DOUGLASS HANLY MOIR PATHOLOGY

Quality is in our DNA

Doctors' Newsletter

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I am delighted to introduce the second Doctors' Newsletter for 2017.

Our special focus in this issue is on medical education, a concept so broad that it can be more easily described than defined. It is, ineluctably, at the core of good medical practice and prerequisite to it. The rate of change in every facet of medicine, and the inexorable accumulation of knowledge, mean that learning how to learn is as important as the facts which are learnt.

Medical education remains an abstract notion, a good intention, without commitment from individuals to learn and to teach and commitment from organisations to resource the process. With commitment at both levels, we see the abstract become real. This Newsletter is one expression of Douglass Hanly Moir's commitment to education; in it I take the opportunity to highlight several others and the individuals behind them.

Much of the content of each Newsletter is provided by DHM pathologists; in this issue, Dr Annabelle Farnsworth outlines the changes in the national cervical screening program, due to be introduced in December, 2017. The move from cytological screening to molecular detection of oncogenic HPV subtypes has had profound implications and its successful implementation is a challenge. Dr Kym Mina introduces us to a screening test for Spinal Muscular Atrophy, available through Sonic Genetics at DHM Pathology. This is followed by Dr Karl Baumgart's discussion of targeted allergy testing and by Dr Fiona Maclean's overview of the significance, the pathology and the approach to diagnosis of arthritis.

Dr Colin Goldschmidt
MBBCh, FRCPA, FAICD
CEO – Douglass Hanly Moir Pathology

Cover: Fruiting body of *Aspergillus* species

Commitment to Education

Whether the comparator is a public or a private one, Douglass Hanly Moir Pathology has occupied a leading position in diagnostic pathology for many years. Key to that position is respect and a key predicate to that respect is our demonstrable and ongoing commitment to education at both an individual and an organisational level.

The development and delivery of the pathology curriculum at the University of Notre Dame, Sydney, the provision and/or sponsorship of innumerable educational workshops, registrar training, scholarships for scientific staff attest to this and form a record unmatched by any other private pathology provider.

Over the last 12 months DHM has provided face-to-face education, primarily to GPs, for more than 300 doctors. This has taken the form of RACGP- and ACRRM-approved Category 1 and 2 events which have earned those attending up to 40 Category 1 points per event. The events have covered subjects such as dermatology and skin surgery, genetics and women's health.

The articles provided by individuals to this and other Newsletters are noteworthy not only for their content but also for what they signify. Each represents an investment of time and effort well beyond the call of duty and by giving that time and making that effort each contributor reveals an awareness of professional development as a professional responsibility.

The same commitment to medical education must also exist at an institutional level to enable and to resource the efforts of individuals; such organisational commitment is directly and causally linked to an organisational culture based on Medical Leadership. This is the deeply embedded culture that exists at Douglass Hanly Moir.

Welcoming our recent pathologists

Histopathology

Dr Sophie Corbett-Burns
MB, BCh, BAO, FRCPA

Dr Corbett-Burns graduated with honours in Dublin, training in anatomical pathology and receiving FRCPA in 2016. Her interests include breast pathology, gynaepathology, neuropathology and gastrointestinal pathology.

Microbiology

Dr James Newcombe
BMedSci(Hons), MPH(Hons), MBBS, FRCPA, FRACP

Dr Newcombe is an award-winning researcher and has published peer-reviewed journal articles on infectious diseases and microbiology topics. He has a special interest in paediatric infectious diseases.

Histopathology

Assoc. Prof. Nirmala Pathmanathan
BSc (Med), MBBS, FRCPA

Assoc. Prof. Pathmanathan is an expert in breast diseases. She sits on the Executive Committee for the Australasian Society for Breast Diseases and is a National Clinical Advisory Board Member for BreastScreen Australia.

Histopathology

Dr Vallapan Thiruvilangam
MBBS, DipPath, MD, FRCPA

Dr Thiruvilangam is an anatomical pathologist. Graduating from the University of Jaffna, Sri Lanka, he completed his MD at the National Hospital, Colombo, in 2000, and immigrated to Australia the same year. He has been involved in teaching, conference presentations and laboratory management.

Histopathology

Dr Cristina Vargas
MD, PhD, FRCPA

Dr Vargas undertook postgraduate studies in anatomical pathology (Mexico City), completing her PhD in Australia. Some areas of interest include breast, head and neck and gastrointestinal tract.

