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Medical Newsletter

THE RISE IN STIs POST-COVID

Special Edition

By Dr Sudha Pottumarthy-Boddu, Dr Stella Pendle and Dr Linda Dreyer

The Changing Landscape of STIs: Test, Detect and Treat are the Keys to Control

By Dr Sudha Pottumarthy-Boddu

The impact of the COVID-19 pandemic extends beyond economic and social disruption, with a direct and indirect impact on the health of individuals worldwide. The low coverage for prevention, testing, and treatment services for STIs during the pandemic has led to a resurgence of STIs globally. Over 1 million new sexually transmitted infections are acquired worldwide every day, with the majority being asymptomatic. The World Health Organization (WHO) in 2020 estimated 374 million new infections with one of the four common STIs: chlamydia (129 million), gonorrhoea (82 million), syphilis (7.1 million), and trichomoniasis (156 million). The incidence of genital infection with herpes simplex virus (HSV) among 15 to 49-year-olds is estimated to be over 500 million[1].

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Post-pandemic resurgence: STI trends in Australia

Trends in key bacterial notifiable STIs, as noted in the National Communicable Disease Surveillance Dashboard of Australia, mimic the global trends[2]. Three years, 2020 to 2022, saw a drop in notifications compared to 2019, reflecting the impact of the pandemic (see Table 1). However, 2023 saw a resurgence of STIs, with notifications significantly higher than in 2019, especially for syphilis < 2 years duration (8.6 % increase), gonococcal infection (16% increase), and congenital syphilis (400% increase; 4 each in VIC, WA, and NSW and 5 in QLD) (Table 1)[2].

"2023 saw a resurgence of STIs, with notifications significantly higher than in 2019..."

Rising congenital syphilis cases in the US

Addressing missed opportunities, the CDC (Centers for Disease Control) reported a 755% increase in congenital syphilis cases in the United States from 2012 to 2021 (335 versus 2,865 respectively), with 3,761 cases reported in 2022 (231 stillbirths and 51 infant deaths)[3]. Lack of timely testing and adequate treatment during pregnancy contributed to almost 90% of these preventable cases.

Table 1. Trends in Key Notifiable STIs in Australia – 2019 to 2023

STI	2019	2020	2021	2022	2023
Chlamydial infection	107,396	91,449	87,367	94,365	109,894
Gonococcal infection	34,745	29,801	26,599	33,148	40,404
Syphilis < 2 years of duration	5915	5361	5775	6180	6451
Syphilis > 2 years or unspecified duration	2609	2192	2186	2623	2795
Congenital Syphilis	4	17	15	15	20

New infections and antibiotic resistance

In addition to the ongoing impact of recognised STIs, other concerning facts include:

- New infections that can be acquired by sexual contact have emerged and are leading to outbreaks in some instances. These include mpox, *Shigella sonnei, Neisseria meningitidis*, Ebola and Zika, along with the re-emergence of neglected STIs like lymphogranuloma venerum (LGV)[1].
- Emergence and spread of multi-drug-resistant gonorrhoea: Resistance of *N.gonorrhoeae* to the available antimicrobial options continues to evolve, with recognition of high levels of resistance to ciprofloxacin, increasing resistance to azithromycin, and resistance or decreased susceptibility to cefixime and ceftriaxone[4].

STI co-infections: Implications and recommendations

Accurate rates of STI co-infections are often difficult to discern as the infections are notified separately. However, it is well recognised that persons at risk of STI acquisition are also at risk of co-infection with more than one STI. Co-infection of *Chlamydia trachomatis* in individuals diagnosed with *Neisseria gonorrhoeae* is well recognised. However, there is paucity of data on the co-infection of chlamydia and gonorrhoea among persons with early syphilis.

A recent study from the University of Birmingham in Alabama reported that of the 865 adults enrolled for a controlled trial for treatment of early syphilis, 234 (27%) adults had also had documented STI co-infection, of whom 29% had *N. gonorrhoeae*, 22% had *C.trachomatis*, and 23% had both. Multisite STI screening for multiple pathogens is recommended for sexually active adults at risk to identify both symptomatic and asymptomatic infections.

"Multisite STI screening for multiple pathogens is recommended for sexually active adults at risk to identify both symptomatic and asymptomatic infections."

