IGG4 COMPASS

IgG4-Related Disease

A *Patient's Guide*

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LUC SMET

igg4.org

IgG4-Related Disease: A Patient's Guide

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Luc Smet

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IgG4-Related Disease: A Patient's Guide

First edition, version 1.0.

Published by the author, alongside igg4.org.

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What this is not. This book carries no medical authority. It gathers published sources and says where each one came from. Every clinical decision belongs with a specialist who has your notes in front of them.

The living version, with a working link to every source, is at **igg4.org**.

Front matter

Why this book exists

I was told I most likely had pancreatic cancer.

A lesion on the tail of my pancreas, read as a probable adenocarcinoma. For a while, that was the word I carried.

The tissue told a different story. IgG4-related disease, an immune condition that imitates cancer well enough to be mistaken for it. The diagnosis I feared most gave way to one that gave me my life back, because this disease can be treated.

By then, years had passed with signs in my blood that no one had followed.

The treatment keeps me awake. Some nights I am up with questions about my own body and nowhere good to take them. So I did what anyone does now. I searched.

I found very little. Pages that promised information and led to dead links. Communities that existed mostly in name. For a disease where delay can cause lasting harm, the help a frightened person could reach was thin.

So I decided to build the thing I could not find.

First igg4.org, and now this book. It does the searching for you. It finds what has been published about IgG4-related disease, shows you where each piece comes from, gives you the link, and points you to a specialist. It does not diagnose, and it does not replace your doctor. It hands you what you need to walk into your next appointment knowing more than you did.

I am a patient, not a doctor. That is the point. The authority stays with the sources and the specialists. I am the one who gathered them, so you do not have to do it alone in the middle of the night.

My lovely wife Vanessa and I wrote *Balanced Divinity*, a book inspired by life force, love and also by the life experience this disease gave us, and that book is the only thing behind this project. No company, no sponsor. Two people who decided the next patient deserves an easier road.

If you live with this disease, treat it, or love someone who has it, there is room for you here. Bring a source we missed. Lend your name. Help someone find their footing. I built this for us, and it will be better with you in it.

Luc

How to use this book

You do not have to read this in order.

If you were diagnosed this week, Part 1 is written for you and Chapter 2 is probably the one you need first. If you are looking for your own organ, go to Part 3 and find it. If you have just been handed a prescription for prednisone and want to know what is coming, go to Chapter 12.

Nothing here is urgent reading. It will keep.

Each chapter ends with two things: something you can do this week, and a pointer to the page on igg4.org that covers the same ground and stays current.

When you meet my own case

I have IgG4-related disease. It is why this book exists.

A few times in these pages my own experience appears. Those passages always carry the line *My own case* above them, and they are always in the first person. They are there because some things are easier to recognise when they come from someone who has been through them.

They are not evidence.

One person's disease proves nothing about anyone else's. My organs, my treatment and my course are mine. Where my experience and the research point in different directions, the research wins, and every clinical statement in this book comes from a cited source rather than from what happened to me.

Medical disclaimer

This is the one section of the book written to be read before anything else. It is short on purpose.

This book is information and education. It is not medical advice, diagnosis or treatment, and reading it creates no

relationship of care between you and the author.

The author is a patient, not a doctor. No part of this book has been written, reviewed or approved by a clinician, a medical body or a regulator. The authority lives in the sources named at the back, and the summarising of those sources into plain language is the author's own work, with everything that implies: a summary can be incomplete, it can be wrong, and it goes out of date on its own.

It cannot tell you what is happening in your body. Not what your scan shows, not what your result means, not whether a treatment is right for you. Those questions belong with a specialist who has your notes in front of them and who has treated this disease before. Chapter 19 helps you find one.

Nothing here is a reason to start, stop or change any treatment or any dose. Not a chapter, not a quotation from a medicine label, not a sentence that seems to describe you exactly. Take it to your specialist and decide there.

Where this book and your own doctor disagree, your doctor knows your case and this book does not. Where this book and

igg4.org disagree, the site is the current version.

No liability is accepted for decisions made or actions taken on the strength of anything in these pages. What you do with this book is yours to decide.

In an emergency, contact your local emergency service. Across the European Union that number is 112. Do not wait, and do not look anything up first.

Medicine moves, and this disease is moving faster than most. Check igg4.org before relying on anything here that matters.

Where everything in this book comes from

This is the part most patient guides leave out, and it is the reason you can trust the rest.

Every factual claim in this book carries a citation, and every source had to clear the same bar before it was allowed in:

- It is independent, peer-reviewed and indexed, or it is issued by an independent public body such as Orphanet, a national

rare-disease network, a medicines regulator or a university hospital, or it is an academic thesis or monograph.
- Industry-funded material is excluded, unless it reports the results of a clinical trial published in a peer-reviewed journal.
- If a source does not support a claim, the claim comes out. No hunting for a friendlier source.
- No source is described unless it has been read.

Where the evidence does not exist, this book says the evidence does not exist. You will find several places where the honest answer is that nobody has studied the question yet. Those passages are not omissions. They are the most useful sentences in the book, because they tell you when to stop searching.

The full reference list is Part 6.

Version and currency

This is version 1.0, first released in September 2026.

Medicine moves, and this disease is moving faster than most. The living version of everything here is at **igg4.org**, in five

languages, and it is updated as the evidence changes. If you are reading this more than a year after the date above, check the site.

What this book costs

The book is free to download from igg4.org, in every language it exists in.

The printed and Kindle editions are priced at the lowest amount the printer or the platform allows. Where a minimum royalty cannot be avoided, it is set as low as the platform permits.

Anything that does reach the author goes back into igg4.org and the work around it. Nothing here supports anyone’s living.

The site itself carries no advertising and takes no sponsorship.

Part 1. What IgG4-related disease is

Before the tests, before the treatment, before the organ that brought you here.

What is this thing, who does it happen to, and why did it take so long for anyone to name it?

Chapter 1. A disease that imitates other diseases

Someone has said the words to you. Maybe a rheumatologist, maybe a gastroenterologist, maybe whoever finally looked at the scan and did not reach for the word everyone had been circling.

IgG4-related disease.

Four characters and a hyphen, and almost nobody you know has heard of it. You will have typed it into a search bar within the hour. Most people do. What comes back is written for doctors, or it is written by someone selling something, and either way it does not answer the question you are asking, which is not *what is the pathophysiology of this condition*.

It is: what is happening inside me, and what happens next.

This chapter answers the first half.

Nobody prepares you for a diagnosis that needs explaining

There is a particular kind of loneliness that comes with a rare disease, and it starts earlier than people expect. It starts the first time you try to tell someone.

With most illnesses, the name does the work. You say it and the other person’s face changes, because they already know roughly what it means and roughly what it costs. Here, the name does nothing. You say it and you watch them wait for more. So you end up explaining your own disease to your own family, days after learning it exists, using words you have only just met.

That is exhausting, and it is not a sign that you are explaining it badly.

It is a structural feature of having something rare. It will happen again with a receptionist, a manager, a nurse on a ward who has not met a case. This book exists partly so that you have somewhere to point.

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What is happening is an immune system building in the wrong places

IgG4-related disease is a condition in which the immune system causes inflammation that forms mass-like lesions or enlarges organs.[1]

That is the whole of it, and it is worth reading twice, because two things in that sentence are doing quiet work.

The first is *the immune system*. This is not an infection, and it is not something that arrived from outside. The cells involved are your own. In the tissues that are affected, particular immune cells build up: B cells, the plasma cells that produce IgG4, and CD4-positive T cells. They release signals that drive inflammation, and over time those signals drive the formation of scar tissue.[2]

Those three names, in plain words

They come back later, especially in Part 4, so they are worth thirty seconds now. If you already know this, skip it.

B cells are a kind of white blood cell whose job is to make antibodies. Antibodies are proteins your immune system uses to tag things it wants dealt with.

Plasma cells are B cells that have matured into full-time antibody factories. The ones involved here are producing IgG4, which is one particular type of antibody, and the one this disease is named after.

T cells are a different kind of white blood cell. Instead of making antibodies, they direct and carry out the response. The ones involved here are called CD4-positive T cells, and they are among the cells giving the orders.[2]

None of that is a fault in the cells themselves. They are doing the jobs they were built for, in a place and at a scale where the result is damage rather than defence.

Why it matters later: several of the newer treatments in Chapter 14 work by removing or quietening B cells. When you meet the phrase B-cell-targeted therapy, that is what is being targeted, and this is why.

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The second is *mass-like lesions*. Most people picture inflammation as redness and swelling that comes and goes. This inflammation builds something. It makes a lump, or it makes an organ larger than it should be. That is why this disease so often walks into a clinic through the door marked cancer, which is where the next chapter goes.

Almost any organ can be affected. Being affected in more than one place is typical, either at the same time or years apart.[1]

Years apart. Hold onto that, because it explains a great deal of what may already have happened to you: the gland that swelled and settled, the scan that showed something nobody could name, the episode filed away as unexplained. Those may not have been separate events.

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It was several diseases before it was one

For most of the last century this was not a disease. It was a scattering of conditions with separate names, in separate specialties, seen

by doctors who had no reason to speak to each other.

The thread was pulled through the pancreas. Recognition of the disease came first through autoimmune pancreatitis, and only afterwards was it understood as one condition capable of appearing in many organs.[2]

This is the reason your diagnosis may have taken years, and the reason your GP may not recognise the name. The single picture arrived long after the separate diseases did, and some of the doctors you will meet trained before it existed.[2]

That is not their failure and it is certainly not yours.

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This is the point where honesty matters more than encouragement

Most people with this disease respond to treatment.[1] That is true, and it is the single most important thing on this page.

Here is the part that sits next to it.

Inflammation that continues over months and years turns into scarring, and scarring is the part treatment cannot undo.[1] Medicines can quieten the inflammation. They cannot return tissue that has already been replaced by scar.

Which means time is not neutral here. The reason specialists press for early recognition is not tidiness. It is that the window in which treatment can protect an organ is a real window, and it does close.

Read that as information, not as an alarm. It does not mean something has already been lost. It means that the appointments, the referral you are waiting on, and the specialist who knows this disease are worth pushing for now rather than after the summer.

You are allowed to push. Most people diagnosed with something rare are far too polite about it for far too long.

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What this chapter cannot tell you

It cannot tell you what caused this in you.

The specialist literature does not answer that question for any individual person.[2] There are findings about susceptibility and about environmental exposures, and this book comes back to them. None of them will tell you why your body and not another one, and why now.

I would rather say that plainly than leave you searching for an answer that is not there yet.

Seven years of a number nobody read

My own case.

In 2019 a routine blood test showed a liver enzyme higher than it should have been. My GGT read 231. The upper limit is 64.