Histopathology

Dr Cherie Wong
MBBS, FRCPA

Dr Wong received FRCPA in 2012 following completion of her training in anatomical pathology. Her special interests include dermatopathology, pulmonary pathology and neuropathology.

Dedication to Excellence

Recognising and supporting the importance of medical education, research and professional advocacy.

Dr Fiona Bonar with His Excellency General The Honourable David Hurley

Adjunct Professor Fiona Bonar – Honoured with an Order of Australia Medal

Adjunct Professor Fiona Bonar was the recipient of a Medal of the Order of Australia (OAM) in this year's Australia Day Honours List. The award acknowledges her service to medicine, particularly in the field of orthopaedic pathology and adds to her 2014 Sonic Healthcare Distinguished Pathologist Award. Working at Douglass Hanly Moir Pathology (DHM) since 1993, Adj. Prof. Bonar is internationally renowned for her expertise in bone and soft tissue pathology, as well as head and neck pathology. She has written chapters in a number of seminal pathology texts, as well as authoring 75 journal articles and published papers. Originally from Ireland, Adj. Prof. Bonar also spent time in New York at New York-Presbyterian Weill Cornell Medical Center and at the Hospital for Joint Diseases before her move to Sydney. She is on the editorial boards of several journals and has spoken at many international conferences. Adj. Prof. Bonar is congratulated on her well-deserved award.

Dr Paul Richmond – A Devoted Histopathologist Retires

Dr Paul Richmond, a well-known and respected DHM pathologist whose career spanned nearly five decades, retired in May, 2017. As an individual who never tired of learning and teaching, his absence will be sorely felt in all parts of the laboratory. A graduate of the University of Sydney, Dr Richmond trained in pathology at Royal North Shore Hospital and obtained further postgraduate experience in dermatopathology in the USA and the UK.

Returning to Sydney, Dr Richmond began working at Posney and Kerr Pathology in 1973 and became a partner in that practice in 1974. In the years that followed, Dr Richmond and colleagues built a practice that provided high-quality diagnostic pathology services to south-western Sydney and western NSW. In the process, he developed relationships of similarly high quality with his referring practitioners, which continued beyond Posney Richmond's merger with Hanly Moir Pathology and into its final incarnation as Douglass Hanly Moir Pathology. The longevity of these relationships and the loyalty to which they testify are huge achievements and a reflection of Dr Richmond's professional expertise and his personal charm.

From L to R: Dr Denis Moir, Dr Colin Goldschmidt, Dr Stephen Fairy, Dr Paul Richmond and Adj. Professor Warick Delprado

Serving the community and the pathology profession for more than 46 years gave him both insight and perspective when dealing with the tremendous changes facing us all. Always smiling, always affable, always curious and always respectful, Dr Richmond is a pathologist and a person whose absence will be felt keenly. As much as we will miss him, we also wish him happiness and fulfilment in his retirement.

Yardsticks in Surgical Pathology

'Yardsticks in Surgical Pathology', a two-day seminar designed for registrars in anatomical pathology, was conducted at Douglass Hanly Moir Pathology's main laboratory in Macquarie Park. This seminar was organised and convened by Dr Esther Myint (Histopathologist – DHM) who, with a background in teaching, was determined to share her knowledge. Aptly named after a standard of comparison, the aim of this Yardsticks workshop is to measure the registrars' anatomical pathology knowledge, which they must have in their respective RCPA training year (from beginning to year 5).

Having been initiated in 2016, the seminar held in January this year attracted a higher level of attendance and was expanded in nature – both with additional groups available and more pathologists contributing to the cases presented. There were 92 registrars from all over Australia, New Zealand and Hong Kong. Along with keynote speakers, Professor Peter Russell and Adjunct Professor Fiona Bonar, the pathologists who presented at the seminar were Dr Suzanne Danieletto, Dr Kambin Nejad, Dr Cathy Lim, Dr Anita Muljono, Dr Yasmin Matthews, Dr Kathleen Young, Dr Erin Morris, Dr Melanie Edwards, Dr Alison Cheah and Dr Sophie Corbett-Burns. The cytology lectures were presented by Dr Irene Ngu and Dr Bryan Knight.

Our pathologists are committed to imparting their knowledge and expertise, and the feedback was very positive, with registrars commenting on the excellence in presentations and the comprehensiveness of the course material.

