ePathWay
THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

Issue #051

SEPTEMBER 2015 | Published by RCPA

In This Issue

Interesting Facts

145

The projected number of male breast cancer diagnoses in 2015 in Australia.

20

The approximate number of men who develop breast cancer in New Zealand each year.

Welcome to the September edition of ePathWay

Breast cancer is associated with the colour pink, but we've changed its 'colour' to 'blue' (just for this month) for Blue September. This is because men can and do develop breast cancer, although it's not on the 'man cancer' radar - yet.

Genetic breakthroughs continue to happen at a cracking pace, so why don't related pathology tests crop up at the same rate? We asked an expert to talk us through getting a test to market, including why it usually takes a few years.

An infected appendix may have killed the great Houdini, but this organ has other 'tricks' up its sleeve as well. We look at appendiceal tumours, and why they can be the stuff nightmares are made of.

And finally, summer is approaching which means more sun-seeking behaviour. Now is the time to check the moles on your body, including any dysplastic naevi. Don't know what they are? Then it's time to find out.

Make sure you keeping checking in to our Facebook page (we've passed 1000 likes). You can follow our CEO Dr Debra Graves (@DebraJGraves) or the College (@PathologyRCPA) on Twitter to keep up to date with pathology news.

Breast cancer is not just a woman's disease - it's also a 'man cancer'

10 - 20%

The percentage of male breast cancers associated with an inherited fault in the BRCA genes.

Source: Cancer Australia, The New Zealand Breast Cancer Foundation

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Fantastical discoveries don't lead to pathology tests overnight

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Professor Graeme Suthers

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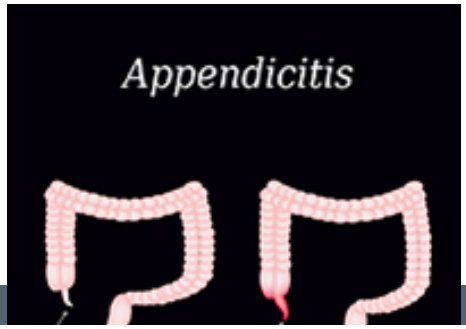

cancers that are often discovered *after* it has been removed because of appendicitis.

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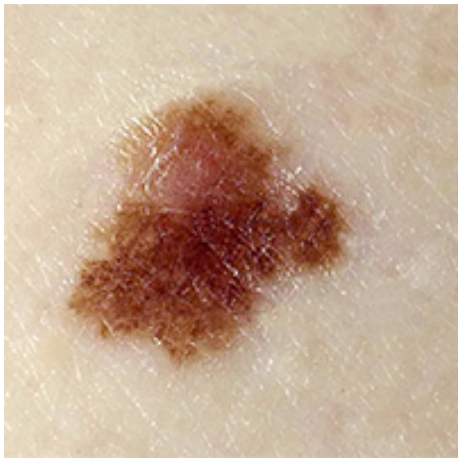

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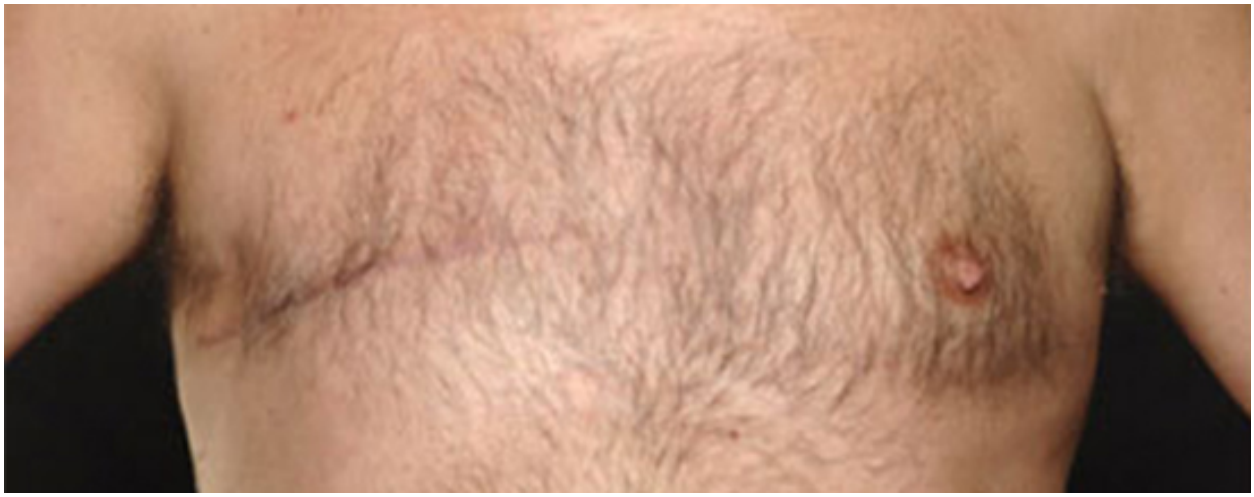

