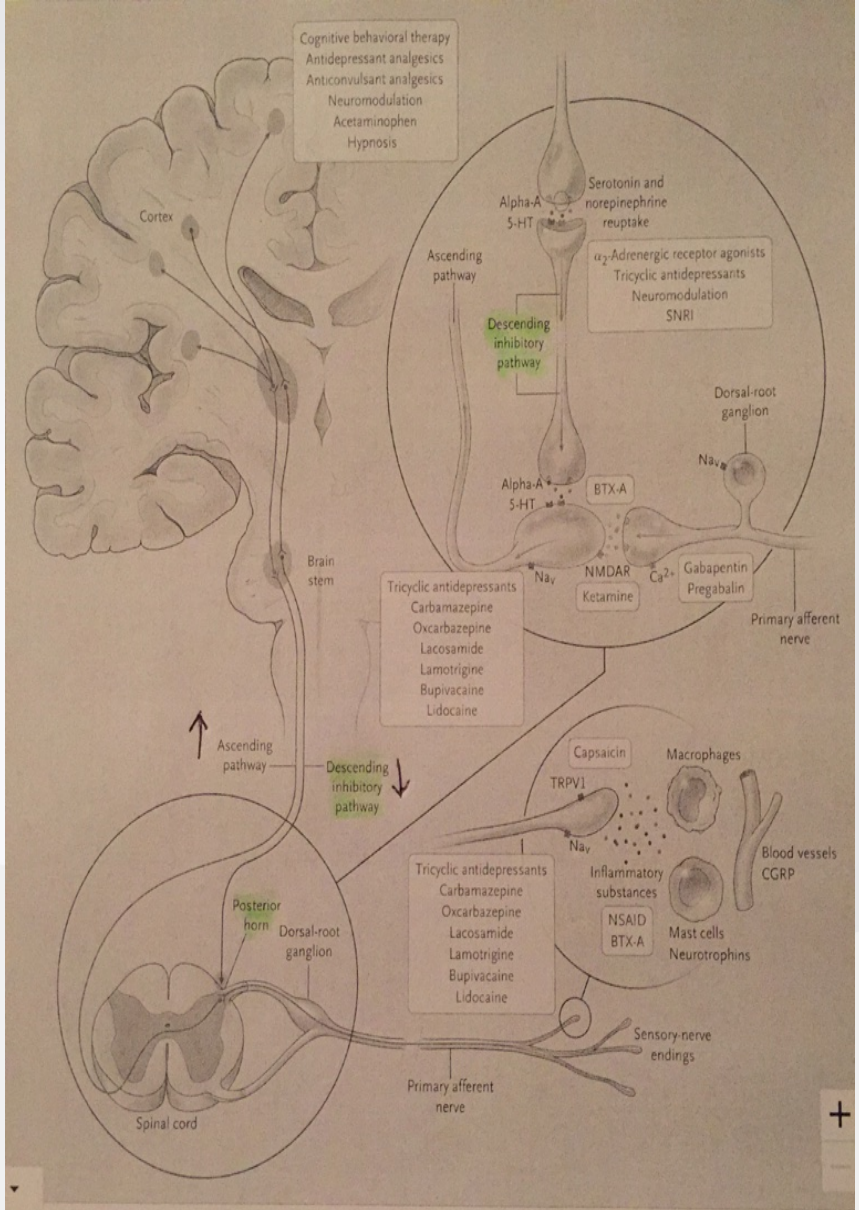

Figure 1. Sites of Action of Various Methods of Pain Management.