It was noted. It was filed.

Over the next seven years that number climbed. 354. 477. 517. 783. 933. Each time it appeared it was put down to a family history of liver disease, and each time I accepted the explanation, because it came from someone who knew more medicine than I did. In that

same first year an ultrasound found a lymph node in my right groin, described as probably benign.

I was running a group of companies. Reading signals from incomplete information was the job. I applied none of it to myself.

What I understand now is that those were not seven unrelated events. A liver marker rising for years, in my case, belonged to this disease, and it was never investigated as such until much later.

That was mine, and yours will be different. Different organ, different marker, different years, and quite possibly no years at all.

What might transfer is only the question. If something in your own history has been explained away more than once, it is worth asking whether it belongs to this.

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What you can do with this

Write the name down and keep it somewhere you can hand over. IgG4-related disease. You will be asked to spell it more

times than seems reasonable, often at moments when you are least able to. A note on your phone is enough.

Ask, at your next appointment, which organs are involved in your case, and whether any others are being watched. The wording can be plain: *"Which organs does this affect in me, and is anything being kept an eye on?"* This disease works across specialties, and the person in front of you may be looking at only one part of it.

Ask whether you have seen someone who has treated this disease before. Not to challenge anyone. To find out. The phrasing that works is: *"Is this something you see often, or would a specialist centre add anything?"* Chapter 19 has the directory.

Which leaves the question this chapter kept stepping around.

If this disease builds masses and enlarges organs, and if it does that in the pancreas more than anywhere else, then how does anyone tell it apart from cancer? And what happens to the people where nobody does?

That is the next chapter.

Chapter 2. Why it is so often taken for cancer

For a great many people, the word cancer arrives before the word IgG4 does.

It arrives in a corridor, or in a phone call that begins with someone asking whether you are somewhere you can talk. It arrives as a shadow on a scan that a radiologist has described carefully and a clinician has read plainly. It arrives, often, weeks before anyone can tell you it was wrong.

If that happened to you, this chapter is about why, and about what it means that it did.

The fear does not leave when the diagnosis changes

Something strange happens when a cancer scare resolves into something else.

Everyone around you exhales. Cards get sent. The relief in the room is real and it belongs to them, and it is good news, and you are supposed to feel it too.

What people rarely mention is that some of it stays with you. You have already had the conversation in your head, the one where you worked out what you would tell your family. That conversation happened. It does not unhappen because the biopsy came back differently.

You may also find you no longer trust scans the way you used to, and that the week before an appointment is worse than it used to be.

None of that is you failing to be grateful. It is the ordinary aftermath of having been told something enormous, and it is worth telling someone about rather than carrying quietly because the outcome was good.

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The resemblance is real, and it is a resemblance of shape

IgG4-related disease forms masses and swelling, so it can look like cancer on a scan. The pancreas is where this happens most often, and it also happens in the kidneys, in the lymph nodes and elsewhere.[3]

Notice what that sentence is not saying. It is not saying doctors are careless, and it is not saying the scan was read wrong. On an image, a mass formed by inflammation and a mass formed by a tumour can look alike, because what a scan sees is shape and density rather than cause.

Which is why some people are investigated, biopsied, or operated on for a suspected cancer before IgG4-related disease is recognised.[3]

That sequence is common enough to have its own literature.

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Ruling out cancer carefully is the system working

This is worth saying without hedging, because people carry unnecessary anger about it.

Ruling out cancer carefully is a normal and important part of the process, and it is not a sign that anything has gone wrong.[3]

A clinician who sees a mass in a pancreas and does not think about cancer is not being kind. If the tests, the waiting and the second opinion felt disproportionate, they were proportionate to a question that had to be answered before anything else could be.

What improves the odds of the two being told apart is reaching a specialist who knows this disease, early.[3]

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It is not only cancer that this disease resembles

The list is longer than most people are told.

Doctors work through lymphoma, infections, sarcoidosis and some forms of blood vessel inflammation. There is also a group of rarer conditions that overlap with this one: Erdheim-Chester disease, Rosai-Dorfman disease, and idiopathic multicentric Castleman disease.[4]

Those three matter for a specific reason. They can affect the same organs, and they can show raised IgG4 as well. So the one blood test whose name is in the disease cannot separate them.

Telling them apart usually needs a biopsy read alongside scans and blood tests, and sometimes a second opinion from a centre that sees the disease often.[4]

If your own diagnosis took a long time, or changed once along the way, this is the reason. It was not indecision.

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The honest part of this chapter is about surgery

Sometimes nobody tells the two apart in time.

When this disease forms a lump in an organ, scans can look enough like cancer that surgery goes ahead before anyone considers IgG4-related disease. A published series of four patients with masses in the kidney and ureter describes exactly that, with the diagnosis made only from the tissue afterwards.[5]

In two of those four, the IgG4 blood test was normal.[5]

Sit with that for a moment, because it is the single most practical fact in this chapter. A normal IgG4 result did not mean the disease

was absent. Chapter 7 deals with that test properly, and this is the first of several places where it will disappoint you.

The authors of that series argue for taking a small tissue sample early where the picture is unusual, rather than going straight to major surgery.[5]

Four patients is four patients. It is a case series, not a trial, and it cannot tell you what the right decision is in your own case. What it can do is tell you that the question is a real one, asked in print, by surgeons.

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What you can do with this

If you are facing surgery for a mass and IgG4-related disease has been raised as a possibility, it is reasonable to ask whether a biopsy first would change anything.[5] Those are close to the corpus's own words, and they are close to the words you can use: *"Would a tissue sample before surgery change the plan at all?"*

Ask what your own IgG4 blood level was, and write it down. Whatever the number, Chapter 7 will help you read it. A normal result is not the reassurance it appears to be, and a high one is not the verdict it appears to be.

If you went through a cancer scare, say so to someone. To your GP, to a specialist nurse, to whoever asks how you are and waits for the answer. The scare is part of your medical history and it is also part of what this has cost you.

Five words in a car park

My own case.

On the 22nd of May 2026 I had an endoscopic ultrasound and a guided biopsy at a hospital in Cádiz. Vanessa drove me the two hours there and sat with me through the consent forms.

I read the discharge report in the car park.

Masa en cola de páncreas, probable adenoCa. A mass in the tail of the pancreas, probably adenocarcinoma.

I know now what those words are. They are the endoscopist's clinical impression, formed from what she saw through the scope: hard tissue on elastography, no contrast enhancement, a picture that fits cancer better than it fits inflammation. They are not a histological diagnosis.

Standing in that car park at four in the afternoon, I did not know that. I only knew the five words.

Five days later the tissue came back. Fibrosis in a storiform pattern. A dense inflammatory infiltrate. An IgG4 to IgG plasma cell ratio of fifty per cent. Pancreatic involvement by IgG4-related disease.

Not cancer.

The sound my wife made when I told her is the best sound I have ever heard.

Four nights sit between those two moments and I will carry them for the rest of my life. That was mine. Yours will have its own shape and its own waiting, and I would not pretend to know what it costs you.

What I would hand you from it is one sentence.

A clinical impression is not a histological diagnosis. Ask for the tissue.

So the disease imitates. It imitates cancer, and it imitates several other conditions well enough to be mistaken for them by specialists.

Which raises a question with an uncomfortable edge to it. If it is this hard to recognise, how many people have it? And are you as alone in this as it currently feels?

Chapter 3. Who it happens to, and how rare it really is

The first thing almost everyone does is look for the numbers.

How many people have this. How many people like me. Whether anyone in this country, this city, this age bracket is walking around with the same thing.

The numbers are thinner than you would expect, and the reason they are thin turns out to be worth knowing.

Rare is not a number, it is an experience

Being told you have a rare disease can feel isolating, as though nobody else knows what you are facing.[6]

That feeling has a particular texture. It is not only that few people have it. It is that the systems built around illness assume you are common. The leaflet does not exist. The support group in your town is for a different condition. The doctor pauses before saying the name, or reads it off the letter.

You are one of many, spread across many countries, and there are patient groups where people who live with this disease share what they have learned.[6]

Both of those things are true at once: the loneliness is real, and the company exists. It is just further away than it would be with a common illness, and you generally have to go and find it.

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Nobody knows how many people have this, and the reason matters

How many people have IgG4-related disease is not known precisely, and estimates drawn from whole populations are still limited.[7]

You will find figures online anyway. Treat them carefully, and notice how few of them say where they came from.

The reason for the uncertainty is not that nobody has tried. It is that recognition of the disease has grown over the past twenty years, which means counts based on diagnosed cases are likely to understate how many people are living with it.[7]

Read that sentence the right way round. It does not say the disease is becoming more common. It says we are getting better at spotting it, and that the people who were always there are only now being counted.

Some of them were counted as something else for years. Some of them have not been counted yet.

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It is found everywhere, in everyone

IgG4-related disease is found in people of all ethnic backgrounds, around the world.[7]

This is worth stating plainly, because much of the early research came from Japan, and a reader who notices that can conclude something that is not true. That the literature is Japanese says where the research began. It does not say where the disease lives.

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The pattern in who gets it is real, and it is not a rule about you

Taken as a whole, this disease affects men about twice as often as women, which is unusual among conditions of this kind.[8]

That has a consequence in a clinic. A disease that is commoner in men, sitting in a category of illness that is usually assumed to run the other way, is a disease that gets missed in both.

The pattern also depends on which organs are involved.[8]

- Disease of the pancreas and bile ducts, and disease of the area behind the abdomen, affects men more often.
- Disease limited to the head and neck most often affects women.

Men are also more likely to have several organs involved, and to have more severe disease.[8]

Most people are diagnosed between their mid-fifties and their seventies, with men on average a few years older than women at diagnosis. It is uncommon in children.[8]

If you are a woman, or you are thirty-four, or your disease is in an organ that does not fit the pattern above, none of this makes your diagnosis less likely to be right. These are descriptions of a population. They are the shape of a crowd, and you are one person in it. The pattern is useful to your doctor when deciding what to suspect. It has no authority over what you have.

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The honest paragraph here is a small one

There is no prevalence figure in this book because there is no prevalence figure worth giving you.[7]

Some guides print one anyway. When you meet a number for how many people have this disease, look for what it is attached to. Several of the figures in circulation trace back to a source that did not cite anything either.

An honest “not known precisely” is more use to you than a confident number that turns out to be nobody’s.

What I found when I looked, and what I found when I asked

My own case.

During the weeks when nobody could tell me what I had, I searched the way frightened people search. At two in the morning, with glucose readings on the table and pain under the sternum.

What came back was fragmented, technical, out of date, or behind a paywall. Almost nothing written for someone without a medical background. Almost nothing in Spanish, in the country where I live.