The Blue September campaign raises funds to fight cancer in men. Man cancer campaigns tend to spotlight testicular and prostate cancer, but there is another type that's not well known. We're talking about breast cancer, and while it's not common in men, it is the same disease that affects women.

Men can develop breast cancer because they have breast tissue, mostly behind the nipple. It doesn't matter how toned those pecs are, there is still breast tissue present. Symptoms for breast cancer are the same as for women such as:

- a painless lump (the most common symptom)
- a fluid discharge from the nipple
- a change in the way the nipple and/or breast looks
- pain in the breast
- lumps in the armpit.

Associate Professor Jane Armes, Director of Anatomical Pathology at Mater Health Services in Brisbane, says male breast cancer isn't common, but it's very important to know it can occur.

"Less than one percent of breast cancers affect men, but there is a perception that males can't get this disease. But they can develop it, and it can advance through the skin more quickly than it would for women if it's left long enough, simply because men have less breast tissue."

Diagnosis and treatment of breast cancer for men is the same as for women: breast examination,

radiological imaging and biopsy of the lesion. Treatments are generally the same for both sexes as well - including mastectomy – and the risk factors are mostly similar to those of women such as age and a family history of breast or ovarian cancer.

“The risk factors for male breast cancer are not well understood but they are definitely associated with the BRCA2[1] gene mutation. For this reason the family history is very important because this mutation gives men an increased risk of developing breast cancer compared to men who don’t have the mutation.”

A/Prof Armes says breast cancer in men is usually hormone sensitive, and most are oestrogen receptor-positive. Men with Klinefelter’s syndrome also have a higher risk.

“Men who have Klinefelter’s syndrome have two X (female) chromosomes and one Y (male) chromosome. This means they are XXY instead of XY, and have lower levels of male hormones and higher levels of female hormones in their body.”

A/Prof Armes advises men who have breast cancer symptoms to treat them seriously because early diagnosis leads to the best outcomes. The other take home message is that breast cancer is not just a woman’s disease. It’s also a man-cancer. Just ask the (approximately) 145 Aussie and 20 Kiwi blokes diagnosed with it each year.

[1] BRCA2 (and BRCA1) are human genes that help stabilise a cell’s genetic material. They are more likely to develop additional genetic alterations that can lead to cancer when they are mutated or altered. A harmful BRCA1 or BRCA2 mutation can be inherited from either parent.

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"Science is never right in an absolute sense, but it's less wrong today than it was yesterday. In the end, turning a genetic discovery into a pathology test is a judgement call in terms of being satisfied there is enough information for it to be reliable," explains Professor Graeme Suthers, Director of Genetics at Sonic Healthcare Australia.

Prof Suthers reviews genetic test applications to identify the ones that can be applied in clinical practice. He says genetics is bedevilled by fantastical new discoveries, and getting the balance right between enthusiasm and healthy scepticism can be tricky.

"Genetics is a new field and we don't have a gold standard to go by. We are forging the gold standard as we go along because we simply can't wait the 20 or 30 years for genetics to mature before we offer genetic tests."

Prof Suthers says there are three main hurdles to clear before a test can be considered for clinical practice.