Dr Esther Myint

Dermpath On The Harbour

Dr Vicki Howard, left, with DHM Pathologists Dr Erica Ahn, Dr Lisa Lin, Dr Francesca D'Souza and Dr Ana Varallo-Nunez

Dermpath On The Harbour is an internationally recognised biennial event, hosted by Douglass Hanly Moir Pathology, Macquarie Park, and organised by our well-known dermatopathologist, Dr Vicki Howard. The course is an intensive, week-long tutorial, encompassing both neoplastic and inflammatory diseases of the skin. The inaugural conference, hosted in Australia in 2012, generated a very positive response from attendees, with many of the dermatopathologists stating that they would be very keen to attend the next event.

The 2016 course was at full capacity, with 48 dermatopathologists in attendance, comprising of international, national and local participants. They benefited from a selection of 450 kilos of glass microscopic slides, imported from the extensive and world renowned Hammersmith, UK, slide collection, specifically for this event. The key speakers were Dr Eduardo Calonje, (Director of Dermatopathology, St John's Institute of Dermatology, London), Dr Bostjan Luzar, (University of Lujbljano, Slovenia) and Dr Thomas Brenn, (University of Edinburgh, UK).

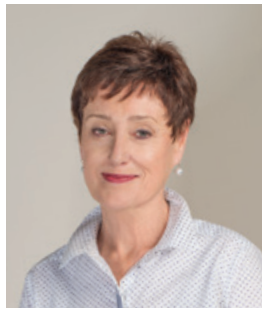
Dr Marcella Roman – Acknowledged by Monash University

In a recent Monash University newsletter, Dr Marcella Roman was recognised for her educational contributions, donating her time to provide weekly tuition to 3rd Year Medical students in Pathology at Rural Health Mildura (RHM). Finding that medical students, who have gone through an extensive selection process, are very keen and extremely engaged in their learning, Dr Roman took the opportunity of maximising her two-day rural visits in her role as Laboratory Director for Barratt & Smith Pathology. Accordingly, she fills her schedule with voluntary lessons – a rewarding experience and an exceptional example of Medical Leadership.

In addition to teaching at the medical school for more than 16 years, Dr Roman also provides educational opportunities to GPs and specialists, with informative and interactive presentations. She has been with Barratt & Smith Pathology since 1987 and has become a well-respected and integral part of the medical community in the Mildura region.

The Cervical Screening Program will change forever

The renewed cervical screening program, due to be implemented on December 1, 2017, differs from the current program in almost all aspects. While the objective, to reduce the incidence of cervical cancer, remains the same, it is the most significant revision of a public health program to have occurred in decades.



Adj. Professor Annabelle Farnsworth
MBBS (Hons), FRCPA, FIAC, DipCytopath (RCPA), RANZCOG (Hon)
Medical Director – Douglass Hanly Moir Pathology
Director – Cytopathology and GynaePath

As Australia will be one of the first nations in the world to make this change, the general information covered in this article will be of interest to all medical practitioners.

Why the change?

For nearly three decades, Australia has had a highly successful cervical screening program based on two-yearly cytology Pap tests for women aged between 18 and 70 years. This program has reduced the incidence of cervical cancer by more than 50%, with most cases of cervical cancer occurring in women who have been under-screened or never screened.

Research has shown that 99% of cervical cancers are associated with persistent infection with certain high-risk or oncogenic HPV viral types. This knowledge led to the development of the HPV vaccine, which targets the two HPV subtypes most commonly associated with cervical disease, HPV types 16 and 18. Since 2007 (for girls) and 2013 (for boys), Australia has had a school-based vaccination program for these types of oncogenic HPV.

The improved knowledge of HPV's role in cervical cancer, together with modelling of the impact of the vaccine in reducing abnormality rates over time, has led researchers to propose that a more sensitive screening test, which looks for the presence of the oncogenic viral types rather than the cellular changes caused by infection, would be more effective in reducing cervical cancer in both vaccinated and unvaccinated women.

What is the new program?