That is the loneliness this chapter is about, and it is not only social. It is informational. The thing you most need at two in the morning has not been written for you.

Then, at half past midnight on the worst night of that week, I sent a message to the Spanish patient association for this disease.

They answered the same morning.

Their scientific committee escalated my case within hours. A professor in Newcastle replied to a letter I had sent and backed my Spanish team's approach before the biopsy result existed. The system does work when you know how to reach into it, and I did not know how until I was forced to learn.

That was mine, and your route will be different, in your own country and your own language.

What holds is smaller and more useful than my story. The people who have this disease have found each other. Some of them answer at midnight.

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What you can do with this

Find the patient group before you need it. Not because today is hard, but because the day you have a question at eleven at night is not the day to start searching. igg4.org lists the groups that exist.

If you are the first case someone has seen, say so out loud, kindly. *“I gather this is uncommon. Would it help to have someone who sees it often look at this with you?”* That sentence protects the relationship and gets you what you need.

Stop reading prevalence statistics. They will not tell you anything about your own disease, and the good ones do not exist yet.

Rarity explains the loneliness. It does not explain the confusion.

That comes from something else: this is one disease that appears in a dozen different places, and where it appears changes almost everything about how it looks.

Chapter 4. The shape of the disease

Two people with this diagnosis can have almost nothing in common.

One has a swollen gland in the jaw and a slightly odd blood test. Another has a pancreas that looked like a tumour and six weeks of fear behind them. Another has scarring behind the abdomen that was found because a kidney stopped draining.

Same disease. Same name in the letter. Almost no overlap in the experience.

This chapter is the map, and it is the reason Part 3 is organised the way it is.

Where it turns up, and roughly how often

IgG4-related disease can affect many organs, and most people have only some of them.[9]

The common areas are the pancreas and bile ducts; the salivary and tear glands; the eyes and orbits; the kidneys; the lungs and chest;

the space behind the abdomen, called the retroperitoneum, and the aorta; and the lymph nodes.[9]

To give a rough sense of how often: the salivary glands are involved in between a quarter and a half of people, the kidneys in around one in six, the lungs in around one in seven, and the aorta in around one in ten.[9]

Being affected in more than one place, either together or years apart, is typical.[9]

And because it can appear in so many places, it is easy to miss and easy to confuse with other conditions.[9] That is the whole of Chapter 2 restated as arithmetic: a disease with a dozen addresses will be met by a dozen specialties, most of which are not looking for it.

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The disease falls into four broad patterns

A study from a specialist Italian centre looked at 179 people and confirmed that the illness tends to fall into four patterns, depending on

which organs are involved.[10]

- Mainly the pancreas and bile ducts.
- Mainly the retroperitoneum or the aorta.
- Limited to the head and neck.
- A wider pattern, known as Mikulicz, with systemic involvement.

Experienced doctors could sort patients into the same four patterns from the clinical picture alone.[10]

The patterns were more than descriptive. They tracked differences in age: people with head and neck disease tended to be younger, around 52, and people with pancreas and bile duct disease tended to be older, around 67. They tracked differences in blood IgG4 levels, highest in the pancreas and bile duct group. And they tracked differences in the course of the illness over the first two years.[10]

Head and neck disease needed the highest cumulative dose of steroids and was harder to control. Diabetes was more common in the groups with pancreatic involvement.[10]

One thing the patterns did not predict: the rate of relapse itself was not clearly different between them.[10]

That last finding deserves its own line,

because it cuts against what you would expect. Harder to control is not the same as more likely to come back.

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What a study from one country shows, and what it does not

Here is where a patient guide usually smooths things over, and this one is not going to.

A Chilean study looked back at the records of 52 adults seen at six medical centres. In that group, the organs most often involved were the lungs, the eyes and the kidneys.[11]

Compare that with the frequencies a few paragraphs above, where the salivary glands led. These are different pictures of the same disease.

Neither is wrong. They are different groups of patients, in different countries, reaching different hospitals through different routes. Which is precisely why the Chilean authors' own framing is the right one to carry: this is one country's experience, not a rule for you.[11]

The other findings from that group are worth having:

- About one in three patients had only one organ affected. The rest had two or more.[11]
- Everyone with kidney or lung involvement had disease in more than one organ at the same time.[11]
- Blood IgG4 was above the reference range in about four out of ten of those tested, which means a normal blood test does not rule the disease out.[11]
- All of them were treated with steroids. About two thirds also needed an additional immunosuppressant medicine, and about one in six needed rituximab because the disease kept coming back.[11]

That last line is a preview of Part 4, and it is a realistic one. Steroids for everyone, something more for most, and a further step for a minority.

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Why your pattern matters, and how far that goes

Knowing which pattern you fall into tells your specialist something real about what to expect: which organs to watch, roughly what age profile fits, how much steroid the disease may demand.

What it cannot do is tell you your own course.

The Italian study reports averages across 179 people, and averages are made of individuals who mostly sat somewhere other than the middle. What all of this means for your own case is a question for your specialist, who has your scans, your bloods and your history, none of which appear in any study.[10]

That sentence is going to recur in this book. It is not a disclaimer bolted on for safety. It is the actual limit of what a book can know about you.

— ✦ —

What you can do with this

Ask which of the four patterns your disease looks like. *"Does mine fit one of the recognised patterns, and does that change what you are watching?"* It is a question specialists in this disease will recognise immediately.

Ask whether anything beyond the affected organ is being monitored. Given how often more than one site is involved, this is a reasonable question rather than an anxious one.

Read only the organ sections in Part 3 that apply to you. The rest will be there if you ever need them. Reading about organs you do not have involved is a way of frightening yourself with someone else's disease.

That is the map: what it is, who it happens to, and where it goes.

Part 2 is about how anyone recognises it. It starts with five red flags that were written down precisely so that a doctor who has never seen this disease might still spot it.

Part 2. How it is recognised

Part 1 was about what this disease is. This part is about how anyone works out that you have it.

It takes longer than it should, it takes several tests rather than one, and the test named after the disease is the least reliable of them. Those three facts explain most of what happens to people in the months before they get an answer.

Chapter 5. The five red flags

If you take one thing from this book and hand it to a doctor, make it this chapter.

Researchers across Europe agreed on five signs that should make a doctor think of IgG4-related disease and refer to a specialist.[12] Five, because a disease that appears in a dozen organs cannot be caught by one specialty watching one organ. Somebody needed to write down what makes any doctor, anywhere, stop and consider it.

The five

- Swelling in one or more organ or area.
- Involvement of the pancreas or the bile

ducts.
- A raised level of IgG4 in the blood.
- Certain tissue findings under the microscope.
- A specific kind of vein inflammation, called obliterative phlebitis.[1][2]

Three of those are things a doctor finds. Two of them, the swelling and the pancreas or bile ducts, are things you may already know about yourself.

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What they are for, and what they are not for

They are not a test.

They cannot tell you whether you have this disease, and counting how many apply to you will not give you an answer.[1][2] They are the trigger for a conversation and a referral, which is a different job entirely, and a more useful one at this stage than a score would be.

They also come from expert agreement rather than from a trial, and they are still being studied.[1][2] That is worth knowing rather than

hiding: a group of specialists agreed on what should raise suspicion, and the agreement is doing the work.

One of the five deserves an early warning. A raised IgG4 in the blood is on that list, and it is the single most misread result in this disease. Chapter 7 is about why.

— ✦ —

What you can do with this

Print the five and take them to an appointment. Not to argue. To ask: *“Do any of these fit my picture?”*

Use them when you are being sent between specialties. This disease is often met by one specialist looking at one organ. The red flags are the thing that crosses those boundaries, and you may be the only person in the room holding all of your own history.

Which raises the obvious question. If five signs only raise suspicion, what settles it?

Chapter 6. How the diagnosis is put together

There is no test for this.

That sentence surprises people, so it is worth saying at the start of the chapter rather than burying it. Diagnosing IgG4-related disease means putting several pieces together, because no single test confirms it on its own.[13]

The pieces

A specialist looks at blood tests, at imaging such as CT, MRI or PET, and usually at a tissue sample.[13] Alongside those, part of the work is deliberately ruling out the things this disease resembles, cancer and infection above all.[13]

The French national protocol sets out what the first round of blood tests usually covers: serum IgG4, a protein electrophoresis, a full blood count, kidney and liver tests, and complement levels.[14]

None of those is the answer on its own. They are the raw material for a judgement.

— ✦ —

Who makes that judgement matters

The picture is usually assembled by several specialists working together rather than by one.[14]

That is not bureaucracy. A disease that can sit in the pancreas, the kidneys, the eyes and the lymph nodes needs people who between them can read a pancreas, a kidney, an eye and a lymph node. When your case is discussed in a meeting rather than in a single clinic, that is the system doing the right thing, even though it feels slow from where you are sitting.

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The criteria are for research, not for you

You may come across the classification criteria, and if you go looking you will find people scoring themselves against them.

They were written to identify patients for research studies, so they are deliberately strict, and people who have this disease can fall outside them.[13] They are a tool for doctors rather than a checklist for patients.[13]

Which means a clinician can be confident you have this disease while you do not meet the criteria, and both of those things can be true at once. If someone tells you that you do not meet the criteria, the useful question is not whether you scored enough. It is what they think you have, and why.

— ✦ —

The honest part of this chapter is about timing

Here is a practical detail that is easy to miss and hard to undo.

Where a tissue sample is needed, it is taken before steroid treatment starts where that is possible, because steroids change what the

sample shows and can produce a false negative.[14]

Steroids work. That is the problem. They quieten the inflammation that the pathologist is looking for, so a sample taken after treatment has begun may come back showing nothing much, and the chance to see the disease clearly has gone.

This does not mean treatment should be delayed. Sometimes an organ cannot wait, and the specialist decides that. It means the order of events is a real clinical question rather than an administrative one, and it is a reasonable thing to ask about.

— ✦ —

What you can do with this

If a biopsy and steroids are both being planned, ask about the order. *"Is the biopsy happening before the steroids start, and if not, does that affect what it can show?"* Ask once, calmly, and accept the answer.

Ask what each test is looking for. *"Which tests are planned, and what is each one meant to tell you?"* It turns a series of appointments into something you can follow.

Do not score yourself against the criteria. They were not built for that, and they will mislead you in both directions.

Of everything on that list, one test carries a name that makes it sound decisive. It is not.

Chapter 7. The blood test, and what it cannot tell you

The disease is called IgG4-related disease. There is a blood test called IgG4. It would be reasonable to assume the second settles the first.

It does not, and the gap between what that test sounds like and what it does is where a great deal of avoidable fear and false reassurance lives.