"I have just been examining applications for a number of new tests that examine the activity or expression of genes that lead to breast cancer. These tests predict the recurrence of breast cancer

over the next five years. All of them passed the first two hurdles, but only a few cleared the last one."

The first hurdle is checking the test will have analytical validity by accurately reflecting the change happening in the breast. The second hurdle is checking the test has clinical validity, that is, that the test result is relevant to the area of interest. For example, does the test accurately predict recurrent risk of breast cancer or does it measure something else? If the answer to these two hurdles is 'yes', then a third one awaits, and Prof Suthers says it's often the 'humdinger'.

"We need to find out if the test also has clinical utility. For example, does it give us useful information that we can't already obtain from existing tests both inside and outside of genetics?"

Clearing these three hurdles doesn't automatically mean the test gets the nod either. Prof Suthers says he still has to make a judgement call by making sure the information is precise enough to be applied in clinical practice. To do this he turns to his peers, scientific publications and independent research to confirm that all reach the same conclusions.

So how long does it take to turn a discovery into a test? About three to five years with very few exceptions, says Prof Suthers, to make sure it's a valid and reliable test. Those years probably feel like a lifetime in a field of fantastical discoveries where getting the right balance between enthusiasm and healthy scepticism needs a steady hand.

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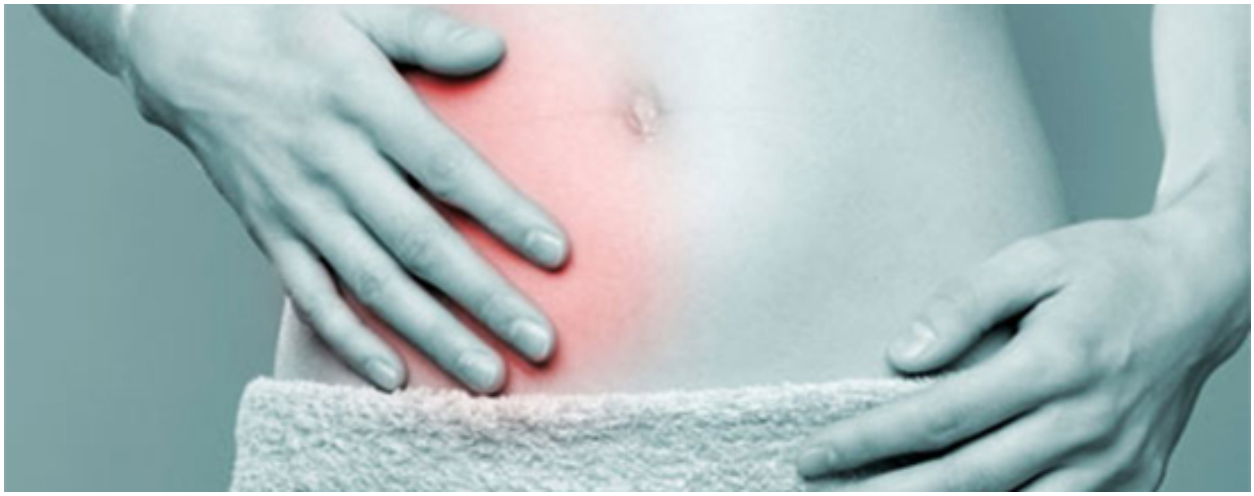

The appendix is an obscure tubular organ, no longer than your little finger and much thinner, that is tucked away in your right lower abdominal cavity. It is best known for causing abdominal pain due to acute inflammation, or appendicitis. It is less well known that the appendix can harbour some rare cancers that are often discovered *after* it has been removed because of appendicitis.

Dr Mee Ling Yeong, Anatomical Pathologist and Clinical Leader of Anatomical Pathology Services in Auckland, says appendiceal neuroendocrine tumours (NETs), previously called carcinoids, are the most common type of cancer that affects the appendix.

“These tumours are slow growing, asymptomatic and usually confined to the appendix, but they can spread to the regional lymph glands. They are most commonly an incidental finding, and an appendectomy is usually a curative treatment. In the event of a lymph node spread or spread to the covering of the appendix by a larger tumour that is greater than two centimetres, excision of a length of the attached large and small intestine, called a right hemicolectomy, is generally curative.”