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THE RISE IN STIs POST-COVID

Neisseria meningitidis: A newly emerging sexually transmitted infection

By Dr Stella Pendle

N. meningitidis and *N. gonorrhoeae*: Causes and risks

Neisseria meningitidis (NM) is typically found as a commensal in the upper respiratory tract of humans and is a leading cause of sepsis. It has the unique ability to cause outbreaks of invasive meningococcal disease, which can be fatal. *Neisseria gonorrhoeae* (NG) traditionally causes gonorrhoea, a sexually transmitted infection involving the genitals, rectum, and throat. These species usually occupy distinct niches but may cause reciprocal diseases. NM may also occasionally be found in the genital tract as a commensal. It has long been recognised that urethral NM infections could be spread by oral sex and were more common in men who have sex with men[1].

Urogenital and anogenital infections due to *N. meningitidis*

In recent years, there have been increasing reports worldwide of urogenital and anogenital infections attributed to NM. These may mimic the symptoms of gonorrhoea, causing urethritis, proctitis, cervicitis, and pelvic inflammatory disease, which is indistinguishable from gonorrhoea. In addition, meningococcal urethritis has been documented in long-term monogamous relationships in which the partner has no disease[2,3].

Changing patterns of meningococcal urethritis

At the beginning of the 21st century, meningococcal urethritis was considered to be a rare condition, found almost entirely in MSM and transmitted by oral sex. More recently, clusters of meningococcal urethritis were identified predominantly in heterosexual men, mainly in the 20 to 30 years age group. Symptoms included urethral discharge (>90%) and dysuria, with symptoms ranging from 2 to 7 days. Almost all men with meningococcal urethritis reported oral sex encounters. However, genital-genital and ano-genital infection can also occur. Like *N. gonorrhoeae, N. meningitidis* can also cause cervicitis, vulvovaginitis, pelvic inflammatory disease, salpingitis, endometritis, and proctitis. Neonatal conjunctivitis and pre-term birth have also been reported. Cases of invasive meningococcal disease (IMD) secondary to infection and colonisation of urogenital or anorectal sites have been reported, mainly in females.

Diagnostic considerations: Co-infections

In patients who present with urethritis or other symptoms suspicious for a sexually transmitted infection, it is important to consider co-infections with other STIs. 15 to 19% of men may have a concurrent infection with *Chlamydia trachomatis* (CT). It is therefore important to test for both chlamydia and gonorrhea by nucleic acid tests (NATs). Either a first-void urine or urethral swab is suitable for these tests. In addition, a further swab for bacterial culture should be ordered.

Laboratory diagnosis of meningococcal anogenital infection

Gram stain is routinely performed on all genital swabs. The presence of Gram-negative cocci on the gram stain, and increased numbers of leucocytes, predominantly neutrophils, is suggestive of urethritis but cannot distinguish between NG and NM.

Bacterial culture is, therefore, the mainstay of diagnosis. Depending on the site of infection, collection of a urethral, genital, or anorectal swab for bacterial culture is required.

NM will not be detected by routine STI screening if only nucleic acid amplification tests (NATs) are used, but testing should be performed to rule out other infections. Dual infections with both *Neisseria meningitidis* and *Neissseria gonorrheae* can also occur, and previous infections with NG are common in MSM.

PCR testing of NG and CT without bacterial culture could lead to a missed diagnosis as the PCR can only detect *Neisseria gonorrhoeae*; it will not detect *Neisseria meningitidis*. Currently, there is no TGA-authorised PCR test available for the detection of meningococcal urethritis or anogenital infection.

There have been over 30 cases of NM at a urogenital or anorectal site reported in NSW since September 2023, and it is likely that many have gone undetected. The importance of actively testing, detecting, and treating cannot be overemphasised.

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THE RISE IN STIs POST-COVID

Mycoplasma genitalium: An Emerging Concern

By Dr Linda Dreyer

***Mycoplasma genitalium* is a bacterium that causes non-gonococcal urethritis (NGU) in men and disease in the lower and upper reproductive tract of women.**

Prevalence and risk factors

The prevalence of *Mycoplasma genitalium* in young adults (18-27 years old) is estimated to be approximately 1%, but is as high as 15-25% in men with symptomatic NGU and up to 15% of women with pelvic inflammatory disease (PID). In Melbourne, asymptomatic infection was detected in 9.5% of men who have sex with men (MSM). Rectal positivity was higher than urine (7.0% vs. 2.7%), and co-infection with other STIs was found in 17%.

Collection recommendations for accurate diagnosis

Mycoplasma genitalium presents with clinical symptoms and signs very similar to other STIs like chlamydia and gonorrhoea, which may complicate its diagnosis. Nucleic acid amplification tests (NAATs) are the recommended diagnostic method, offering high sensitivity and specificity. The best sample to obtain is a first-pass urine sample in male patients or a high vaginal swab in female patients. A cervical swab is slightly less sensitive, with a first-pass urine sample being the least sensitive in female patients. In high-risk populations, a rectal swab should also be collected. As pharyngeal infection is uncommon, a throat swab is not indicated.