A normal result does not rule it out

The test measures the level of IgG4, a type of antibody. It is raised in many people with this disease, but not in everyone. Depending on the study, somewhere between one in ten and nearly half of people with the disease have a normal level.[15]

Read that range again, because the top of it is the part that matters. In some studies, nearly half.

There is a harder version of the same finding, from a place where the stakes were as high as they get. A meta-analysis pooled ten studies of people who went to surgery because their pancreas was suspected of cancer, and looked at those who turned out to have autoimmune pancreatitis, the pancreatic form of this disease. Among the type 1 cases with a pre-operative result available, fewer than half had a raised serum IgG4: 43 per cent, twenty-one patients out of forty-nine.[16]

So in the situation where getting it right matters most, the test named after the disease missed the majority of the people who had it.

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A raised result does not confirm it either

The test fails in the other direction too.

Allergic, immune and cancerous conditions can raise IgG4.[15] Even when the level is more than five times the upper limit of normal, around one in four people turn out to have a different diagnosis altogether.[15]

Five times normal is the kind of number that looks conclusive on a screen. One in four of those people have something else.

This is why the red flags in Chapter 5 list a raised IgG4 as a reason to think, not as a reason to conclude, and why Chapter 6 said the diagnosis is assembled rather than read off.

— ✦ —

Where it does earn its place

The test has a real job, and it is a different one from diagnosis.

Where the level was raised before treatment started, it becomes useful for following how things are going over time, and a rise can be an early sign that the disease is returning.[15]

That is worth understanding, because it changes what your own number means depending on when it was taken. A raised level before treatment gives your specialist something to track. The same number in isolation, with no before, tells you much less.

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This is the point where honesty serves you better than reassurance

If you have been told your IgG4 was normal and therefore this is not what you have, that conclusion is not safe on its own.

If you have been told your IgG4 is high and therefore this is what you have, that is not safe either.

Neither of those is a reason to distrust your doctor, who is almost certainly reading the number alongside everything else, which is

exactly what the sources say to do.[15] It is a reason to ask what else the judgement rests on, and to be careful with what you read online, where this test is routinely described as if it decided the matter.

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What you can do with this

Find out what your level was, and when it was taken. Before treatment or after changes what it can be used for.

If your result was normal and the question is still open, say so out loud. *"I know my IgG4 was normal. Does that rule this out, or not?"* A specialist who knows the disease will have a clear answer.

Be careful about tracking the number on your own between appointments. In isolation it moves for reasons that have nothing to do with you, and watching it alone tends to cost more peace of mind than it buys.

Which is why the next step is so often tissue, and why the next chapter is about what tissue can and cannot settle either.

Chapter 8. The biopsy

Looking at a small piece of the affected tissue under a microscope is often the most telling step in the whole process.[17]

It is also the step people dread most, and the one they are given the least information about beforehand.

What the pathologist is looking for

Three findings point towards this disease.[17]

- A dense build-up of immune cells.
- A swirling pattern of scarring, which pathologists call storiform fibrosis.
- Inflammation that narrows small veins.

A high proportion of IgG4-positive cells supports the picture.[17] The pathology literature puts a number on that proportion: more than 40 per cent of IgG plasma cells staining for IgG4 counts in favour.[18]

If those words appear on a report you are given, that is what they mean. They are not a verdict on their own.

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Why none of it proves the diagnosis

Because the same findings appear in other conditions.[17]

A pathology review sets out the overlap plainly. Raised IgG4, in the blood or in the tissue, is also seen in certain cancers, in infections, in Sjögren’s syndrome, in granulomatosis with polyangiitis and in Castleman’s disease.[18] The three classic features are not always all present, and they look different depending on the organ: tear glands and lymph nodes often do not show the classic scarring at all.[18]

So a biopsy from a tear gland that lacks storiform fibrosis has not ruled anything out. It has behaved the way tear glands behave.

— ✦ —

And why a biopsy can miss

This is the part worth knowing before yours rather than after.

The changes are patchy, and a small needle sample can come from the wrong part of the tissue.[17]

That is not a mistake by anybody. It is the nature of a disease that does not distribute itself evenly through an organ. A negative biopsy in someone whose whole picture points at this disease is a reason to keep looking, not a closed door.

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The conclusion the pathologists themselves reach

The review that documents all this overlap ends where you would want it to end. A biopsy alone is rarely enough. The diagnosis is best made when a specialist team, including a pathologist familiar with this disease, looks at the clinical picture, the scans, the blood tests and the tissue together.[18]

Which is why an unclear case gets taken to a multidisciplinary meeting rather than settled by one test.[18] If you are told your case is going to be discussed by a group, that is good news wearing the clothes of a delay.

— ✦ —

What you can do with this

Ask whether the pathologist looking at your sample has seen this disease before. Phrase it as a question about the service, not about the person: *"Is this being read by someone who sees IgG4-related disease regularly?"*

If your biopsy was negative and your picture still fits, ask what happens next. *"Given everything else, does a negative biopsy settle it, or does it need another look?"*

Ask for the report and keep it. You will be asked about it again, possibly years from now, possibly by someone in another country.

Between the blood and the tissue sit the scans, and a quieter piece of work about how the whole sequence should be organised.

Chapter 9. Scans, and the work being done on the sequence

Imaging is how most people’s story starts. A scan finds something, and the something needs a name.

What is being worked on

A doctoral thesis from the Universitat Autònoma de Barcelona takes on two practical questions.[19]

The first is how to use quantitative PET/CT, a whole-body scan that measures activity in tissues, to see whether treatment is working.[19]

The second is how to bring the steps of diagnosis and treatment into an algorithm that a specialist team in Europe can follow: what to check in the blood, what to look for on imaging, when to take a biopsy, when to start steroids, and when to add another medicine such as an immunosuppressant or rituximab.[19]

It also reviews how the disease is defined today, the different clinical patterns it takes, and how response is followed over time using a disease responder index.[19]

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Why this is in a patient guide at all

Not because you can use it. You cannot, and it is not a self-check tool.[19]

It is here because of what it tells you about where things stand. Specialist centres are actively working on shared ways to reach this diagnosis faster and to measure whether treatment is helping.[19] The sequence that was improvised for people diagnosed ten years ago is being turned into something a team can follow.

If your own path felt disorganised, it may well have been. That is being worked on, by people who noticed.

Your own scans, tests and treatment plan remain a matter for your specialist.[19]

— ✦ —

What you can do with this

Ask what a scan is being repeated for. Following treatment response and looking for new disease are different purposes, and knowing which one you are in makes the wait easier.

Ask whether your response is being tracked in any structured way. Some centres use a responder index. Knowing whether yours does tells you how your progress is being judged.

All of which describes a process that works. The last chapter of this part is about how long it takes to get into it.

Chapter 10. Why it takes so long, and what shortens it

This disease is still not widely known, even among doctors, so it is often recognised late.[20]

That single sentence explains more about the experience of getting this diagnosis than anything else in this book.

What the delay costs

The time between the first symptoms and a clear diagnosis can be long, and it matters, because inflammation left untreated can cause lasting damage to an organ before treatment begins.[20]

That is the same point Chapter 1 made about scarring, arriving from the other direction. The clock does not stop while the system works out what to call it.

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Numbers, from one hospital that counted

A hospital in Buenos Aires reviewed its own sixty patients and put figures on that wait.[21]

Half were diagnosed within about nine months of their first symptoms. One in ten waited more than ten years.[21]

And the finding that matters most: those who already had organ damage by the time they were diagnosed had waited significantly longer for it.[21]

This is one centre rather than a whole country, so the figures illustrate the pattern rather than measure it everywhere.[21] The direction of the finding is what to carry, not the exact numbers.

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What shortens it

Reaching a doctor who knows the disease, and a centre of expertise, shortens that path. And treatment usually works well once it starts.[20]

Both halves of that deserve equal weight. The delay is real and it has a cost. The thing on the other side of it responds to treatment.

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My own case

My own case.

Nobody was going to assemble my history for me.

Seven years of results sat in different systems, in two languages, gathered by doctors who each saw a piece. No single one of them had ever seen all of it, which meant the story those results told together had never been told to anyone.

So I built it. A structured dossier out of seven years of medical records, twenty-eight pages, in one document, in one order. And then letters to specialists in this disease, in four countries, from a patient who had done the work and had a clear question to ask.

They answered. One of them backed my Spanish team’s approach before my biopsy result even existed. The Spanish patient association I messaged at half past midnight escalated my case within hours.

I want to be careful about the lesson here, because it would be easy to draw the wrong one. I did not get better care because I deserved it more than the next patient. I got it because I happened to have the skills to assemble a dossier and the confidence to write to strangers, and most people are given neither of those things along with their diagnosis.

That was mine, and yours will look different. What transfers is smaller and it is real: the story your records tell together is one nobody has read yet, and you are the only person in a position to put them in the same place.

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What you can do with this

Gather your records before you need them. All of them, from every hospital, across every year. Not to diagnose yourself. So that the next specialist you see can read in one sitting what is currently scattered across a decade.

Put them in date order and write one page at the front. What happened, when, and what the question is now. That page is what a busy clinician reads.

If you have waited a long time already, say the length out loud. *"This started four years ago."* Duration is clinical information, and it changes how a specialist reads everything else you tell them.

Ask about a centre of expertise. *"Would it be worth having this looked at somewhere that sees the disease regularly?"* Chapter 19 has

the directory.

That is how the diagnosis gets made: five signs, several tests, a biopsy read in context, and usually more time than anyone would want.

Part 3 goes organ by organ, and you should read only the parts of it that apply to you.

Part 3. Where it shows up

One disease, a dozen addresses. This part is the map, and it is built to be read selectively.

How to use this part

Read your own organ. Leave the rest.

That is not a throwaway instruction. This part covers twelve places this disease turns up, and almost nobody has twelve. Reading about organs you do not have involved is a way of

frightening yourself with somebody else's illness, and there is no benefit in it that would outweigh the cost.

If a new organ becomes involved later, this part will still be here.

Each section covers what the disease does in that organ and what it feels like or looks like. Where the sources carry it, a section also says what the disease is mistaken for there, and what is worth asking. Where they do not, it stops. They are short by design, and each is as short as the evidence behind it.

Before you go further: the things not to wait on

Most of what this disease does develops over months, and most of it is not urgent. Three exceptions run through this part, and they are collected here so that nobody has to find them by reading a section that does not apply to them.

New or changing vision. If swelling behind the eye presses on the optic nerve, sight can worsen. New or changing vision is worth reporting quickly rather than at the next appointment.[22]

New or worsening breathlessness. Worth raising promptly.[23]

Chest pain, breathlessness, or symptoms that worry you. Tell your treating team rather than waiting for a routine appointment.[24]

None of those means something terrible is happening. They mean the clock matters more than the appointment schedule.