From December 1, 2017, the following changes will apply:

- The oncogenic HPV test will replace the Pap test as the primary cervical screening test
- The cervical sample is collected in the same way as a Pap test, with the collection device being rinsed into a ThinPrep® vial – NB. no glass slide is required
- Asymptomatic Australian women aged 25-74 years who test negative for oncogenic HPV will be classified as **'Low Risk'** and offered a repeat HPV test in 5 years
- Women who test positive for oncogenic HPV will also have a ThinPrep® cytology slide made from the same vial and, depending on the result, may be classified as **'Higher Risk'** with referral for colposcopy, or **'Intermediate Risk'** with a recommendation to return for repeat testing in 12 months
- Symptomatic women (e.g. those with abnormal bleeding) and those in follow-up after a significant abnormality will be offered both HPV and ThinPrep® testing
- A self-sampling HPV test option supervised by a clinician will be offered in special circumstances

How will the new program be administered?

Integral to the success of the new program is the establishment of a new National Cancer Screening Register (NCSR). This will be an 'opt out' register, meaning all women presenting for cervical screening will be included in the register unless they specifically elect to opt out.

The NCSR will invite women into the program when they turn 25 and will recall women in the program at the appropriate intervals.

The NCSR will collect cervical HPV, LBC, colposcopy and histology results and will eventually integrate HPV vaccination status for women in the screening program.

More information

As we approach December, 2017, DHM GynaePath will continue to provide updates on the clinical interpretation of these changes for our referrers.

For general information on the new cervical screening program, see the National Cervical Screening Program website:
www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/cervical-screening-1

Carrier Screening for SMA

Dr Kym Mina
MBBS, PhD, FRCPA (Genetics)
Director of Genetics – Douglass Hanly Moir Pathology

Spinal muscular atrophy (SMA) is an autosomal recessive disorder characterised by degeneration and loss of the anterior horn cells in the spinal cord that results in symmetrical muscle weakness and atrophy. It has an estimated incidence of 1 in 10,000 live births and is the most common genetic cause of mortality in children under the age of two.

The clinical severity of SMA occurs on a spectrum, and as such this disorder is further subdivided into types according to age of onset, motor milestone achievement and life expectancy. The clinical course is further complicated by respiratory, nutritional and orthopaedic comorbidities. SMA is not curable and management is supportive.

Importantly, approximately one person in forty is a carrier of an SMN1 gene mutation that can cause SMA. Carriers are asymptomatic and often have no family history of SMA, and so it is common for individuals to be unaware of their personal carrier status. Joint HGSA/RANZCOG guidelines recommend that pre-pregnancy carrier screening for common genetic conditions, including SMA, be offered to all women.

Sonic Genetics, through Douglass Hanly Moir Pathology, now offers a test that can identify the great majority of SMA carriers by detecting deletions of the SMN1 gene. The test can be requested by any medical practitioner, and as is the case with all genetic tests, the importance of providing relevant family history cannot be overstated. It should also be remembered that any test which detects heritable mutations has important implications for other family members. Therefore testing should not be performed without consideration of the need for appropriate genetic counselling.

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New *CERTAIN* Profiles

Clinically Effective Rational Testing Allergy INformation

Allergy testing is frequently performed on people with suspected allergic rhinitis, allergic conjuctivitis, asthma or reactions to insects, foods or medicines. Testing is of greatest utility when targeted according to the clinical problems, the patient's age and duration of residence in their current environment; in fact, results cannot be interpreted without seeing them in this context. Allergy testing should not be undertaken as a screening exercise.

Dr Karl Baumgart
BSc (Med), MBBS, PhD, FRACP, FRCPA
Director – Immunology

In the context of suspected food allergy, testing is performed in order to confirm suspected sensitisations and also to determine the safety of high-risk allergen foods. This is especially important when the foods which may be involved are 'disliked' and 'usually avoided'.

In the context of respiratory symptoms, allergy testing is intended to define the clinically important sensitisations and exposures, bearing in mind the potential for cross-sensitisation between airborne and food allergens. Up to 5% of patients with dust-mite allergy may show cross-sensitisation to crustaceans, while birch pollen sensitisation has an association with allergy to seemingly unrelated nuts, fruits and vegetables.

Patient age is a key determinant of sensitisation to both food and respiratory allergens. At any point in time an individual's allergy problems, and the results of their allergy tests are like still-shots from a long and complex film. This film is titled 'The Allergic March' (see Figure 1) and depicts the transition from sensitisation to food allergens (mainly gastrointestinal and skin symptoms) to progressively greater sensitisation to airborne allergens (otitis, rhinitis, asthma and conjunctivitis).