The growing challenge of antibiotic resistance

The primary concern in treating *Mycoplasma genitalium* is its increasing resistance to antibiotics. Azithromycin (macrolide) resistance is widespread, prompting a shift towards alternative regimens like moxifloxacin. However, resistance to moxifloxacin is also emerging, creating a significant challenge in management. In Australia, the current resistance rate of azithromycin exceeds 60% in the majority of cases and is even as high as 80% in the MSM population.

Treatment is based on the test results and clinical presentation. See STI guidelines.

A doctor's role in prevention

Preventive measures are crucial in managing *Mycoplasma genitalium*. Regular STI screening, safe sex practices, and public health campaigns can significantly mitigate its spread. It is vital for doctors to counsel patients on safe sex practices and the importance of regular screening. However, the significance of *M. genitalium* in asymptomatic individuals remains uncertain. Currently, local guidelines advise against testing asymptomatic patients unless they were exposed to known contact.

Managing the *Mycoplasma genitalium* challenge

Mycoplasma genitalium represents a significant and growing challenge in sexual health. The evolving nature of its antibiotic resistance profile necessitates a vigilant approach to diagnosis, treatment, and public health strategies. Continuous education and updated guidelines are essential to effectively manage this emerging STI.

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Important Updates from STI Guideline Changes 2020-2022

For more information, please visit sti.guidelines.org.au/whats-new.

Standard asymptomatic check-up: HIV and syphilis testing should be included whenever STI testing is indicated.

Chlamydia: To improve antibiotic stewardship, immediate treatment is not recommended for all sexual contacts of chlamydia – instead, offer testing of exposed anatomical sites and await results.

Sex-associated diarrhoea: Among reports of increasing drug-resistant shigellosis among MSM, there is a need for expert local advice and stool culture when treating diarrhoea in MSM.

Skin rash and lesions: Primary care clinicians are encouraged to think about STIs when examining, testing and managing clients with rashes, lumps and lesions that might not be on the genital skin.

The Changing Landscape of STIs: A GP's perspective

By Dr David Baker

Dr David Baker, a GP and Director of East Sydney Doctors, has worked in Darlinghurst for over twenty years. He has a special interest in Sexual Health and HIV Medicine and has completed additional training at The University of Sydney – obtaining a Diploma in Medicine (Sexual Health).

As we have all seen over the last few years, we need to expect the unexpected in health care. This remains true in the world of Sexually Transmitted Infections (STIs), as we saw with the rise and fall of monkeypox (now renamed mpox).

Some things don't change. GPs continue to play a vital role in the prevention, diagnosis, and treatment of STIs. Getting to know our patients is very important, especially when it comes to screening for STIs. With a new patient, we can ask about their background in terms of sexual behaviour, relationship status, and risk factors such as travel history. STI testing will depend on the clinical situation as well as the patient's background.

Testing guidelines: asymptomatic patients

Current guidelines recommend testing for asymptomatic patients to include first-catch urine for chlamydia and gonorrhea PCR testing, along with a blood test for HIV antigen/antibody, syphilis serology, and hepatitis B serology (HBsAg, anti-HBs, anti-HBc)[1]. Patients should be vaccinated for hepatitis B if not immune.

Additional guidelines: MSM

Men who have sex with men (MSM) are recommended to also have anal and rectal swabs for chlamydia and gonorrhea PCR testing, to undergo sexual health screenings every 3 months, and to receive an annual hepatitis C antibody test (hepatitis C is rarely an STI but can be transmitted in MSM).

HIV cases decline thanks to PrEP

HIV infections in Australia have markedly declined to 552 HIV notifications in 2021, a 48% decline since 2012[2]. Increasingly, infections are occurring in females and people born overseas. HIV rates have fallen in the MSM population largely due to the increased use of Pre-exposure Prophylaxis (PrEP) – antiretroviral medications taken prior to sex. All MSM should be encouraged to use PrEP. Even though HIV rates are falling, it is very important to continue regular HIV testing, as HIV is now manageable with modern treatment but has a much better outcome if diagnosed early.