A more aggressive appendiceal cancer is a goblet cell carcinoid tumour. These tumours grow at a faster rate than appendiceal neuroendocrine tumours, and can spread to other organs, especially the ovaries, which may yield the first signs that lead to the discovery of the appendiceal tumour.

Another type of cancer is so extraordinary it could star in a horror movie. It’s called is an appendiceal mucinous neoplasm, which may present as a mass in the lower abdomen.

“These tumours arise from the mucous lining of the appendix, and are cysts of varying size filled with mucus. Some are benign, while others are malignant and spread through the wall of the appendix. Mucinous carcinomas can spread to the peritoneum (the serous membrane that forms the lining of the

abdominal cavity) and produce abundant mucus in a condition known as pseudomyxoma peritonei," explains Dr Yeong.

If the thought of mucous-producing tumours has raised your heart rate, then it's probably a good time to add (for peace of mind!) that appendiceal tumours are rare and only found in less than 1% of appendectomy specimens. Dr Yeong says the important message is to be aware that the appendix can harbour tumours, some of which may spread widely, even if it's a classic appendicitis presentation.

"Acute appendicitis is so common most people don't think of cancer. It is not known if the tumour or the infection develops first, or if the events are coincidental, but it's important to know that these synchronous lesions can occur," explains Dr Yeong.

Most appendiceal tumours are treated successfully with an appendectomy, but a few can result in significant disease if they are detected late. And this is why it's important to know there is more to the appendix than appendicitis.

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If we compiled a list of awkward medical names, dysplastic naevus would be on it. A dysplastic naevus is an atypical mole, but a non-medical person may have a hard time joining the dots between its medical name and meaning. We therefore asked an expert to fill us in on dysplastic naevus, including its link to melanoma.

Professor Richard Scolyer, skin pathologist at the Royal Prince Alfred Hospital (RPAH) and Melanoma Institute Australia, says it's common for people to have a small number of dysplastic naevi (the plural of naevus). He says they can form any time in life, most commonly between ages 10 and 50 years.

"Dysplastic naevus were first recognised and described in the 1970s, and affect between seven and 30 percent of the Caucasian population. While naevus means a mole on the skin, the term dysplastic is a bit misleading. In other medical settings, dysplasia means a precursor to invasive cancer, but that doesn't apply in this case."

Prof Scolyer says most dysplastic naevi don't progress to melanoma, but they are a risk factor. The risk of melanoma is double compared to the rest of the population if you have one dysplastic naevus, and 12 times greater if you have more than 10.

"It's very important to understand that a dysplastic naevus is a potential precursor, and not an obligate precursor, to melanoma. They are a marker of increased risk of melanoma developing anywhere on the body, and not inside the actual mole. Only about one dysplastic naevus in 10,000 progresses to melanoma each year. This is why excising them prophylactically to reduce the risk of melanoma is not recommended."

So how do we tell a dysplastic naevus from other moles?

“They are usually bigger than other moles, have irregular borders, variable colour and can look a bit red if they are inflamed,” explains Prof Scolyer.

“They are also dynamic and can change over time. If a lesion is new, changing or becomes an ‘ugly duckling’ sign, where it looks different to other moles, or if you are concerned, then it should be checked by a doctor.”

Prof Scolyer lists the risk factors for dysplastic naevus as sun exposure, skin type and genetics, and there is a familial condition called the Dysplastic Naevus syndrome. This is where a person has hundreds of atypical moles all over their body, not primarily in areas exposed to the sun. This syndrome also confers a higher risk of developing melanoma (but not just inside the actual moles themselves).

So we know dysplastic naevus means atypical mole. And we know it is a risk factor for melanoma. And we know they don’t look like other moles. But we don’t know why they were landed with such an awkward name. This may be water under the bridge anyway. Dysplastic naevus is increasingly being called atypical naevus or atypical mole, which are straightforward enough to avoid a spot on our list of awkward medical names.

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