The full spectrum of airborne allergen sensitisation is not apparent until around the age of 8 years, or 8 years after arrival in a new environment. These sensitisations become progressively stronger over the subsequent 10 years so that results of early allergy tests are not as impressive as those performed a few years later.

Both skin prick tests (intracutaneous, *in vivo*) and laboratory tests (*in vitro*, specific IgE, or 'RAST') are clinically useful tools to investigate allergy symptoms in patients. The skin prick test is a more qualitative point-of-care test; laboratory tests provide a broader menu, including allergens not available in skin test systems, a re-check when skin test reactions are weak or discordant, and the opportunity to know more detail about which individual allergen molecules are the target of allergic responses.

The Medicare rebate is insufficient to cover the cost of either skin prick tests or laboratory allergy tests. Historically, laboratory test panels included mixed allergens that could be used as a negative screen to provide more allergen test coverage within a Medicare rebate. However, low, moderate and even quite high false positives occur in mixed allergen testing when there is plenty of low affinity, low avidity antibody. Therefore strategies based on mixed allergen screens which are then individually characterised are clinically inefficient and can be misleading. Neither skin prick nor laboratory tests can confirm non-IgE mediated food intolerances or T cell contact sensitisations.

> Testing that answers only part of the clinical question should be avoided. When allergy testing is indicated, that testing should be comprehensive.

TYPICAL EVOLUTION OF ALLERGIC DISEASES

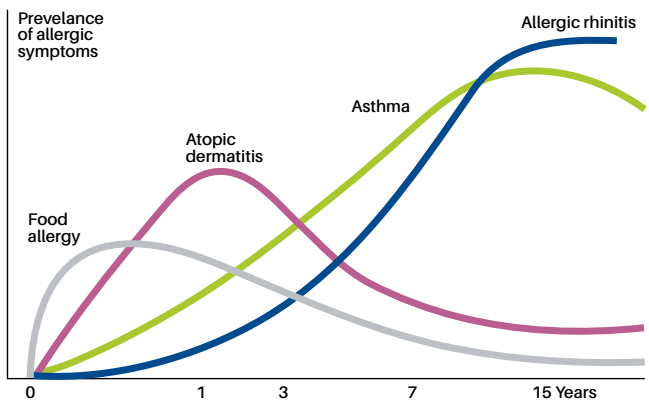

Figure 1. The Allergic March *(Adapted from Immune Tolerance Network, LEAP Study 2011; http://www.leapstudy.co.uk)*

CERTAIN Profiles

The CERTAIN profiles are designed to provide efficient baseline allergy assessment for most of the circumstances encountered in clinical practice. The composition of each profile is given below and each can be requested as CERTAIN Profile (or CP) 1,2,3 etc. Additional allergens can be added if necessary (sera are kept for 4 weeks from the date of collection) but when more than four allergens are tested a fee will be charged ($5* per individual, $10* per mixed allergen and $40* per component allergen). Current Medicare Benefits Schedule (85%) rebates for total IgE (Item 71075) are $19.55* and $22.80* for an episode of *in vitro* specific IgE allergen testing (Item 71079).

CP	TOTAL IgE AND SPECIFIC IgE	CLINICAL APPLICATIONS
CP1	egg white, egg yolk, cow's milk, ovomucoid alphalactalbumin, betalactoglobulin, wheat, soy, oats, potato, peanut, cashew, sesame, almond, codfish, beef, chicken, kiwi, banana, avocado, latex, strawberry	21 allergens, designed for allergic children in the first 18 months
CP2	egg white, egg yolk, cow's milk, ovomucoid alphalactalbumin, betalactoglobulin, wheat, soy, oats, potato, peanut, cashew, hazelnut, walnut, macadamia, sesame, almond, codfish, beef, chicken, prawn, kiwi, banana, avocado, latex, strawberry, dustmite, cat, dog, fescue grass	30 allergens, designed for allergic children between 19 and 36 months
CP3	peanut, cashew, pistachio, walnut, hazelnut, almond, brazil, pecan, macadamia, pine nut, sesame, pumpkin seed, linseed, coconut	14 allergens, designed for children, teenagers and adults with uncertainty about 'nut allergy' and follow-up after previous positive tests or reactions
CP4	codfish, tuna, salmon, crab, prawn, lobster, oyster, mussel, scallop, octopus, squid, anisakis	12 allergens, designed for children, teenagers and adults with uncertainty about fish and seafood or follow-up of previously seafood sensitised persons
CP5	alpha-gal, milk, pork, beef, lamb	4 allergens and one component allergen, designed for tick-meat-milk sensitised persons initially or in follow-up
CP6	birch, parietaria, latex, apple, peach, apricot, plum, kiwi, banana, avocado, hazelnut	11 allergens, designed for persons with birch pollen-induced food allergy or oral allergy symptoms, usually following time in New Zealand, Europe or North America and sometimes Canberra or Melbourne
CP7	rockmelon, watermelon, eggplant, cucumber	4 allergens, designed for persons with reactions to melons
CP8	down-feathers, dustmite, fescue grass, bahia (paspalum) grass, couch (Bermuda) grass, rye grass, cat, dog, horse, birch pollen, olive tree pollen, acacia, eucalyptus, cypress, casuarina, plane tree, privet, plantain, ragweed, alternaria, aspergillus, penicillium, hormodendrum	22 allergens and one mixed allergen, designed for persons over age four with significant aeroallergen symptoms including allergic rhinitis, allergic conjunctivitis and asthma

