

## SPECIAL POINTS OF INTEREST:

- CADF has a new website!
- One CADdy's experience with coronavirus
- How to interpret your laboratory results
- Guest blogger Dr. C. Connolly
- A second product giveaway!

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## Welcome from the editors!

Welcome to the second edition of CADdy News!

Thank you to everyone who provided feedback on our first edition, we will endeavor to incorporate all of the excellent content suggestions into our future editions.

Congratulations to JoAnn Domitrovich who was the winner of the giveaway competition! We hope you enjoy your OCOOPA rechargeable hand warmers.

In this edition, we bring you the second part of Dr. Catherine Connolly's blog as she explores the topic of anemia. We also hear from CADdy member, Dee Ryan, who recounts her experience of contracting the novel coronavirus. Dr. Rana Walley, a CADdy care partner and laboratory scientist, provides tips and advice on how to interpret your blood results. We also introduce a new section called "Chitter-Chatter" where we direct some light-hearted questions to a featured member of the Cold Agglutinin Disease Foundation.

If you haven't already done so, please complete your member profile at <https://form.jotform.com/201154877602050> as this will ensure you get the first release of CADdy News direct to your email. We will also archive newsletter issues on the CADF website and our Facebook group CADdy Chatter.

*Until next time, stay safe and warm!*

## CADF's new website

You may have noticed a new look for the Cold Agglutinin Disease Foundation at <https://coldagglutinindisease.org>. Our website has undergone a makeover to make it more user-friendly. Please check it out to find more information about CAD, including information about CAD treatments, clinical trials, news, research, and personal stories shared by CADdys and their care partners.

If you would like to share your CAD story, we'd love to hear from you! Please contact us at: [info@cadfadvocacy.org](mailto:info@cadfadvocacy.org)

*Dr. Catherine Connolly*

*My father has been living with Cold Agglutinin Disease for the last 4 years – a rare condition that leads to the breakdown of red blood cells when he’s exposed to cold weather. In this blog series, I explore his disease from the personal side and the professional side, as his daughter and as a qualified medical doctor.*

*Through telling our story, piece-by-piece, I hope to raise awareness, share knowledge, and build friendships within the CAD community.*



The unique Australian Rules Football (AFL) goal posts are seen on many Aussie ovals

“Learning to adapt to life with this condition”

Parkrun results can be a yardstick for monitoring anemia



## Part 2: Slowing down

Since his youth Dad has always been a keen runner. On our last family trip to Ireland, we stumbled across an old diary cataloguing the times it took for him and his siblings to race each other around an 8-kilometre loop starting and finishing at their summer holiday beach cottage. After meeting Mum, starting a family, relocating to Australia, and working more than ever, it would be natural to assume Dad’s love for running would be put on the side burner. This was not the case. Instead, running became one of the ways our family would spend quality time together. Almost as far back as I remember, Dad would round up my brothers and sisters and I for relay races around our local grass oval. As we grew older and stronger, our starting handicaps were changed to always result in a close finish, particularly on the last lap which was “winner takes all.” Now we’re all adults, we still try to have a family meet up at our local 5km ParkRun event on Saturday mornings whenever we have the time.

Some years ago we noticed Dad’s time for the 5km ParkRun course began to slow down, and we all assumed it was a normal part of getting older. But after discovering he has CAD, we now know there’s more to it than his age alone. Since he was diagnosed with CAD, Dad’s had a Haemoglobin level (a red blood cell marker) that’s fluctuated from 110 right down into the 60’s- at which point he experienced palpitations and other symptoms, which required a blood transfusion plus specialised therapy. To give perspective, we

found an old blood test of Dad’s which showed his Haemoglobin used to be 160 (the normal reference range for a male lies approximately between 130 – 165g/L). With the benefit of hindsight, it’s likely that his new habit of afternoon naps on the weekend and occasional irritable moods were related to his declining Haemoglobin level, which dropped by 50 points before we found out that he had CAD and needed a treatment plan.