Rise in syphilis: Be aware of generalised rashes

Syphilis rates have greatly increased over the last 10 years, particularly in MSM populations as well as in Aboriginal and Torres Strait Islander people. Syphilis has been called the 'Great Mimic' as it causes a wide range of symptoms. Primary syphilis is a painless ulcer at the site of infection but is often missed. Secondary syphilis occurs 6 weeks or so later with a wide range of symptoms, particularly a rash. Tertiary syphilis occurs usually years later and involves many organ systems. Most patients are diagnosed by serology. An important take-home message is to order syphilis serology for any generalised rash. Treatment is usually with intramuscular penicillin.

"GPs continue to play a vital role in the prevention, diagnosis, and treatment of STIs."

Drug resistance amidst the rise in gonorrhoea cases

Gonorrhoea rates have also increased. Multidrug-resistant gonorrhoea is emerging around the world and has been reported in Australia. It is important to follow treatment guidelines and, if possible, obtain a sample for resistance testing[1].

Order *mycoplasma genitalium* for symptomatic patients

Mycoplasma genitalium is an uncommon cause of urethritis and cervicitis. Order this test if patients are symptomatic (e.g., urethral discharge) but not as a screening test. A swab or first-catch urine PCR test should be collected. Treatment is complex and is guided by sensitivity testing.

Mpox prevention through vaccination

This infection is largely in the MSM population, with exposure mostly occurring while travelling. The usual symptoms are lesions or ulcers around the body. If suspected, a swab for PCR should be taken, and the laboratory notified. Case numbers have dropped, with only 26 cases in Australia in 2023, making this a rare STI[3]. Note: Mpox can now be prevented by vaccination.

Genital wart cases declining thanks to HPV vaccination

A good news story is that genital wart infections are on the decline, thanks to universal HPV vaccination.

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Bulk-Billed Genetic Carrier Screening: A milestone for preventative medicine

By Associate Professor Mirette Saad

MBS UPDATE
Bulk-Billed
Genetic Carrier Screening
Now Available

On 1st November, 2023, Genetic Carrier Screening for cystic fibrosis (CF), spinal muscular atrophy (SMA), and fragile X syndrome (FXS) was added to the MBS, marking a significant milestone in accessible healthcare for all Australians. In the following article, we provide information on the covered conditions, outline the Medicare eligibility criteria, and share insights from several GPs on the transition to bulk-billing for this testing. This shift represents a significant advancement in preventative medicine within the domain of general practice, ultimately enhancing accessibility and affordability for patients.

Screening for CF, SMA, and FXS

Clinical Labs' Genetic Carrier Screening test for CF, SMA, and FXS provides patients with information regarding their chances of having a child with any of these conditions.

- One in 20 people are carriers of at least one of these conditions;
- 90% of carriers have no family history;
- One in 160 couples will be found to be at risk of having an affected child.

Cystic fibrosis (CF)

- CF is a severe autosomal recessive genetic condition that causes lung and gastrointestinal problems
- Approximately 1 in 25 people are carriers of CF
- Clinical Labs' CF screening covers more than 75 common mutations in the CFTR gene
- CF affects approximately 1 in 2,500 people

Spinal muscular atrophy (SMA)

- SMA is an autosomal recessive inherited neuromuscular disease historically associated with high morbidity and mortality
- Approximately 1 in 35 people are carriers of SMA
- Clinical Labs' SMA screening identifies deletions of the SMN1 gene (one copy), which account for approximately 96% of the mutations in this gene
- SMA affects approximately 1 in 6,000 people

Fragile X syndrome (FXS)

- FXS, an X-linked condition, is the most common inherited form of intellectual disability
- Approximately 1 in 330 people are carriers of FXS
- FXS carrier screening is recommended for females, as it is inherited in a different way to CF and SMA. Female patients who have the gene change (number of CGG triplet repeats) in the FMR1 gene are found to be at risk of having a child affected by FXS, as the abnormal gene may expand over generations
- The size of these CGG triplet repeats determines the chance of the FXS gene failing to function in a normal way and, therefore, the clinical presentation
- Males can also carry the faulty FMR1 gene on their one X chromosome and may pass it on to their daughters. (Testing would incur a private fee - not eligible for Medicare billing)
- FXS affects approximately 1 in 3,600 men and 1 in 6,000 women

In addition to bulk-billed screening, Clinical Labs also offers expanded carrier screening options at an out-of-pocket cost for patients who want a broadened assessment of their risk of having a child with a genetic condition. For information about our Comprehensive and Ashkenazi Jewish Carrier Screening tests, visit antenatal.clinicallabs.com.au/doctor/carrier-screening.

