Galactorrhoea

Synonym: *lactorrhoea*

Galactorrhoea is milky secretion from the breasts. The term usually refers to milk secretion not due to breastfeeding. It is bilateral and from multiple ducts. The milk volume may be large or small, and milk may be secreted spontaneously or expressed.

Physiology of lactation and prolactin [1] [2]

Lactation requires prolactin (PRL). Other hormones are involved in priming the breast prior to lactation: oestrogen, progesterone, insulin, thyroid hormones and glucocorticoids. Oxytocin is involved in milk release. Conversely, oestrogens and progesterone can also have an inhibitory effect on lactation: the fall in levels after delivery facilitates lactation, whilst an injection of oestrogen was used in the past to inhibit lactation.

PRL is unique amongst the pituitary hormones in that it is regulated by an inhibitory factor from the hypothalamus, whilst the other hormones are regulated by a releasing factor. This inhibitor is mainly dopamine. However, thyrotrophin-releasing factor (TRF) causes the release of not just thyroid-stimulating hormone (TSH) but prolactin too. Hence, acquired hypothyroidism may be associated with elevated PRL. Serotonin may also be involved in PRL release.

There is a physiological increase in PRL levels in response to pregnancy, breast stimulation (especially sucking), stress, sleep, dehydration, sexual intercourse, seizures, exercise and food ingestion.

Epidemiology

Galactorrhoea is much more common in women than in men. It is most common in women of reproductive age, but can occur in nulliparous women, menopausal women, and men. In women it may be physiological but in men it is always pathological. Nipple discharge (of any type) accounts for 2-5% of referrals to a breast clinic (due to the association with breast cancer) but should not be seen as synonymous with galactorrhoea. [3]

Hyperprolactinaemia is the most common cause, and as many as 90% of women with hyperprolactinaemia have galactorrhoea. The prevalence of non-pregnant hyperprolactinaemia is around 0.2% in the adult population with an incidence of 13.8 cases per 100,000 person-years and is 3.5 times higher in women than men. [4]

Aetiology

When galactorrhoea is accompanied by amenorrhoea, it is usually caused by hyperprolactinaemia.

Physiological

- Pregnancy and post-lactation: women may lactate from the second trimester, and may continue to produce milk up to two years after stopping breastfeeding.
- Fluctuating hormone levels: puberty and the menopause.
- Neonatal: exposure to maternal hormones in utero can produce gynaecomastia and galactorrhoea in the newborn (sometimes known as 'witch's milk'); no action is required and it will subside rapidly and spontaneously.
- Nipple stimulation or suckling.

Non-physiological causes of hyperprolactinaemia

- Idiopathic hyperprolactinaemia (40% of cases of hyperprolactinaemia).
- Prolactinomas (PRL levels are usually very high in this case as the tumour causes hypersecretion of PRL).

- Other causes of hypersecretion of PRL:
    - Addison's disease.
    - Acromegaly.
    - Cushing's disease.
    - Metastatic tumours.
    - Infections such as tuberculosis.
    - Sarcoidosis.
    - Histiocytosis.
- Drugs (see 'Drugs that raise PRL', below).
- Systemic disorders:
    - Chronic kidney disease.
    - Liver failure.
    - Hypothyroidism.
    - Epileptic seizures.
- Chest wall lesions or irritation:
    - Breast surgery.
    - Burns.
    - Herpes zoster.
    - Spinal cord injury.
    - Trauma.

- Pituitary stalk infiltration or interruption, due to:
    - Sarcoidosis, tuberculosis, or schistosomiasis.
    - Multiple sclerosis.
    - Resection of the pituitary stalk.
    - Tumours: meningioma, craniopharyngioma, dysgerminoma, dermoid cyst, pineal gland tumours.
    - Empty sella.
    - Rathke's cyst.
    - Irradiation.
    - Trauma.

Drugs that raise PRL

Typically the level of prolactin will be lower than 200 ng/ml.[5]

The following list is not comprehensive but drugs which raise PRL include:

- Antipsychotics - the most common drugs to cause hyperprolactinaemia:
  - Traditional phenothiazine antipsychotics (chlorpromazine, prochlorperazine, thioridazine, trifluoperazine) and haloperidol.
  - Atypical neuroleptics may also be implicated, but less frequently. Risperidone is the most likely to cause a raised PRL, also amisulpride. Olanzapine is less likely to do so.
- Antidepressants, especially the **selective serotonin reuptake inhibitors** (SSRIs). Monoamine-oxidase inhibitors (MAOIs) and some tricyclic antidepressants (TCAs) less often.
- H_2 antagonists, especially cimetidine.
- Antihypertensives, including beta-blockers, methyldopa and verapamil.
- Contraceptives, including combined oral contraceptives and depot contraceptives.
- Prokinetics: domperidone, metoclopramide.
- Illicit drugs, including cannabis, opiates and amfetamines.
- Various others, including digoxin, spironolactone, opiates, danazol, sumatriptan, isoniazid and valproate.