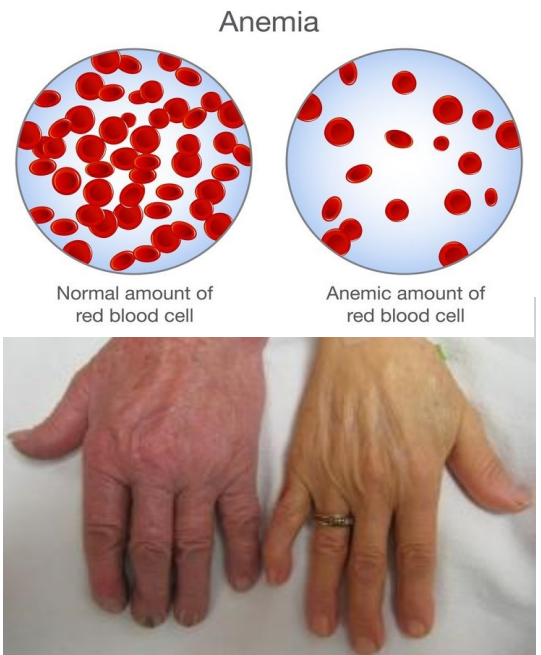
Nowadays, with the help of therapy, Dad’s been able to maintain a fairly steady Haemoglobin level of about 90. However, in the earlier stages of his disease around the time of starting treatment, there were times it dipped dangerously low and he was very pale. In these instances, it was usually Mum who’d be the first to notice a change in Dad’s colour and energy and suggest he get another blood test done to check his levels. Getting a blood test was not always the most straightforward task - as I’m sure many CADdys know - and this will be the focus of a future blog post. For Dad, who’s been challenged to adapt to life with this condition, it’s been a learning curve to be able to identify the difference between what’s normal tiredness and what’s CAD-related exhaustion that requires medical input. Dad still joins in ParkRun whenever the weather permits, and for him, his run-times have pretty well matched the peaks and troughs of his Haemoglobin level. These days, when he sees and feels he’s slowing down, this is a useful prompt that shouldn’t be ignored, and suggests he might need some medical input.

In part 3 of this blog, I explore Dad’s experience of jaundice (turning yellow) - how his appearance led people to believe he might have cancer, and how this assumption affected us.

## Part 2: Slowing down (cont.)

### *Medical Spotlight: Anemia*

Anemia is the medical term used to describe a low Haemoglobin or low red blood cell count. Haemoglobin is the protein subunit in red blood cells that carries oxygen around the bloodstream and delivers it to organs and tissues in the body. Anemia can occur in many different medical conditions or nutritional deficiencies. When it develops gradually over time, it's not always easy to spot. Some clues might be feeling tired or weak, appearing pale, experiencing dizziness or a 'whooshing' sensation in the ears and, in more severe cases, shortness of breath and/or chest pains. In CAD, anemia occurs by a disease process called "hemolysis" which refers to the breakdown of red blood cells within the body. For people with primary CAD (i.e. not related to an underlying malignancy or infection), the breakdown of red blood cells is triggered by a disorder in the immune system, typically a clonal proliferation of B-cells. These abnormal cells produce CAD antibodies which tag red blood cells for destruction by the body. Haemoglobin levels are important to monitor in CAD, but please keep in mind when sharing and reading stories with other CADdys that there are slight variations in the ways different laboratories test this marker, and the results may be presented with different units or normalised reference ranges.



## “Chitter Chatter”: *Meet our members*

**Name: Pat Watson**, President of the Cold Agglutinin Disease Foundation

**What 3 words describe you?** Proactive, optimistic, introverted

**Who do you most admire and why?** Anyone who has CAD and adapts and moves on.

**How has CAD changed your life (one positive, one negative)?**

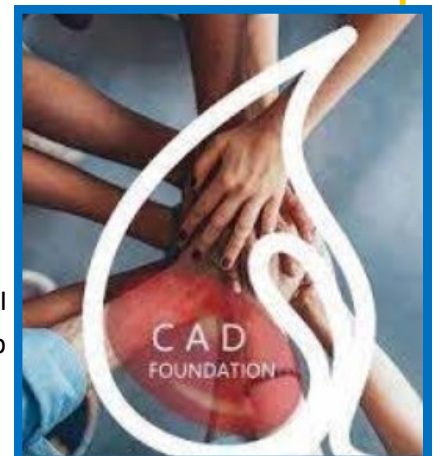
**Positive** – Met some really great people through the Foundation and CADdy CHATTER.

**Negative** – I hate the lack of physical stamina.

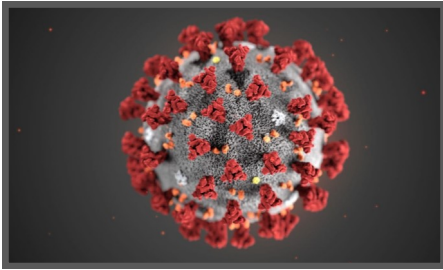
**What is your favorite hobby?** Genealogy

**What's one thing that annoys you the most?** When everybody wants a piece of me. I simply don't have time for everything.