Medicare Eligibility Criteria

Bulk-billed genetic carrier screening is now available to determine a couple's combined risk of having a child with a genetic condition. Testing is available for all individuals, even those with no symptoms or family history. Male partners of the biologically female positive cases for CF or SMA (not FXS) are eligible for testing under Medicare cover. Please see below for specific Medicare criteria. Private fee may apply if criteria are not met.

New items 73451 and 73452

The patient who is planning pregnancy or already pregnant should be tested first under MBS item 73451 prior to testing the reproductive partner patient under MBS item 73452 to ensure an informative and clinically relevant test result is obtained in the relevant gene.

73451

Testing of a patient who is pregnant or planning pregnancy to identify carrier status for pathogenic or likely pathogenic variants in the following genes, for the purpose of determining reproductive risk of cystic fibrosis, spinal muscular atrophy, or fragile X syndrome:

a. CFTR;

b. SMN1;

c. FMR1.

One test per lifetime.

The intent of MBS item 73451 is to test an asymptomatic female chromosomal sex patient who is either planning a pregnancy or is already pregnant.

73452

Testing of the reproductive partner of a patient who has been found to be a carrier of a pathogenic or likely pathogenic variant in the CFTR or SMN1 gene identified by testing under item 73451, for the purpose of determining the couple's reproductive risk of cystic fibrosis or spinal muscular atrophy.

One test per condition per lifetime.

The intent of MBS item 73452 is to test an asymptomatic male chromosomal sex patient who is the reproductive partner of the patient planning pregnancy or already pregnant and has been tested under item 73451.

Recommended by clinical guidelines

Genetic Carrier Screening should now be a routine part of pre and early pregnancy clinical management by GPs and specialists, with both RANZCOG[1] and RACGP[2] guidelines recommending that genetic carrier screening be offered to every woman and couple who are planning or in the first stage of pregnancy, regardless of their risk factors.

The importance of early screening

It is always recommended that testing is undertaken prior to pregnancy so that this vital information is known early, offering greater reproductive choices, such as:

- pre-implantation genetic diagnosis through IVF,
- using donor eggs (or donor sperm for CF and SMA),
- donor embryos, or
- adoption.

Early detection is paramount as it also allows more time for counselling.

GP

The Impact of Preventive Care in General Practice

By Dr Jung Yoon Huh
Medical Principal of The Madison Medical Practice Northbridge, NSW

General practice holds a unique place in the healthcare system due to its focus on preventive care. It's the very reason I chose this specialty and a sentiment shared by many of my colleagues. While it may not have the glamour of high-profile surgeries often depicted in medical shows, its significance runs deep.

I was thrilled when reproductive carrier screening became accessible through Medicare last November. This test targets two autosomal recessive disorders and one X-linked disorder: cystic fibrosis (CF), spinal muscular atrophy (SMA), and fragile X syndrome (FXS). The process is remarkably straightforward—a simple blood test with results delivered within weeks. If a woman is not a carrier, the journey ends there. However, if she is a carrier, the next step involves testing her current partner and providing genetic counselling as needed.

Although this can be conducted during pregnancy, a positive result can lead to more complex and distressing implications. That's why I seize every opportunity to introduce this screening test during various consultations. Whether discussing contraception, STI screenings, routine vaccinations for infants, or addressing concerns like heavy menstrual bleeding and iron deficiency, I broach the topic. Recognising the time constraints many women face—juggling work and family—I provide written materials and a request form, allowing them to choose the most convenient time for the test.

The brilliance lies not only in the test's accessibility and simplicity but also in its potential to transform lives. For prospective parents, it offers a chance to prevent these conditions in their children—an opportunity that is priceless and life-changing. In the realm of general practice, prevention and education are as vital as treatment. So, let us continue our proactive journey, championing health and well-being.

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How to interpret test results

Status: Confirmation of patient's carrier status for the tested condition (CARRIER/NON-CARRIER).

Interpretation: Patient's risk of having a child with the specific genetic condition.