The digestive organs

The pancreas

IgG4-related disease can cause a swollen pancreas, which is called autoimmune pancreatitis.[25]

The usual first sign is painless jaundice, a yellowing of the skin or eyes, caused by a blockage in the bile ducts.[25] The word painless is doing real work there, because it is what makes people wait.

Some people have vague abdominal discomfort or weight loss instead, and only a minority have the symptoms of a sudden pancreatitis attack.[25]

This is where the disease is most often mistaken for pancreatic cancer, because the two can look alike on a scan and cause the same symptoms.[25] Careful diagnosis matters a great deal here,[25] and Chapter 2 is about exactly this.

Over time, pancreas involvement can affect digestion and blood sugar, so both are usually monitored.[25]

Worth asking: what is being monitored, and how often. Digestion and blood sugar are followed for a reason, and knowing that turns a repeated blood test into something you understand rather than endure.

— ✦ —

The bile ducts

The bile ducts are the tubes that carry bile from the liver to the gut. This disease can inflame and scar them, which doctors call IgG4-related sclerosing cholangitis.[26]

It very often occurs alongside autoimmune pancreatitis,[26] which is why these two sections sit together.

The usual signs are jaundice, together with itching, and sometimes weight loss.[26] The itching surprises people. It is not a skin problem.

On imaging it can resemble two other conditions: primary sclerosing cholangitis, and bile-duct cancer, called cholangiocarcinoma. Telling them apart can be difficult and matters a great deal, because their treatment and outlook are very different.[26] This is another of the situations where this disease is mistaken for cancer.[26]

When a blocked duct is causing jaundice, it may need to be drained with a small tube, called a stent, while the inflammation itself is treated.[26]

That is worth understanding before it is offered to you. A stent deals with the blockage. It is not the treatment for the disease, and having one does not mean the treatment is failing.

The head and neck

The salivary and tear glands

The major salivary glands are among the most commonly affected sites in this disease, involved in somewhere between a quarter and a half of people.[27]

It shows as painless swelling of the glands around the jaw, in front of the ears, and around the eyes. The swelling is usually gradual, on both sides, and not painful, which makes it easy to overlook.[27]

Read that list again if your own diagnosis took years. Gradual, symmetrical and painless is a combination that gets noticed by other people before it gets noticed by doctors, and often not for a long time.

Swelling of the tear glands shows as puffiness of the upper outer eyelids.[27]

Dryness of the mouth and eyes can occur but is usually mild, which is one of the things that distinguishes this from Sjögren's disease.[27]

Worth asking: if you have been told you have Sjögren's and the dryness has never really fitted, that is a reasonable thing to raise.

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The mouth

The most common sign in the mouth is a painless, rubbery swelling on the roof of the mouth, on one side or both. It can be the same colour as the surrounding tissue, or reddish or purple.[28]

The tongue and the jaw bones can also be involved, and the gums can swell and feel like they are burning.[28]

Swelling of the glands under the jaw belongs to the same picture, and was known by other names before this condition was described.[28] If you were given one of those older names years ago, that may be why.

Most people with mouth involvement also have signs of the disease elsewhere, and most have a raised IgG4 level in the blood.[28]

And the sentence that matters most in this section: because these lesions look like other things, they are sometimes removed surgically before anyone suspects IgG4-related disease.[28]

That is the argument of this whole book, in one organ. A dentist or an oral surgeon may be the first person to see this disease and the last to think of it.

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The eyes and the eye socket

This disease often affects the tear glands, which shows as painless swelling of the upper outer eyelids. It can also spread into the eye socket itself, inflaming the soft tissue or the muscles that move the eye.[22]

That can cause the eyes to bulge, double vision, redness or pain.[22]

If the swelling presses on the optic nerve, sight can worsen, which is why new or changing vision is worth reporting quickly.[22]

Diagnosis usually involves an MRI or CT scan of the eye socket, blood tests, and often a small tissue sample, commonly from the tear gland.[22] Because the disease can be active elsewhere in the body at the same time, an eye specialist will usually work alongside an internist or immunologist.[22]

Some centres have particular expertise in this, including the Orbitacentrum at Het Oogziekenhuis Rotterdam, a recognised Dutch expertise centre for rare orbital conditions.[22]

Worth asking: whether anyone is looking at the rest of you. An eye clinic can treat an orbit expertly and never ask what else is going on, and in this disease the orbit is usually not the whole story.

— ✦ —

The thyroid

The thyroid is affected less often than organs like the pancreas or the salivary glands.[29]

When it is, the recognised form is Riedel's thyroiditis, in which the thyroid becomes hard and fibrous, meaning scarred.[29]

This can be felt as a firm swelling in the front of the neck. If it presses on nearby structures it may cause a hoarse voice, or difficulty breathing or swallowing.[29]

New difficulty breathing or swallowing is one of the things the opening of this part said not to wait on. It belongs in the same group, and it wants raising promptly rather than at the next appointment.

Because a hard thyroid mass can resemble other thyroid conditions, careful diagnosis matters.[29]

Thyroid involvement can change the gland's hormone levels, so thyroid function is usually checked and followed. A specialist assesses whether treatment is needed.[29]

The chest and the abdomen

The lungs

The lungs are affected in around one in seven people with this disease.[23]

Many have few or no symptoms, but some have breathlessness, a cough, or symptoms resembling asthma.[23]

What it looks like on a scan varies widely, from solid nodules to hazy patches to thickening around the airways, which is part of why lung involvement can be hard to pin down.[23]

It is assessed with imaging and followed by a specialist. **New or worsening breathlessness is worth raising promptly.**[23]

Worth asking: if you have been treated for adult-onset asthma that never quite behaved like asthma, whether the lungs have been looked at in the context of this diagnosis.

— ✦ —

The kidneys

The kidneys are affected in around one in six people.[30]

The usual form is inflammation of the kidney tissue itself, which can reduce kidney function and show up as protein in the urine.[30]

Less often, the disease forms a mass in the kidney that looks like a tumour on a scan, which is one reason a tissue sample is sometimes needed.[30] Chapter 2's four patients were exactly this situation.

Kidney involvement is followed by a specialist with blood tests and urine tests, **because changes can appear before anything is felt.**[30]

That last clause is the reason to keep the appointments when you feel well. Kidneys do not complain early.

— ✦ —

The retroperitoneum and the aorta

The retroperitoneum is the space behind the abdomen. This disease can cause a band of fibrous tissue to form there, called

retroperitoneal fibrosis, sometimes involving the aorta, the large blood vessel running down through the abdomen.[31]

It is one of the most commonly affected sites and the clearest example of the scarring form of the disease.[31] It affects middle-aged and older men more often than women, by roughly four to one in an American population study that followed a county for twenty years.[31]

Many people have no symptoms at all, and others have only vague back or flank pain.[31]

Because the inflamed tissue sits close to the tubes carrying urine from the kidneys, it can press on them and cause a backup of urine, so the kidneys are usually checked even when nothing is felt.[31]

What treatment does here

Steroids are the usual treatment and they work well.[31]

An Italian randomised trial found that adding methotrexate allowed a much lower steroid dose to achieve the same result: roughly a quarter less prednisone over nine months, with no more side effects.[31] In that trial the

fibrous tissue shrank by about 60 per cent, kidney function improved, and nobody's kidneys failed.[31]

Coming back after treatment stops is common, in about a third of people within the following year and a half.[31]

That is a useful set of numbers, and it is the only place in Part 3 where a randomised trial speaks directly to one organ.

The caveat that travels with all of it

Most research on retroperitoneal fibrosis includes people whose disease is not classed as IgG4-related, so these findings describe the condition broadly rather than only its IgG4 form.[31]

The same American study found that survival was no different from the general population, although it followed only eleven people.[31]

Eleven. Reassuring, and thin, and both of those are worth holding at once.

Some centres run dedicated services for this, including the retroperitoneal fibrosis and IgG4-related disease service at Imperial College Healthcare NHS Trust in London.[31]

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The blood vessels

This disease can involve blood vessels of any size, from the smallest up to the aorta.[24]

Taking all the larger arteries together, the aorta and the arteries supplying the head, the gut and the heart, involvement is found in around half of people.[24] The aorta on its own is involved in about one in ten.[24]

Half is a larger number than most people expect, and it is worth reading calmly. Involvement means the vessel wall can thicken, the vessel can narrow, or it can widen into an aneurysm.[24] It does not mean half of people have a dangerous artery.

Involvement of the heart arteries is uncommon. In one large hospital group it was found in about four in every hundred people with the disease, all of them men, and all with disease that had been present for many years and with very high IgG4 levels.[24]

Because the disease reaches vessels of so many sizes, some specialists argue it should be counted as a form of blood vessel

inflammation.[24]

If you have chest pain, breathlessness or symptoms that worry you, tell your treating team rather than waiting for a routine appointment.[24]

Elsewhere

The lymph nodes

This disease can cause lymph nodes to become enlarged, often without any other symptom. It is a common finding, and the nodes most often involved are those in the chest, the abdomen, the armpits and the neck.[32]

Enlarged nodes have many possible causes, so they are one of several things a specialist weighs alongside the rest of the picture rather than a finding that points anywhere on its own.[32]

Which cuts both ways, and it is worth saying both. A swollen node is not evidence that this disease is active. It is also not nothing.

— ✦ —

The nervous system

This disease usually affects glands and organs, and only uncommonly the nervous system.[33]

When it does, the two forms most often reported are separate from each other, and either can occur on its own.[33]

One is a thickening of the tough lining around the brain and spinal cord, called pachymeningitis, which can cause headaches and sometimes affects vision or raises the pressure inside the skull.[33]

The other is inflammation of the pituitary gland, called hypophysitis, which can disturb the body’s hormones.[33]

The brain tissue itself is only rarely involved, described in occasional case reports as an inflammatory mass rather than a widespread problem.[33]

All of this is uncommon, and it is recognised and followed by specialists using scans such as MRI and, when needed, further tests.[33]

And the sentence to hold on to: neurological symptoms have many possible causes, most of them unrelated to this disease, so anyone experiencing them should see a doctor who can look at the whole picture.[33]

If you have started attributing every headache to your diagnosis, that sentence is for you.

What this part could not tell you

It could not tell you which organs are involved in your case. Only your own scans and your own specialist can do that.

It could not tell you what will happen next in the organ you read about, because the sections describe what the disease does across many people rather than what it will do in you.

And it does not cover every organ this disease can reach. It covers the twelve that the vetted material supports. If yours is not here, that is a limit of this book rather than evidence that your organ is not involved.

Part 4 is treatment, and it is the longest part of this book by a distance, because that is where most of the evidence sits.