**What's the best piece of life advice you've heard?** From my Dad – I always want to know all the “whys, hows, whats” etc. right now. He said “Stop wanting to know everything too soon.”



# Novel coronavirus and COVID-19



The novel coronavirus, or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus, and COVID-19 is the associated illness.

In our last issue, we outlined our top 5 tips for staying safe during the pandemic. Below, CADdy member **Dee Ryan** outlines her experience of contracting the novel coronavirus.

## Coronavirus: my experience

*I wondered  
“Is this the  
night I start  
having  
trouble  
breathing?”*

As early as February, I was monitoring China’s outbreak and wondering if I could believe what I was reading. I cancelled a road trip in the first week of March, feeling ridiculous and blaming CAD for my overly cautious decision. It would be another three weeks before Massachusetts went into a two-week shutdown. Remember when we all thought it would be for two weeks? There was still snow on the ground when I went grocery shopping for the last time, March 19th. I was so worried about getting sick that I told my college-age son to get permission to shelter in his dorm after college was shut down. I felt very vulnerable.

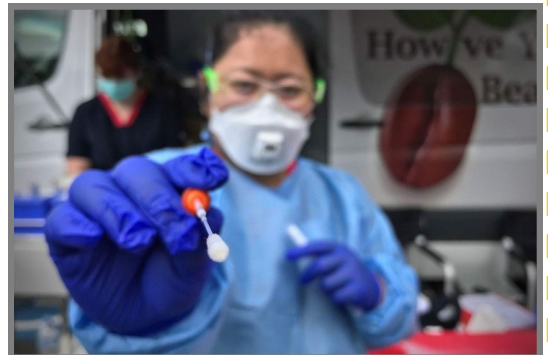
On April 3<sup>rd</sup>, I developed a cough and fever. For the first five days I had a low-grade fever, but otherwise I mostly felt brain-fog and sleepiness. Because of my CAD, I have an oximeter. These inexpensive devices are placed on the finger and show oxygen saturation (typically around 98%) along with your heart rate. Until COVID-19, I used it exclusively to watch my heart rate, which gets “tachy” (tachycardia is an above normal heart rate) sometimes due to my severe anemia. My oxygen held steady at 95% while my chest felt like a case of bronchitis. The Centers for Disease Control and Prevention (CDC) website stated that you only had to worry once the oxygen saturation fell below 93%.

On day six I started to perk up and enjoyed thinking that I was a mild case, only to crash on day seven. I was having terrible morning headaches and nightly fevers in addition to worrying “*is this the night I start having trouble breathing?*”. My CAD is caused by an indolent lymphoma (very indolent! I was diagnosed 13 years ago and am still on “watch and wait”). Night sweats can be a symptom and, like other patients, I have on occasion wondered if I have had one. Well, I don’t wonder anymore! For five nights I suffered the most incredible COVID-19 night sweats along with vivid, strange dreams.

By Monday, April 13th, I started to grow worried about how long my fevers had lasted. I have significant anemia, but it does not slow me down too badly- it holds very steady, unless I get a fever. In the past, when I have gotten sick, I have had a fever for 4 or 5 days and become very pale. It was now day 11! I wondered what on earth my blood was doing. Would I make it through the COVID-19 only to have a CAD disaster?

That evening my oxygen reading went to 91% and it was time to go to the ER. I tested positive for Covid-19, but the EKG and chest X-Ray eliminated any immediate worry. On the other hand, my blood work caused quite a reaction with the doctor who assumed that I was having a crisis. However, once I heard the results, I was happy to know that the fever had not lowered it much from the typical level.

I was still quite sick for another five days, and it took weeks before I really felt like myself, but it was great news to know that CAD did not complicate my COVID-19 experience.



A coronavirus nasal swab test

# Understanding laboratory results in CAD



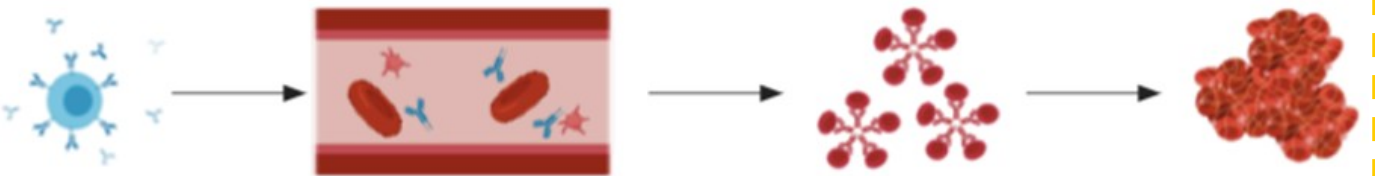
*Dr. Rana Walley is an American Society for Clinical Pathology (ASCP) certified Medical Laboratory Scientist with a PhD in Clinical Health Science from the University of Mississippi Medical Center. Her father suffers from severe CAD and she has shared in his frustration trying to find understanding healthcare professionals and consistent lab practices.*