DHM Pathology provides, arguably, the foremost and most comprehensive clinical allergy service in Australia. Major components of that service include the most extensive *in vitro* specific IgE (RAST) menu in Australasia. We also offer eosinophil cationic protein (ECP) and tryptase, as well as the ISAC microarray and genetic tests for Types I and II and Type III hereditary angiodema – specialised tests not otherwise available. Our goal is to offer a test menu which provides you, the clinician, with the most comprehensive and robust diagnostic information possible for the investigation of your patients with allergy symptoms. Our clinical immunologists are available to assist with the interpretation of results and provide any clinical guidance required.

*correct at time of printing

Arthritis

Arthritis is the leading cause of disability and chronic pain in most industrialised countries and represents a huge social and economic cost. In 2011–2012, approximately 15% of the Australian population (3.8 million individuals) were diagnosed with arthritis and their painful, swollen joints were the eighth most frequently managed problem in general practice. Estimates of the total annual cost of arthritis to the health system are in the region of $5.5 billion. Arthritis-associated disability and early retirement cost the government $1.1 billion in extra welfare payments and lost taxation revenue and costs the economy $7.2 billion in lost GDP alone.[1]

Dr Fiona Maclean
MBBS (Hons), BAppSc, FRCPA
Deputy Director – Histopathology

Of the many distinct types of arthritis, osteoarthritis, rheumatoid arthritis and gout account for more than 95% of cases and will be the focus of this article.

What is arthritis?

While having the specific meaning of joint inflammation, the term has acquired a broader usage and is often used when referring to joint pain or joint disease. Common symptoms of arthritis include pain, stiffness and decreased range of motion. Symptoms may be intermittent, they may vary in severity, they may remain stable for years or may progress rapidly over time. Severe arthritis can cause chronic pain, an inability to perform daily activities or to gain and retain employment. Co-morbidities are very common and include diabetes, cardiovascular disease, obesity, chronic obstructive lung disease and mental health problems.

What causes arthritis?

Arthritis can be a manifestation of altered geometry of the joint (e.g. fracture, Paget's disease), loss of integrity of its constituents (e.g. cartilage, synovium) or a change in its mechanical properties (e.g. haemochromatosis); often, there are multiple factors involved in the pathogenesis of an individual case. In all forms, the ultimate morphology and histology are those of osteoarthritis, making elucidation of the initial cause challenging.

Non-inflammatory (degenerative) arthritis

While osteoarthritis (OA) is the archetype of the non-inflammatory (degenerative) category of arthritis, an inflammatory component does play a role in disease progression.[2] OA is characterised by combined loss of hyaline cartilage and its attempted regeneration. In areas of complete cartilage loss, sclerosis of subchondral bone contributes to disease progression related to altered plasticity and shock absorption. Osteophytes at the perimeter of the joint and along the surface represent attempted repair of the articulating surface.

The development of osteoarthritis is our uniform destiny, inevitable for those with a preceding form of arthritis as for those without. The changes of osteoarthritis may obscure all others to an extent which prevents the diagnosis of any antecedent pathology. An example is rheumatoid arthritis leading to secondary osteoarthritis; the changes caused by the latter can preclude recognition of the former.