Recommendations: Pathologist's advice on next steps regarding partner or follow-up testing/genetic counselling:

- If **patient** is found to be a **CARRIER for CF or SMA →** testing of reproductive partner is RECOMMENDED for that specific condition
- If **Patient** is found to be a **NON-CARRIER for CF or SMA →** testing of reproductive partner is NOT REQUIRED
- If the **reproductive partner** is also found to be a **CARRIER for CF or SMA →** genetic counselling is recommended (see below for details)
- If the **patient** is found to be in the **pre-mutation or full mutation range for FXS →** genetic counselling is recommended (see below for details)

Figure 1. Extract from Clinical Labs Genetic Carrier Screening Report for CF, SMA, and FXS

Test Results		
CONDITION / GENE	**STATUS**	**RESULT**
Cystic Fibrosis (CFTR)	**CARRIER****	**Heterozygous carrier for NM_12345.6: c.1521_1523del, p. (F508del)**
Spinal muscular Atrophy (SMN1)	Non-Carrier	At least two copies of the SMN1 gene detected
Fragile X syndrome (FMR1)	**Premutation Range**	**Premutation range allele(s) detected 70,30**

Interpretation		**Recommendations**
Cystic Fibrosis (CF)	**HIGH RISK. This individual is a heterozygous carrier for a variant in the CFTR gene. The risk of having a child with CF is 1 in 100.**	**Genetic counselling and partner testing are recommended.**
Spinal muscular Atrophy (SMA)	This individual has at least two copies of the SMN1 gene.	N/A
Fragile X syndrome (FXS)	**HIGH RISK.**	**Genetic counselling recommended.**

Supporting you with genetic counselling for positive cases

For positive cases (tested by Clinical Labs), Clinical Labs offers one genetic counselling session per couple at no cost. Any follow-up consultations, if necessary, will incur an out-of-pocket fee.

- We will notify the referring clinician and provide contact details for the genetic counselling service.
- The referring doctor can either contact the genetic counsellor to schedule the appointment, or the consultation can be organised through the lab.
- Appointments are conducted over the phone and are generally available within 48 hours of referral.

During the call, which lasts 15-20 minutes, the genetic counsellor will discuss the risk of having a child carrying this condition with the patient and their partner. It is also optional for the referring clinician to be on the call.

Please note: The genetic counselling request must be made within two weeks of receiving the partner's CARRIER test results. For FXS, only pre-mutation and full mutation cases are offered genetic counselling.

Supporting you through every stage of your patient's pregnancy journey

In addition to genetic carrier screening, Clinical Labs also offers a wide range of routine and advanced antenatal pathology tests for patients, including our non-invasive prenatal test (NIPT), Harmony.

Australian clinical guidelines (RANZCOG[3]) recommend that doctors discuss NIPT with all pregnant women. Harmony NIPT screens for common foetal chromosomal abnormalities, including Down syndrome. It also evaluates foetal sex, sex chromosome aneuploidy conditions, and offers optional screening for 22q11.2 deletion (DiGeorge syndrome) at an additional cost to the patient. DiGeorge syndrome affects an estimated 1 in 1,000 pregnancies[4,5] and is the second most common genetic cause of heart defects and developmental delay after Down syndrome[6].

For more information about Harmony NIPT and other antenatal tests offered by Clinical Labs, visit antenatal.clinicallabs.com.au/doctor.

The Role of Genetic Carrier Screening in Women's Health Consultations

GP

By Dr Sumudu Udapitiya
General Practitioner providing Shared Obstetric Care, Cranbourne West Medical Centre, VIC

I have been working as a GP in Australia since 2018 and am currently working at Cranbourne West Medical Centre in Victoria. My special interests include women's health, and I also provide shared obstetric care for women. This places me in an ideal position to discuss preventive health and pregnancy planning with patients.

Having a healthy baby is the expectation of every woman planning a pregnancy. Genetic carrier screening, along with other general health assessments, plays a significant role in achieving this goal.

I have been offering pre-pregnancy genetic carrier screening from the start during all pregnancy planning consultations and have been discussing it opportunistically in women's health consultations. I usually explain it with pictures to illustrate how genetic conditions are inherited and carried hidden among generations when the condition is autosomal recessive and X-linked. I also provide figures about carrier status to emphasise the importance of testing. Since there is no longer an out-of-pocket cost, I have seen a marked increase in acceptance for testing by most women.

As this is also a once-in-a-lifetime test, it gives the patient a sense of reassurance for future pregnancies if they are not a carrier or helps them plan for future pregnancies if they are a carrier. Testing in pre-pregnancy allows women to access genetic counselling in a timely manner and plan for a healthy baby.

Ordering Genetic Carrier Screening with Clinical Labs

How to order: To order bulk-billed screening for CF, SMA, and FXS, please complete the Clinical Labs Genetic Carrier Screening Request Form located at antenatal.clinicallabs.com.au/doctor/carrier-screening. This form is also available as an .rft file that can be uploaded to Best Practice or MedicalDirector, and will be hosted in Best Practice as a template in March. Please also provide any relevant family or partner history when completing the request form.