Lab results are central to understanding many disease processes. The CDC Division of Laboratory Systems states that 70% of medical decisions depend on lab test results. As a patient, it is helpful to understand quality control of laboratory results in order to better advocate for your own health care. The many different tests ordered, in addition to variable reporting units and reference ranges, may make results interpretation complex and confusing.

This article is intended to provide general information about why selected common lab tests are ordered and how CAD may affect these results. This article is not intended to provide a medical diagnosis or be used to interpret lab values. Always discuss your results and their meaning with your treating doctor. The full article will be uploaded to the CADF website shortly.

The blood of CAD patients interferes with laboratory tests in two ways: agglutination (clumping together) and lysis (cell breakdown). A few tests commonly affected by these processes are explained below:

**Hemoglobin (HGB or Hb)** is done to assess the oxygen carrying capacity of the blood (Hb is an oxygen-carrying protein in a red blood cell (RBC)). Normal ranges vary but are generally 13 –17g/dL for males and 12-15g/dL for females (European ranges 130-170g/L and 120-150g/L). In CAD, the agglutination of red cells interferes with the test because red cells are typically counted by automatic counting methods that require cells passing through a type of “gate” in single file. If cells are stuck together they are measured as one large cell, not several cells stuck together.

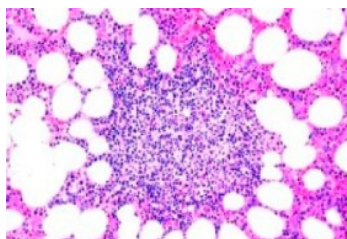


*The process of Agglutination:* 1. Abnormal B-cells produce CAD antibodies. 2. The antibodies are released into the blood stream. 3. The antibodies bind onto RBCs (multiple at once). 4. Clumping/agglutination of bound RBCs occurs.

**Hematocrit (HCT)** is the volume that RBCs occupy within whole blood and is reported as a percentage. Hemolysis invalidates results as it is impossible to get an accurate volume of RBCs without all cells being intact. The HGB and HCT (H&H) share a unique relationship in that the HGB x3 should equal the HCT (+/- 3%). This is called the ‘rule of three’. For example, if the HGB is 12g/dL the HCT should be 33-39%. Laboratory professionals use this quick mathematical check to see if the H&H ‘match’. If the instrument HCT does not agree with the ‘rule of three’, laboratory professionals must investigate for an instrument problem or a patient pathology (such as CAD hemolysis) that interferes with test results. The lack of agreement with the ‘rule of three’ is often the first indication that sample may need to be warmed and rerun or, in severe cases, the plasma may need to be replaced with saline and retested. This is one reason blood work in CAD may take extended time.

**Bilirubin** is a breakdown product of hemoglobin. The normal life span of a RBC is 120 days. Normally there is a steady breakdown and regeneration of RBCs and the bilirubin level will remain steady. The body is very efficient in recycling parts of RBCs and delivering the iron and protein to the bone marrow where new RBCs are created. RBCs lysed by CAD pass through the liver where bilirubin is made. Excess bilirubin (from the excess lysed RBCs in CAD hemolysis) will be excreted via the gastrointestinal tract and urine (causing dark urine). In hemolysis the bilirubin level will be elevated. (Cont. over page)

## Is primary CAD a bone marrow disorder?



Dr Sigbjørn Berensen, Medical Advisor and friend of the Cold Agglutinin Disease Foundation, has previously collated the bone marrow findings of 54 patients with CAD and he published his research in the American Society of Hematology Journal in 2016. (see article at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6142439>).

He discovered that the marrow findings were surprisingly similar for 40/54 patients, with nodular groups of lymphoid tissue being a common finding (see example image top left). He termed this appearance “Primary Cold Agglutinin-associated lymphoproliferative disorder”. It is different to other types of recognized lymphomas such as Waldenstrom’s (Lymphoplasmacytic lymphoma) or marginal zone lymphoma.

While it is therefore likely that CAD is due to an underlying lymphoma (not previously diagnosed), it is important to note that this discovery does not change the management or outcomes for patients who have been given a diagnosis of ‘primary’ CAD. It is exactly the same condition, but researchers continue to find out more about it all the time, thereby enabling new treatments to be developed.