Part 4. Treatment

This is the longest part of the book, because it is where most of the evidence is.

It is also the part where the tone changes. Everything before this was about what is happening and how anyone found out. From here on, things are being done.

One reminder before you start, because this is the part where it matters most. Everything ahead describes medicines in general and none of it describes you. No dose, taper, interval or decision in this part is advice, and nothing in it is a reason to change what you are taking. Take what you find here to the person who prescribes for you.

Chapter 11. What treatment is trying to

do

Start with the good news, because it is real and it is the frame for everything else.

IgG4-related disease often responds well to treatment, especially when it is caught early.[34]

Three aims, not one

Treatment sets out to calm the inflammation, to protect the affected organs, and to prevent relapse.[34]

Those are three different jobs and they run on different clocks. Calming the inflammation is fast. Protecting the organs is the reason for the speed. Preventing relapse is the long one, and it is the reason treatment does not simply stop when you feel well.

Steroids such as prednisone are still the standard first treatment, and more than eight in ten people respond to them.[34]

Beyond steroids, treatment is moving towards therapies that target the B cells involved in the disease. Rituximab has been used off-label for years, meaning it is not licensed for this

disease although specialists use it in it. In 2025 inebilizumab became the first medicine approved specifically for IgG4-related disease. Other B-cell-directed and immunomodulatory agents are in later-stage development.[34]

Chapters 13 and 14 take each of those in turn.

— ✦ —

The sentence to sit with

Treatment aims to control the disease rather than cure it.[34]

Many people do well for long stretches, but staying in remission with no treatment at all is uncommon, so this is followed over the long term rather than finished and closed.[34]

That is not the sentence anyone wants at the start of a treatment chapter. It is put here rather than buried at the end because knowing it changes how the next two years feel. If you expect an ending and do not get one, every continuing appointment reads as failure. If you expect a long relationship with a manageable condition, the same appointments read as maintenance.

— ✦ —

How long the first course runs

Months rather than weeks.[35]

Most people are started on 20 to 40 mg of prednisone a day, or the equivalent, and that dose is tapered down over two to four months.[35]

Those figures are here so that the shape of it is not a mystery. They are not your dose. Nobody's dose comes from a book.

— ✦ —

Feeling better comes long before finishing

Improvement usually shows within two to four weeks of starting, and some people notice a change within days.[35]

Most people respond, and the book has already given you the figure: more than eight in ten. Response is expected often enough that

failing to respond to a proper dose is a reason for doctors to question whether the diagnosis is right.[35]

That second sentence is worth holding on to in both directions. If you responded quickly, that is the disease behaving as this disease behaves. If you did not, that is information, and it is a reason for someone to look again rather than to increase the dose and hope.

— ✦ —

The part that is unsettled, and nobody will tell you plainly

Here is where honesty matters more than encouragement.

How long maintenance treatment should continue, how often B-cell treatment should be repeated, and who can safely come off treatment altogether are all described in the literature as open questions.[35]

Not difficult questions. Open ones. The evidence to settle them has not been produced yet.

Which means two specialists can give you different answers and both can be practising good medicine. It also means the answer you are given may change as the evidence does, and a changed answer is not a mistake being corrected.[35]

If you have been unsettled by getting different advice from different doctors, that is the reason, and it is worth knowing that the disagreement is among the specialists rather than in your case.

Where B-cell treatments such as rituximab or inebilizumab are used, a response is generally expected within one to three months, or sooner alongside steroids.[35]

Your own timetable depends on which organs are involved and how you respond, so it is one to set with your specialist rather than read off a page.[35]

The fortnight it turned

My own case.

What finally sent someone looking was weight. About twenty kilos in five months.

A liver marker had been climbing for seven years and had been explained away every time it appeared. A lymph node had been called probably benign. Neither of those moved anybody. The weight did.

Then the right treatment started, and this is the part I had not prepared for.

The pain that had woken me every night between two and four in the morning, for four weeks, was gone within days.

The liver marker that had peaked at 933 came down to around 300 over the following three months.

I am not going to tell you that will happen to you, and the reason is arithmetic rather than modesty. I am one person. The studies in this chapter cover thousands, and what they say is that most people respond and that improvement usually shows within two to four weeks.

What I can add to those studies is only this: what it is like from the inside when a thing that has been getting worse for seven years turns around in a fortnight.

That was mine. Yours will run on its own clock, in your own organs, on your own medicines.

— ✦ —

What you can do with this

Ask what your treatment is aiming at right now. Calming inflammation, protecting an organ, and preventing relapse are different goals and you may be in a different phase from the one you assume.

Ask what the plan is after the first course. *"When this taper finishes, what happens next?"* The answer may be uncertain, and hearing why it is uncertain is more useful than being told a number that later changes.

Which brings us to the medicine most people meet first, and live with longest.

Chapter 12. Steroids, and living on them

Prednisone works. That is why it is still the first treatment after all these years, and why more than eight in ten people respond to it.[34]

Everything in this chapter exists because it also costs something, and because most of what it costs can be anticipated, watched for, and often eased.

For many people a course of steroids is the usual first treatment and it often works quickly. A specialist manages the dose and how it is lowered over time. Because long-term steroids carry a burden and relapse after stopping them is common, doctors often work to reduce them, sometimes by adding another medicine, and increasingly by considering B-cell-targeted therapies as steroid-sparing options.[36]

That single paragraph is the whole argument of Chapters 13 and 14 in miniature: the point of the other drugs is largely to need less of this one.

— ✦ —

What the label lists

Listed effects of prednisone include trouble sleeping, mood changes, raised blood sugar, increased appetite and weight gain, and raised

blood pressure. Stomach ulcers and bleeding from the gut are also listed, as is a higher risk of infection, which prednisone can mask.[37]

Reading that list in one go is unpleasant, and it is better than meeting each item separately at two in the morning wondering whether it is the disease.

Each of the sections below takes one of them.

Tell your specialist about anything new or getting worse, and say when it started and whether it followed a change in dose.[37]

That last clause is the single most useful sentence in this chapter. The timing relative to a dose change is often what tells a specialist which thing they are looking at.

— ✦ —

Sleep and mood

Sleep disturbance is a listed effect, alongside mood changes such as irritability, anxiety and low mood.[38]

Those two travel together and they feed each other. It is worth naming that plainly, because people tend to report the sleep and stay quiet about the mood, and the mood is the part that makes everything else harder to carry.

Tell your specialist if poor sleep is affecting how you get through the day.[38]

— ✦ —

Blood sugar

Prednisone can raise blood sugar. Reduced glucose tolerance and diabetes are both listed effects.[39]

There is a pattern to it that almost nobody is told, described in a study of patients given steroids in hospital. When prednisone is taken once in the morning, blood sugar tends to rise over the day, peak between lunch and dinner, and come back down by the next morning.[39]

Which has a practical consequence: **a reading taken only first thing in the morning can miss the rise entirely.**[40] If you have been testing at breakfast and being told your numbers look fine, that may be true and incomplete at once.

And in the other direction: if a dose is reduced too quickly, blood sugar can fall too low.[39]

Tell your specialist if your readings change after a dose change, and keep a note of them so there is something to look at together.[39]

— ✦ —

Keeping a record, and why weeks beat moments

Your team may ask you to measure blood sugar and blood pressure at home. Readings taken over weeks tell a specialist more than a single measurement in the clinic.[40]

Ask when to test and what to write down. Your own target values, how often to measure, and what any reading means are questions for your specialist rather than for a page.[40]

Take the readings with you. Anything that records the number, the time of day, and what you had eaten will do, including paper.[40]

igg4.org offers a free readings log if you want one. It records glucose, blood pressure, pulse and weight and produces a report to bring to an appointment. The readings stay on your own phone, there are no accounts, and it records what you measure without interpreting it.[40]

— ✦ —

Infection, and the way it hides

Prednisone raises the risk of infection. Listed effects include new infections, existing ones getting worse, and dormant ones becoming active again.[41]

It can also mask an infection, so the usual warning signs may be milder than you would expect.[41]

That is the part that catches people out. The fever that would normally send you to a doctor may not arrive, or may arrive small.

Contact your doctor promptly if you have fever, chills, or feel unwell in a way that is new. Say that you are taking steroids.[41]

Those last five words change what happens next in the consultation.

— ✦ —

The stomach

Stomach ulcers, bleeding from the gut and inflammation of the pancreas are all listed effects of prednisone.[42]

Doctors sometimes prescribe a medicine to protect the stomach alongside steroids. European rheumatology guidance recommends this where there is a raised risk of stomach ulcers, including taking anti-inflammatory painkillers at the same time, having an inflammatory disease, and older age.[42]

Having an inflammatory disease is on that list, which means many readers of this book qualify. If nobody has discussed stomach protection with you, that is a reasonable thing to raise.

One limit on that guidance is worth carrying with you, because it applies to everything this chapter draws from it. It was written for people on what it calls medium to high doses,

meaning more than 7.5 mg of prednisone equivalent a day.[42] Further down a taper than that, it is no longer describing you, and whether the protection is still needed becomes a question for your specialist rather than a settled recommendation.

Tell your specialist about stomach pain or discomfort that keeps coming back.[42]

Get medical help the same day for severe stomach pain, vomit that looks like coffee grounds, or stools that are black or tarry. These can be signs of bleeding.[42]

— ✦ —

Burning or tingling in the hands or feet: the one that is not a steroid effect

This section is here because of what it is not.

A burning or tingling feeling in the hands or feet is worth taking seriously, and **it is not among the listed effects of prednisone**.[43]

So it does not get filed under “probably the steroids” and left there. It is a symptom looking for its own explanation, and blood sugar is one of the things worth checking.

Tell your specialist about burning, tingling or numbness in the hands or feet. Say how long it has been going on and when your blood sugar was last checked.[43]

New numbness or weakness, burning with severe pain, or a change in the colour of a hand or foot needs prompt medical attention.[43]

— ✦ —

Sex, which nobody is going to raise with you

This section exists because the effect is in the labels and almost never in the conversation.

The Spanish medicines agency lists abnormal excretion of sex hormones, including impotence, among the adverse reactions of prednisone, in a list it introduces as effects seen especially at high doses and in prolonged treatment.[44]

The American regulator's prednisone labelling describes the mechanism rather than the symptom. It states that corticosteroids cause reduced sex hormone production. And it goes further than describing: it tells prescribers that sex hormone replacement, testosterone in men, should be offered to patients who are hypogonadal, in anyone expected to be on at least the equivalent of 5 mg of prednisone for at least three months.[45]

Two things follow, and both are worth having.

The direction is down, not up. If your sex life has changed since treatment started, that is a recognised effect of the medicine rather than a separate misfortune that happened to arrive at the same time.