Testing locations: Your patients can visit any of our 1,300 collection centres for their carrier screening blood test. Locations can be found at clinicallabs.com.au/location.

Turnaround time: Results for CF, SMA, and FXS testing will be available within 5-7 business days from the time we receive the sample at our laboratory.

Test cost: Genetic carrier screening for CF, SMA, and FXS is bulk-billed once in a patient's lifetime. Please see above for Medicare eligibility criteria.

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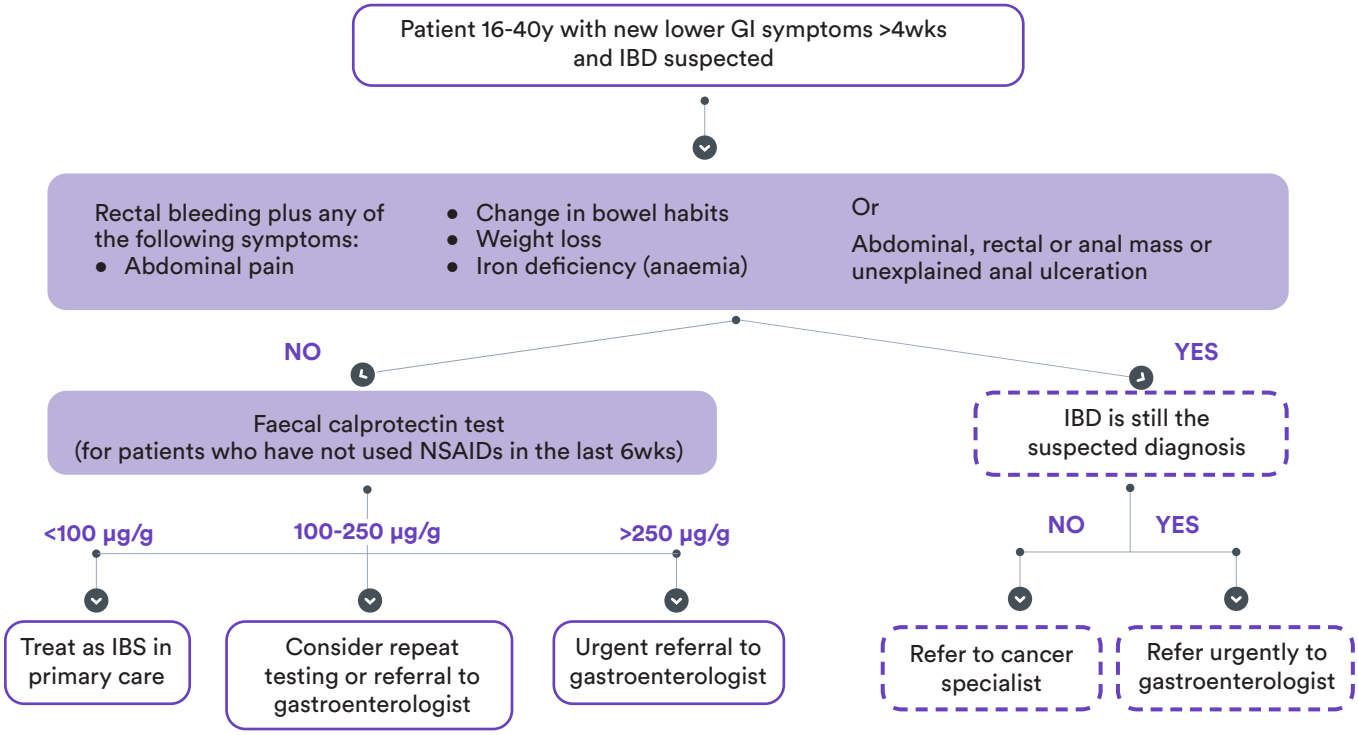
The Role of Calprotectin Testing in the Diagnosis and Management of IBD

By Associate Professor Louise Smyth

MEDICARE-Rebatable*

Faecal calprotectin concentration is a useful, non-invasive method for distinguishing between organic and functional diarrhoeal disorders and for monitoring disease activity in established cases of gut wall inflammation.

Figure 1. Use of faecal calprotectin test in primary care



(After Lamb, Kennedy, Raine, et al., 2019)

Faecal calprotectin

Widespread clinical application of measuring calprotectin levels has evolved for the non-invasive investigation of diarrhoeal gut disease since the beginning of this century. Calprotectin in faeces has been shown to be a robust measure of neutrophilic inflammation of the intestinal mucosa. However, it is not specific for inflammatory bowel disease (IBD), as it is variably increased in other causes of gut wall inflammation and in various gastrointestinal malignancies, as well as due to ingestion of some common drugs. Nevertheless, faecal calprotectin concentration has been shown to vary with the degree of inflammation (Bressler, Panaccione, Fedorak, & Seidman, 2015) and, according to some authors, to predict relapse in IBD (Chang, Malter, & Hudesman, 2015).