## Understanding lab results in CAD (cont.)

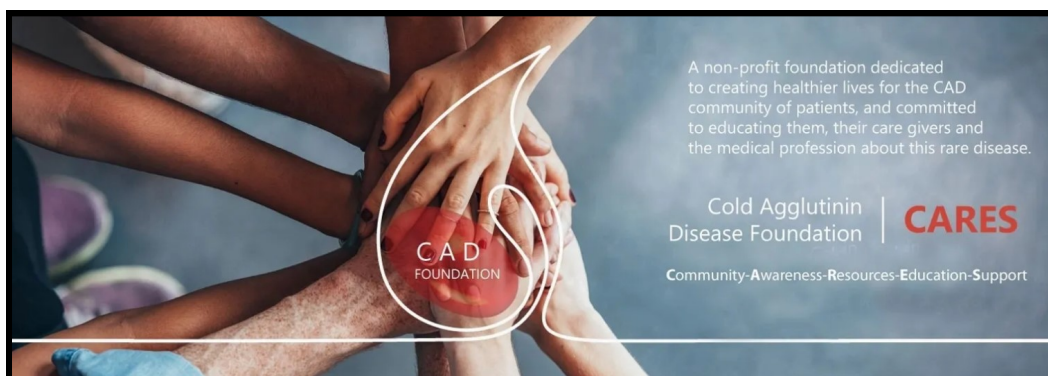
“Laboratory professionals are taught to reject hemolysed samples”.

**Lactate Dehydrogenase** (LD or LDH) is an interesting enzyme that is found in almost all body tissues and is released after cell trauma. The highest fractions of LDH are found in cells in the heart, liver, kidneys, skeletal muscle and RBCs. For example, LDH is 200X more concentrated INSIDE the red cell compared to outside. Lysis of red cells (e.g. during CAD hemolysis) releases LDH into serum/plasma producing an extremely high result. LDH can therefore be a marker for the presence of hemolysis in CAD. Of note, laboratory professionals are taught to reject hemolysed samples submitted for LDH. This is because a difficult blood draw that causing excess lysis to RBCs (as they pass through the needle/test tube) is a common cause of a falsely elevated LDH. A newly diagnosed CADdy might have their initial bloods rejected for this reason, until the laboratory realizes that the blood in a CAD patient is always/often partly hemolysed and they should report the results regardless.

## CADF: new CARES logo!

As part of our CADF website upgrade, we have developed a new logo!

Our new logo explains the many roles of CADF in supporting patients with CAD, their care partners and clinicians.





A non-profit foundation dedicated to creating healthier lives for the CAD community of patients; we are committed to educating CADdys, their care partners and the medical profession about this rare disease.



### Cold Agglutinin Disease Foundation

E-mail: [info@cadfadvocacy.org](mailto:info@cadfadvocacy.org)

Website: <https://coldagglutinindisease.org>

#### Facebook:

Business page- Cold Agglutinin Disease Foundation

Support group- CADdy Chatter

Complete your online profile at:

<https://form.jotform.com/201154877602050>

to receive up to date information about virtual meetings, events (like the CADF summit), volunteer opportunities, promotion and more!

## Product review and giveaway!

The Gintao electric heated foot warming pad is a great product to keep your feet warm— particularly for those who suffer with Raynaud’s phenomenon or other conditions with poor peripheral circulation. It has a soft, thick 20 x 22” flannel cover containing a central heating pad that heats quickly to warm your toes! On Amazon it scores a 4.2-star rating from almost 600 reviews. It is adjustable with 3 levels of temperature options and an automatic turn-off function to prevent overheating. According to some reviews this item is also popular with cats, so be warned you might have to share it if you have a pet cat!

\*This product has no affiliation or promotional relationship with CADF— we just picked it because of the great reviews! We are providing this product as a:

### FREE GIVEAWAY!

To enter, you need to have registered with CADF previously by completing the **member profile survey** on the CADF website (see link above, top right).

Then email: [info@cadfadvocacy.org](mailto:info@cadfadvocacy.org) with answers to the questions in the “Chitter Chatter” section of this newsletter. CAD Foundation will randomly draw a name from those who answer all the interview questions.

By participating, you agree to be featured in the “Chitter Chatter” section of future newsletter editions. One lucky winner will be selected for the next issue AND win the product giveaway!

\*Odds of winning are based on the number of entries received

**Entry deadline:** Midnight October 24, 2020 EST (USA)

**Draw date:** October 25, 2020