Normoprolactinaemic causes of galactorrhoea

Idiopathic galactorrhoea. When all else has been excluded, what remains is labelled as idiopathic. Female patients with galactorrhoea but normal PRL levels, normal thyroid function and regular periods can probably be observed.

Presentation

History

- Duration of symptoms, progression, nature, colour and amount of fluid.
- Unilateral or bilateral discharge (unilateral suggests local pathology, and needs breast clinic referral).

- Ask whether it is spontaneous or has to be expressed.
- Note the timing of the last menstrual period. Suspect pregnancy until proved otherwise.
- Drugs: prescribed, over-the-counter and illicit; herbal treatments and dietary supplements.
- Ask about acne, hirsutism, menstrual irregularity, reduced libido, infertility and erectile dysfunction (symptoms of hyperprolactinaemia).
- Thyroid and other endocrine symptoms.
- Ask about headaches, visual symptoms and cranial nerve symptoms (for pituitary tumours).

Examination

- Thyroid gland, signs of hypothyroidism, Cushing's disease or acromegaly.
- Neurological examination including visual fields (if an intracranial or pituitary tumour is suspected).
- Abdominal palpation for pregnancy.
- Examine the breasts:
    - Note whether discharge is seen and, if so, whether it looks milky or bloodstained. If no discharge is apparent try gently massaging the breasts, or ask the patient to do so, to try to express some fluid. Note whether it is bilateral and from multiple ducts.
    - Note any previous breast surgery or abnormality of the surrounding skin.
    - Palpate for lumps and nodes.

Differential diagnosis

Breast disease

- Mammary duct ectasia can cause nipple secretions which may be milky or discoloured in appearance. The discharge can be bilateral and from multiple ducts.
- Duct papilloma typically causes serous or bloodstained discharge from a single duct. Underlying malignancy is rare but needs excluding.
- Persistent discharge through a fistula following an abscess.

Investigations

Initial investigations

- PRL levels (see the separate Hyperprolactinaemia and Prolactinoma article). Very high levels suggest prolactinoma. If PRL levels are not elevated, further investigations (such as hormone levels and scans) are not required.
- TFTs (it is important to exclude hypothyroidism).
- Renal and liver function.
- Pregnancy test if appropriate.

Further investigations

May be needed:

- Formal testing of visual fields: defects suggest optic nerve compression and merit urgent referral.
- MRI scan - needed, for example, if PRL levels are significantly raised and not explained by any other cause, or if there is irregular menstruation. CT scans may be used if MRI is unavailable, but MRI is the scan of choice.
- Other endocrine assessments (eg, for Cushing's disease or acromegaly) may be appropriate.
- If the nature of breast secretions is unclear, microscopy may be used.

Management

- Exclude serious pathology: investigations as above; exclude breast disease.
- Identify and treat the cause, if possible:
    - Treat hypothyroidism.
    - Management of prolactinomas is described in the separate Hyperprolactinaemia article.
    - Review/change any contributing drugs.
- If the cause cannot be addressed, consider:
    - Dopamine agonists such as bromocriptine or cabergoline - treatment details are also in the Hyperprolactinaemia article. Cabergoline is thought to be more effective in reducing galactorrhoea.[5]
    - These dopamine agonists may also be used in those with normal PRL levels if galactorrhoea is troublesome and reassurance alone is not sufficient. This usually resolves the galactorrhoea within two months and the medication can then be stopped.
    - Hormone treatment: testosterone for men or oestrogens for women (eg, the combined oral contraceptive pill). These help to prevent osteoporosis and may improve symptoms.

Complications and prognosis

These depend on the underlying cause. There is probably an increased risk of osteoporosis if hyperprolactinaemia is untreated.

Further reading

- Position statement on the use of dopamine agonists in endocrine disorders; Society for Endocrinology (Feb 2009 - reviewed Nov 2011)

- Huang W, Molitch ME; Evaluation and management of galactorrhea. Am Fam Physician. 2012 Jun 1;85(11):1073-80.
- Vroonen L, Daly AF, Beckers A; Epidemiology and Management Challenges in Prolactinomas. Neuroendocrinology. 2019;109(1):20-27. doi: 10.1159/000497746. Epub 2019 Feb 7.

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