Inflammatory arthritis

Rheumatoid arthritis (RA) is a systemic chronic inflammatory autoimmune disease of uncertain aetiology, characterised by chronic destructive synovitis. Clinically, swelling, pain and joint destruction occur. Although declining in prevalence (from 2.4% to 2.1% between 2001 and 2008), RA still imposes significant cost, reflecting debility and premature mortality.

RA represents a complex dysregulation of the immune system. A failure of immunological tolerance results in production of antibodies to citrullinated and carbamylated proteins (ACPAs and anti-CarP), which induce a sustained local inflammatory response if access is gained to the joints. This leads to increased osteoclastogenesis and bone destruction. Extra-articular manifestations are common and include rheumatoid nodules, vasculitis, lung and eye manifestations.

Examples of non-inflammatory versus inflammatory arthritis	
Non-inflammatory (200-2000 WBC x 10^6/L)	Inflammatory (>2000 WBC x 10^6/L)
Avascular necrosis	Crystal-induced monoarthritis (e.g. gout/pseudogout)
Charcot's arthropathy	Lyme disease
Haemochromatosis	Rheumatoid arthritis and juvenile idiopathic arthritis
Osteoarthritis	Septic arthritis
Pigmented villonodular synovitis	Spondyloarthritis
Trauma	Systemic lupus erythematosus

WBC: white blood cell

Diagnosis of rheumatoid arthritis

The diagnosis of rheumatoid arthritis is based on the following:

- Inflammatory arthritis involving three or more joints
- Positive rheumatoid factor (RF) and/or anti-citrullinated peptide/protein antibody (such as anti-cyclic citrullinated peptide [CCP]) testing
- Elevated CRP or ESR
- Exclusion of other diagnoses, such as psoriatic arthritis, viral arthritis, gout etc
- The duration of symptoms is more than six weeks

Crystal deposition disease (gout/pseudogout)

Gout: primary or secondary abnormalities of uric acid metabolism result in deposition of monosodium urate crystals (MSU) into joints and periarticular tissues. Secondary gout can reflect over-production (e.g. chemotherapy effect) or under-excretion of uric acid (e.g. renal failure).

Crystals precipitate in tissue stimulating the innate immune system. An acute inflammatory response occurs and the intense acute arthritis this causes is a common presentation. An interval phase of variable length follows, with some progressing to chronic tophaceous gout. Crystal identification in synovial fluid or tophus is the gold standard of diagnosis.

Calcium pyrophosphate dehydrate deposition disease (CPPD): CPPD (also known as pseudogout) is frequently present in association with degenerative change in OA, where deposition in hyaline cartilage predominates. Although common (seen in 5% of autopsy series), it has a particular association with disorders such as haemochromatosis, Wilson disease and hyperparathyroidism.[3]

Distinction between osteoarthritis and rheumatoid arthritis		
Clinical or laboratory feature	Osteoarthritis	Rheumatoid arthritis
Primary joints affected	Distal interphalangeal Carpometacarpal	Metacarpophalangeal Proximal interphalangeal
Heberden's nodes	Frequently present	Absent
Joint assessment	Hard and bony	Soft, warm and tender
Nature of joint stiffness	Worse after exercise	Worse after rest
Laboratory findings		
– Rheumatoid factor (RF) – Anti-CCP – ESR/CRP	Not detected Not detected Normal	Detected in 80% Appears earlier than RF Elevated

CCP: cyclic citrullinated peptides; **ESR:** erythrocyte sedimentation rate; **CRP:** C-reactive protein

This article was first published in *Diagnostic Histopathology,* October, 2016. With Dr Maclean's assistance and approval, the article has been modified for inclusion in this Doctors' Newsletter by Dr Ian Chambers, Medical Editor.

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Our Doctors' Newsletters contain articles written by our pathologists which focus on current issues and recent developments in pathology. Suggestions from you, which we invite wholeheartedly, are the best guarantee that our Doctors' Newsletter becomes a resource of maximum possible interest, information and relevance. If you have any topics you would like to suggest please feel free to contact Dr Ian Chambers (Medical Editor, DHM Publications) at med.ed@dhm.com.au.

Please note, this Newsletter can also be viewed on our website via the Clinician Publications link.

We look forward to hearing about your topics of interest and encourage your participation.

Dr Ian Chambers
MB, ChB, FRCPA, MASM
Medical Editor

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