Shown are pain treatments that act on the brain, multiple drug targets along the pain pathway in the spinal cord (including facilitation of descending pain inhibitory pathways

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Finnerup:Pain Management NEJM June 2019

- Treatment choice depends on many factors
- No general treatment algorithm is possible (WHO and IASP)
- Overemphasis on pain intensity as an outcome (0-10 scale)
- Does not reflect the pain experience
- Suffering a limited pain may be accepted and tolerated if that pain serves a purpose

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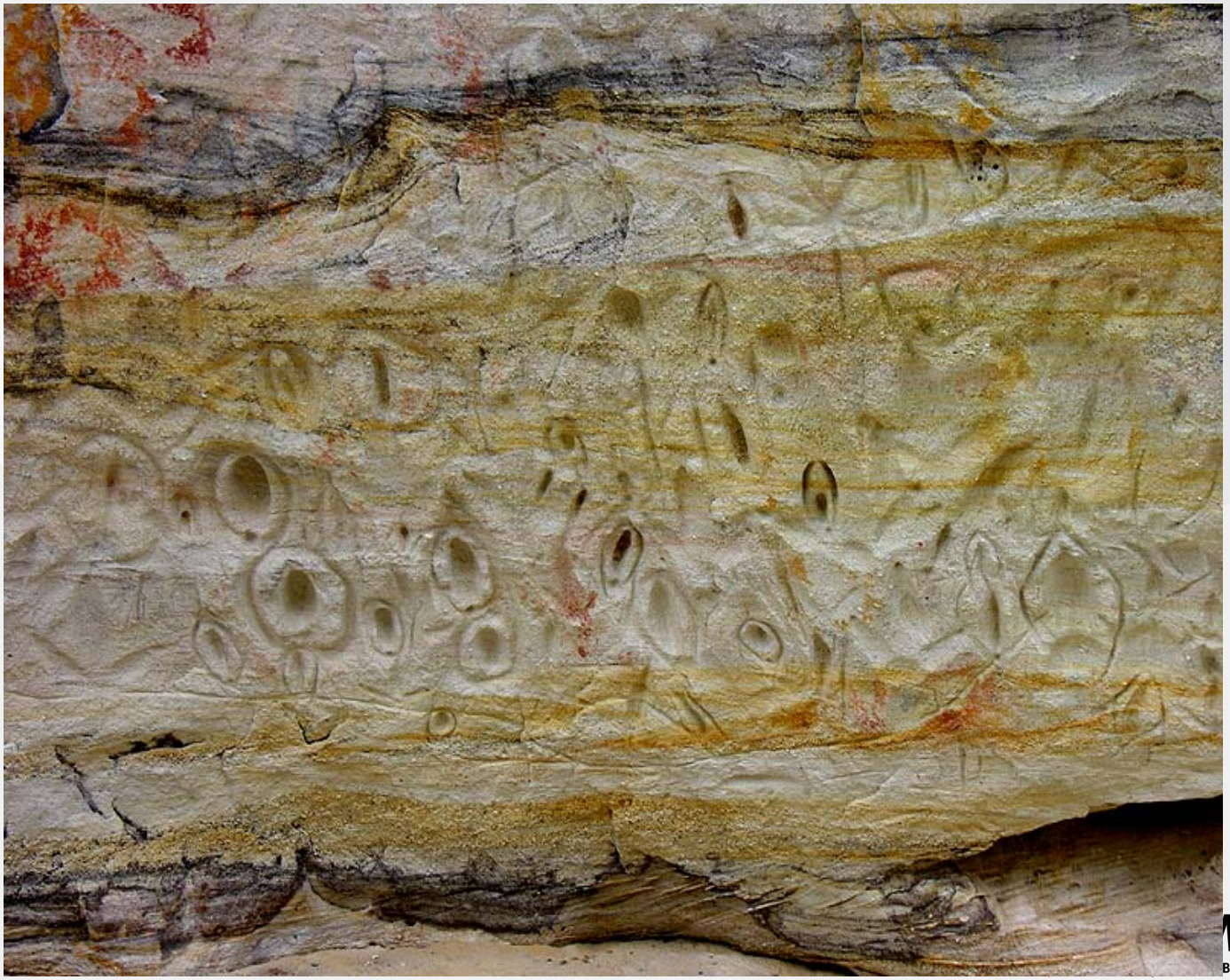
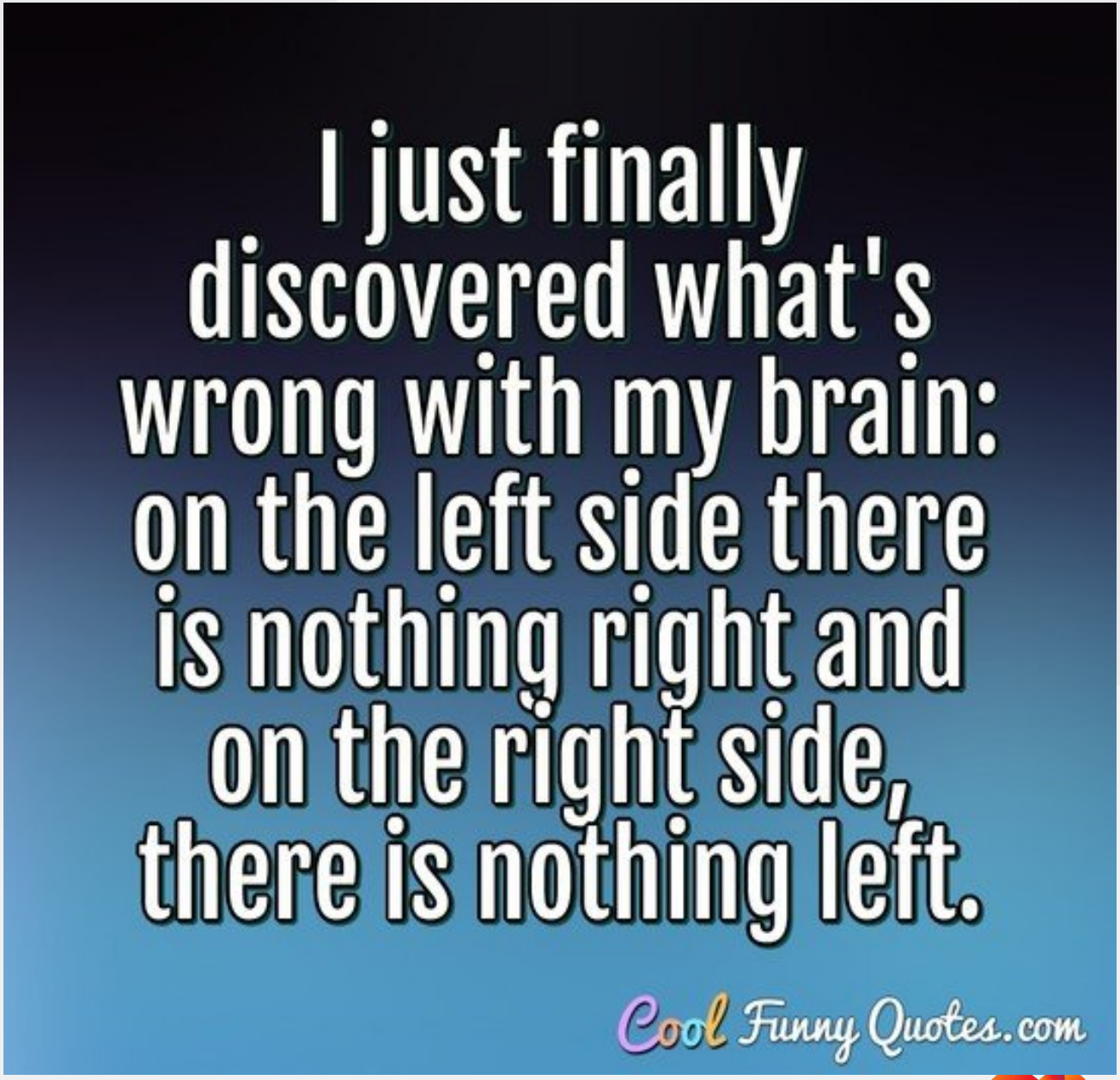
Whose vulva is it anyway?





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