And it is anticipated. The regulator wrote an instruction to prescribers about a group defined by five milligrams for three months, which is a threshold most readers of this chapter crossed long ago. The instruction exists. What it does not tell you, and what this book will therefore not tell you, is how many people in that group are affected.

Neither label says how often it happens, so this book will not give you a figure.

One difference worth knowing, because you may meet either document: the American label does not name erectile dysfunction among its adverse reactions, and the Spanish label names impotence.[44] [45] Both are regulator-approved, and they describe the same territory in different words.

Raise it, because it will not raise itself. *"I have been on steroids for months. Should my sex hormones be checked?"* That is a blood test. The label already says what to do if the answer comes back low.

— ✦ —

The two medicines that arrive because of the steroids

Steroid treatment rarely arrives alone. European rheumatology guidance recommends a stomach-protecting medicine alongside it where the risk of an ulcer is raised,[42] and where blood sugar climbs far enough to need treating, a tablet may be added for that too.

Each of those carries something the prescription does not mention, and the two of them carry the same thing.

The stomach protector. Omeprazole and the medicines like it work by lowering the acid in your stomach, and the regulator-approved label is candid about what long use costs.

It asks that anyone treated for more than a year be kept under regular review.[46] It lists benign polyps in the lining of the stomach as a common finding.[46] It records severe low magnesium in people treated for three months or more, and it says that at high doses used for more than a year these medicines *could* slightly raise the risk of fracture, with that word doing real work in the original.[46] It notes a small rise in infections of the gut.[46] And it states that the medicine can reduce the absorption of vitamin B12, because the acid it suppresses is part of how B12 is taken up.[46]

Read that as an argument for a review date rather than an argument for refusing it. Bleeding from the gut is what the protector is prescribed to prevent, and European rheumatology guidance recommends it precisely where the risk of an ulcer is raised, which for many readers of this book it is.[42]

The review date is the part that tends to go missing. A protector started at the top of a steroid course can still be on the repeat prescription long after the steroid has come down, and the label's own answer to that is the yearly review it asks for.[46]

Metformin. Some readers will be taking metformin already. Others meet it because steroids pushed their blood sugar up, in the way the blood-sugar section earlier described. Where that needs treating with tablets rather than with insulin, metformin is among the ones used: a hospital guideline written for adults on steroid treatment names it for milder cases, and that guideline was written for inpatients rather than for people managing a taper at home.[47]

Metformin lowers vitamin B12. This is not a rare event tucked in a footnote. The label lists reduced vitamin B12 as a common adverse reaction, meaning between one in a hundred and one in ten people, and says plainly that the risk rises with the dose, with the length of treatment, and in anyone who already has a reason to be low.[48]

The British medicines regulator issued specific advice about it in June 2022, asking doctors to test B12 where deficiency is suspected and to

consider periodic testing in people carrying those risk factors.[49]

And here is where the two meet. In that same advice, the regulator names medicines that impair B12 absorption as one of the risk factors, and the example it gives is proton pump inhibitors: stomach protectors.[49]

So a person on a long steroid course can end up on two medicines, prescribed for two unrelated reasons, both of which lower the same vitamin. Neither prescription mentions the other.

What makes this worth a paragraph rather than a footnote is what low B12 looks like. The metformin label names anaemia and neuropathy as the two situations in which levels should be measured.[48] Neuropathy means nerve symptoms, and anaemia is the thing that leaves you tired.

You have already read a section of this chapter saying that burning or tingling in the hands and feet is not a listed effect of prednisone and should be reported rather than absorbed. This is one of the reasons that section exists. Some of what gets filed under *the steroids, presumably* has a name, a blood test, and a treatment.

Ask whether your vitamin B12 has been checked, if you are taking metformin, a stomach protector, or both.[48] [49]

Ask what the review date is for the stomach protector.[46]

Neither question takes a minute. Neither is a request to stop anything, and nothing in this chapter is a reason to stop anything on your own.

What is given alongside, rather than in response

Some things are offered with steroids from the start, before anything has gone wrong.

European rheumatology guidance recommends calcium and vitamin D to protect the bones, and a stomach-protecting medicine where there is a raised risk of stomach ulcers.[50] This is the same guidance written for medium to high doses, with the same limit on who it describes.[50]

Effects of steroid treatment can often be eased, and what helps depends on which effect it is and on the rest of your treatment.[50]

Bring the effects you are having to your specialist rather than living with them. Say when they started and whether they followed a change in dose.[50]

People are remarkably good at deciding that a side effect is the price of being treated and saying nothing. It is worth resisting that, because a good deal of it is adjustable.

The most important thing in this chapter

This section is set apart because it is the one that can hurt you if nobody tells you.

Steroids taken for more than a few weeks should never be stopped suddenly.[51]

While you are taking them, your body reduces its own production of a hormone, and it needs time to start again. A joint guideline from the

European and American endocrine societies puts one line in the sand: a course shorter than three to four weeks can be stopped without tapering, whatever the dose, because there is little concern about your own production having been suppressed.[52] Past that, the picture changes.

Three weeks. That is a low bar, and most people reading this cleared it long ago.

What that guideline declines to give you is a threshold above which it happens. The dose, how long you have taken it, which steroid it is and how it was given all feed in, and the guideline says plainly that predicting the risk in one person remains difficult.[52]

That is less comforting than a number, and it is the truth. Nobody can read your dose and tell you whether your body has started again.

The same applies while you are ill

An infection, an accident, or an operation places extra demand on the body at exactly the point when it cannot produce that hormone itself.[52]

The same guideline is direct about it. Anyone currently or recently on steroids who has not been tested should be given extra steroid cover when the body is under that kind of stress.[52] And if such a person becomes unstable, or cannot keep anything down, or has diarrhoea that will not stop, the possibility of an adrenal crisis should be considered whatever steroid they take, however it was given, and at whatever dose.[52]

At whatever dose. Which is why none of this depends on your number being a high one.

Doctors have rules for this, sometimes called sick day rules, which set out what to do when you are unwell.[52]

And here is the finding that makes this section necessary

The endocrine guideline records something uncomfortable about people in exactly this position. Set beside people whose adrenal insufficiency has some other cause, **people whose adrenal insufficiency came from steroid treatment were found to be less aware of their own diagnosis, and less**

likely to have taken the steps that prevent a crisis, including carrying something that speaks for them when they cannot.[52] Poor knowledge and lack of awareness went with higher rates of adrenal crisis.[52]

Less aware, through nobody's fault. The steroids were prescribed for something else, and the adrenal question was never the headline in the room.

There is a second study worth knowing about, because it answers the thought that your own dose is too small to matter. Among 67 kidney transplant recipients taking maintenance prednisolone, at an average daily dose under 5 mg, 72 per cent failed a test of adrenal function.[51]

Those were kidney transplant patients and not people with this disease, and sixty-seven people at one centre is a small study. Read it for one thing only: a low number on the box is not the reassurance it looks like.

A card tells anyone treating you in an emergency that you take steroids, and the endocrine guideline names a standardised European steroid emergency card for that purpose.[52] It works precisely when you are least able to explain yourself.

What to ask for

Ask your specialist for your own sick day rules and whether you should carry a steroid card.[52]

Your rules depend on your dose, on how long you have been taking it and on the rest of your treatment, so they are theirs to set, not something to read off a website.[52] This book will not give you a rule, and any website that gives you one without knowing your dose is doing you no favours.

The card itself is a different matter, and you can have one today. igg4.org offers a free alert card you print and complete yourself: your diagnosis, your medicines and doses, your specialist, an emergency contact. It exists in the five languages of the site, and what you type into it stays on your own device. It says who you are and what you take, for the moment when you cannot say it. It carries no sick day rule, and it does not replace a steroid emergency card your own health service may issue.[53]

If you are already tapering, this is a conversation for now rather than for the end of the taper.

What you can do with this

Say when it started, and whether it followed a dose change. Attach that to every side effect you report. It is the piece of information a specialist most often has to go looking for.

Ask about bones and about your stomach, once, early. *"Should I be on calcium and vitamin D, and does anything need to protect my stomach?"*

Ask for your sick day rules and a steroid card. If the answer is that you do not need them, that is a fine answer and it took thirty seconds to get. The printable alert card at igg4.org is yours in the meantime.[53]

Ask about vitamin B12 if you take metformin or a stomach protector. And ask what the review date is for the stomach protector.[48] [49] [46]

Do not decide anything is the price of treatment. Bring it. Most of this list is adjustable, and the ones that are not are still worth your specialist knowing about.

Chapters 13 and 14 are about the medicines whose main purpose is to let you need less of the one in this chapter.

Chapter 13. The treatments that let you need less steroid

Chapter 12 was about what steroids cost. This chapter is about the medicines whose main job is to reduce that cost, by keeping the disease quiet on a lower dose or on none at all.

Three are established enough to have real evidence behind them, and they are very different from each other.

Mycophenolate mofetil

Mycophenolate blocks an enzyme that activated immune cells need in order to multiply, so the cells driving the inflammation cannot make more of themselves.[36] It is widely

used in this disease, particularly where the kidneys, the eye socket or the lungs are involved.[36]

It is a tablet, taken daily, and it is the one conventional medicine in this chapter with a randomised trial behind it.

The trial

A randomised trial took sixty-nine people who had just been diagnosed and split them in two. Thirty-five had steroids alone. Thirty-four had steroids plus mycophenolate, at 1 to 1.5 g a day. Everyone was followed at one, three, six and twelve months.[54]

- Relapse within the year: forty in every hundred on steroids alone, about twenty-one in every hundred with mycophenolate added.[54]
- Remission: about fifty-one in every hundred on steroids alone, about seventy-six in every hundred with mycophenolate added.[54]
- No serious adverse reactions occurred in either group.[54]

Where relapses did happen, they were most often in the lungs, the tear glands, the salivary glands, the sinuses and the kidneys.[54]

Read that beside the azathioprine section below, because the two are not the same weight of evidence. This is a randomised trial. Azathioprine's evidence in this disease is ten men at one centre, looked at backwards.

What the trial cannot tell you

Sixty-nine people, in one country. The published summary does not say whether anyone was blinded to which group they were in, and the full report sits behind a paywall, so the figures here come from the summary. No statement of who funded the trial, or of the authors' competing interests, was visible on the page.[54]

And it is not your dose. The trial's own title calls 1 to 1.5 g a day a low dose, and the doses used in practice run higher. The European label's own figures, written for transplant, are 2 g a day after a kidney and 3 g a day after a heart or a liver.[55] Chapter 11 said that nobody's dose comes from a book, and it holds here: if your own number is larger than the

trial’s, that is a question worth one sentence at your next appointment rather than a reason to change anything.