Although faecal calprotectin concentration increases somewhat with age in adults, it has been shown to be a superior non-invasive discriminatory test for the distinction between inflammatory and functional intestinal diseases. The positive predictive value (PPV) is increased by a raised concomitant serum CRP.

Faecal calprotectin in paediatric populations

It is known that young children and infants have higher faecal calprotectin concentration than adults or older children. The literature regarding older children is less clear regarding reference intervals (RIs), but values tend towards adult levels after 4 years of age, with a gradual decline between 12 months and 4 years. In young children, 100 µg/g has been shown to be an acceptable

Table 1 - Factors and conditions associated with elevated faecal calprotectin levels

Infectious	Inflammatory conditions
• Bacterial dysentery • *C. difficile* • Giardia lamblia • *Helicobacter pylori* gastritis • HIV • Infectious diarrhea • Small intestinal bacterial overgrowth • Viral gastroenteritis	• Inflammatory bowel disease • Autoimmune enteropathy • Cirrhosis • Cystic fibrosis • Diverticulitis • Eosinophilic colitis/ enteritis • Gastroesophageal reflux disease • Juvenile polyp • Microscopic colitis • Pancreatitis • Peptic ulcer • Pouchitis • Untreated coeliac disease
Neoplasms	**Other**
• Colonic and gastric polyps • Colorectal cancer • Gastric carcinoma • Intestinal lymphoma • Intestinal polyposis • Pancreatic cancer	• Age <5y • Graft rejection (small bowel) • Immune Deficiency • Protein-losing enteropathy • Radiotherapy • Untreated food allergy
Drugs	
• NSAIDs • PPI	

NSAIDs (Nonsteroidal anti-inflammatory drugs); PPIs (Proton pump inhibitors)

(After Bressler, Panaccione, Fedorak, & Seidman, 2015)

cutoff, although some healthy children have levels up to 150 µg/g. Shimizu et al., in a study of children aged 6-17 years, established that the optimal cutoff of faecal calprotectin (FCP) to predict IBD was 217 µg/g, and that faecal calprotectin concentration increased exponentially as the endoscopic activity score increased. Optimal cutoff values of FCP for predicting mucosal healing were also demonstrated for ulcerative colitis (UC) and Crohn's disease (CD), at 161 µg/g and 367 µg/g respectively.

The longitudinal monitoring of individuals is clinically reliable (Herrera, Christensen, & Helms, 2016).

Necrotising enterocolitis is associated with increased faecal calprotectin concentration. Wide-ranging cutoffs are reported; however, Thuijls et al. (2010) have reported clinically relevant positive likelihood ratio (LR) of 12.29 and negative LR of 0.15 using a faecal calprotectin concentration cutoff of 286.2 µg/g faeces.

Laboratory analysis of faecal calprotectin

Reference intervals

Most healthy adults will have a faecal calprotectin concentration of <10 µg/g faeces. However, as the faecal calprotectin concentration is known to increase with age, RIs are usually established that account for miscellaneous factors, including age. These RIs should not be used for longitudinal monitoring when the patient should become their own reference.

Specimen collection, transport and storage

The time between defaecation might affect the faecal calprotectin concentration; therefore, the first stool of the day is recommended. Stool specimens should be collected into a clean, airtight container without preservative and stored at 2-8°C. The sample must be received at the laboratory within 24hrs of collection. Stool specimens that are liquid or very solid may be technically unsuitable.

Conclusion

Faecal calprotectin concentration is a safe and reliable non-invasive test for inflammation of the bowel wall that can:

- Distinguish between patients with IBD and patients with IBS.
- Determine disease activity and risk of relapse in IBD patients, and assess the level of mucosal healing.
- Help to identify patients with abdominal symptoms who may require further investigative procedures and reduce the number of endoscopies performed for the diagnosis of diarrhoeal disease and monitoring of IBD.

Because it is not specific for IBD, it must be interpreted in the clinical context.

Certain Patients may be Eligible for a Medicare Rebate

Two Medicare Items for faecal calprotectin testing, 66522 and 66523, were added to the MBS on the 1st November 2021.

To determine if your patient is eligible and to access the Medicare eligibility criteria, please scan the QR code.

Article continues over page

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