The independent review that points to this trial is careful about the whole class of these medicines. It describes their use in this disease as largely extrapolated from other autoimmune conditions, and it says the relapse percentages and the possible added toxicity are reasons to keep other options in view.[36] That review received no external funding and its authors declare no conflicts of interest.[36]

— ✦ —

What the label says, and who the label is about

Scope first, because it changes how you read the rest. The European product information for mycophenolate mofetil is written for preventing the rejection of a transplanted kidney, heart or liver. IgG4-related disease appears nowhere among its authorised uses.[55] So it is used here off label, in the way rituximab has been for years. The effects below are the label’s, described in transplant patients taking it alongside other immunosuppressants.

Effects listed as very common, meaning at least one person in ten: diarrhoea, vomiting, nausea, abdominal pain and constipation; a low white cell count; anaemia; bacterial infections; headache; raised blood pressure; cough and breathlessness; raised cholesterol; weakness, fever and swelling.[55]

Three things on that label are worth more than a line each.

Infection. People taking immunosuppressants, mycophenolate included, are at increased risk of opportunistic infections, of fatal infections, and of sepsis.[55] Chapter 12 said that steroids can mask the usual warning signs. On both medicines at once, the same sentence applies with more force: a fever that would normally send you to a doctor may arrive small, or not at all.

Skin. The label states that people on immunosuppressive combinations are at increased risk of lymphoma and other malignancies, particularly of the skin.[55] It gives its own advice for that, and it is the kind you can act on today: limit sun and UV exposure, wear protective clothing, use a sunscreen with a high protection factor.[55]

Chapter 18 covers what is known about cancer risk in this disease itself, and it is worth reading beside this.

Blood counts. The label asks for a complete blood count weekly for the first month, twice monthly for the second and third months, then monthly through the first year.[55] That schedule was written for transplant patients. **Yours is your specialist's to set, and asking what it is takes one question.**

And the level of the medicine itself. Some teams measure mycophenolic acid, which is what mycophenolate becomes in the body, to see how much of the drug is reaching you. The European label mentions this only as something that may be appropriate when a combination is being switched, or where the immunological risk is high, and it gives no target range at all.[55] So this book gives none either. If your own team measures it, the range they read it against is theirs.

And the sentence that belongs in bold wherever it appears: **mycophenolate is a powerful human teratogen**, and the label contraindicates it in pregnancy.[55] Chapter 21 has the detail, and it is the chapter to read before a pregnancy is on the table rather than after.

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Azathioprine

Azathioprine is a tablet, taken daily, and it is used as maintenance: not to bring the disease under control in the first place, but to keep it there once steroids have done that.

The evidence in this disease is thin, and it is worth seeing exactly how thin.

A specialist centre in Graz, Austria looked back at ten men who were given azathioprine after an initial course of steroids. Some because the disease relapsed while the steroids were being tapered, some because the steroids were causing side effects, and some to bring the overall steroid dose down. All ten met the 2019 classification criteria, and they were followed for an average of about six years.[56]

Seven of the ten stayed in remission over that period. Three relapsed, five relapses between them.[56]

Side effects during treatment: infections in two, blood-count abnormalities in four, and raised liver enzymes in one. By the last visit,

five were still taking it, two had been switched to rituximab, and three were off immunosuppressive treatment altogether, two because of blood-count problems and one by their own choice.[56]

The finding worth carrying to your own appointment

Both of the patients with kidney involvement relapsed on azathioprine.[56]

The authors conclude that where the kidneys are affected, a B-cell-directed treatment such as rituximab may be the better maintenance option, and that azathioprine is otherwise a reasonable choice.[56]

Two patients is two patients. It is not proof. It is a specific, published observation that a specialist can weigh, and if your kidneys are involved it is a fair thing to raise.

What this study is not

Ten men, one centre, looking backwards. Not a randomised trial. And it says nothing at all about how azathioprine works in women, because there were none in it.[56]

Which maintenance medicine fits any one person depends on which organs are affected, on other health conditions and on specialist judgement.[56]

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Rituximab

Rituximab is an antibody treatment that targets a marker called CD20 on B cells, the immune cells linked to this disease. It has been used off-label here for years, particularly when the disease returns or when steroids are not enough on their own.[57]

It is given and monitored in a hospital setting, and whether to repeat it is a decision for the specialist.[57]

The evidence is stronger than azathioprine’s, and it comes from three places.

Does it work. In an early open-label trial with no comparison group, meaning everyone received the drug and nothing was measured against it, thirty people were treated, most of them with rituximab alone and no steroids.

Ninety-seven per cent showed a clinical response, and about four in ten were still in complete remission a year later.[57]

What happens when it stops. In a French study of thirty-three people, the disease came back in roughly four in ten after treatment stopped, on average a year and a half later.[57]

And the finding that changes practice. In that same French study, giving rituximab again before a relapse appeared roughly doubled the time people stayed free of disease.[57] A German hospital cohort of twenty-four people, looked at backwards through their records over around four years, found that continuing rituximab as maintenance lowered the share who relapsed from close to nine in ten to under three in ten, with a reassuring safety record.[57]

From nine in ten to under three in ten is a large difference, and it is the argument for planned repeat treatment rather than waiting for something to go wrong. It comes from twenty-four people at one hospital, so hold the direction more firmly than the numbers.

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What you can do with this

If you are on maintenance, ask what the plan is for continuing it. Both drugs in this chapter behave differently when they stop than when they continue, and the plan is worth knowing rather than discovering.

Ask which of the three you are on, and why that one. They have different evidence behind them and different things to watch for, and the answer tells you what your own monitoring should look like.

If your kidneys are involved and azathioprine is proposed, mention the Graz finding. *"I have read that both patients with kidney involvement in one series relapsed on azathioprine. Does that apply to me?"*

Chapter 14. The newer treatments

This is the part of the book most likely to be out of date first.

One of these is approved. Two have published trial results and are not approved. The rest are research.

Inebilizumab, the first approved treatment

In 2025 inebilizumab, sold as Uplizna, became the first medicine approved specifically for IgG4-related disease.[58]

It is authorised across the European Union, where the European Medicines Agency lists IgG4-related disease among its approved uses.[58]

Being authorised is separate from being funded. Each country decides on price and reimbursement itself.[58] If you have read that a treatment is approved in Europe and then found it is not available to you, that is the reason, and it is not a misunderstanding on your part.

It attaches to B cells and destroys them. It is given as a drip, with two doses at the start and then one every six months.[58]

In its phase 3 MITIGATE trial, which was funded by the company that makes it, inebilizumab substantially reduced the risk of the disease flaring compared with placebo, and people taking it needed far less steroid.[58]

Manufacturer funding is not a reason to dismiss a result, and it is a reason to know. A randomised trial against placebo is the strongest design there is, and this book uses industry-funded work only when the results have been through peer review, as these have.[58]

And the other side of that, in the same trial: serious side effects were more common on inebilizumab than on placebo, so the benefit and that risk are weighed together.[58]

One absence is deliberate. Longer-term follow-up from the trial extension was presented at a scientific meeting in 2026 and has not been published in a medical journal, so those figures are not repeated here.[58]

That is this book declining to tell you something it could easily have told you. Conference presentations are not peer-reviewed, and a figure quoted from one can move by the time it reaches a journal.

— ✦ —

Obexelimab, published and not approved

Obexelimab works differently from rituximab and inebilizumab. Rather than destroying B cells, it binds to CD19 on the B cell together with an inhibitory receptor, which quietens the cell without depleting it. It is given as a weekly injection under the skin.[59]

In the phase 3 INDIGO trial, also funded by the manufacturer and published in June 2026, 194 people received either obexelimab or a dummy injection for a year, with everyone coming off steroids by week eight.[59]

- Flares happened in about 27 of every 100 people on obexelimab, and about 55 of every 100 on placebo.[59]
- About 37 in 100 reached full remission at one year, against about 20 in 100 on placebo.[59]
- People on obexelimab needed roughly a third as much rescue steroid.[59]

Side effects reported more often than on placebo were joint pain, allergic-type reactions and diarrhoea. **Serious side effects were less common on obexelimab than on placebo.**[59]

Obexelimab is not an approved treatment for IgG4-related disease.[59]

— ✦ —

Rilzabrutinib, the one that is a tablet

Rilzabrutinib is experimental and it is taken by mouth. It blocks an enzyme called BTK that carries signals inside B cells.[60]

Being a pill sets it apart from rituximab, inebilizumab and obexelimab, which are given by drip or by injection.[60] For anyone who has spent a day in an infusion suite, that difference needs no explaining.

In an early phase 2 study run by the manufacturer, 27 people took it for up to a year: some who had not improved on rituximab, and some who had not tried it. About seven in ten, 19 of the 27, were free of

flares and off steroids and other immune-suppressing drugs by the end, and disease activity fell by week 12 and stayed down through week 52.[60]

Serious side effects occurred in two of the 27, including one death that the trial investigators judged unrelated to the medicine. The most common side effect was diarrhoea.[60]

And here is why those numbers must be held loosely. Everyone in that study received the drug. There was no comparison group, and it was small, so the findings point the way rather than settle it.[60]

Seven in ten sounds better than the obexelimab figures above. It is not comparable to them, because a study where everyone gets the drug cannot tell you what would have happened without it. A larger phase 3 trial, comparing rilzabrutinib against a dummy treatment, is now recruiting.[60]

Rilzabrutinib is not an approved treatment for IgG4-related disease.[60]

— ✦ —

Everything else, honestly labelled

Several other medicines are being explored. According to an independent review of the treatment landscape from July 2025, the evidence for each is still limited: small open-label studies, ongoing trials, or case reports. **None of them is an approved treatment for this disease.**[61]

- **Zanubrutinib**, another BTK inhibitor, in an open-label trial.[61]
- **Abatacept**, which dampens T-cell activation, in a small proof-of-concept study and isolated case reports.[61]
- **Dupilumab**, which blocks IL-4 and IL-13 signalling, in case reports only, mainly in patients with an allergic pattern of disease.[61]
- **Efgartigimod**, which lowers circulating IgG antibodies, with one case report and one ongoing trial.[61]
- **Tocilizumab**, which blocks IL-6, in case reports, particularly in vascular forms of the disease.[61]
- **JAK inhibitors** such as tofacitinib and baricitinib, in early clinical trials.[61]

None of these should be seen as a treatment option today. They are areas of ongoing research, and decisions about trials or off-label use belong with a specialist.[61]

— ✦ —

What you can do with this

If a treatment here interests you, ask whether it is available to you rather than whether it exists. Approval, licensing and funding are three different things and only the last one determines whether you can have it.

Ask about trials if you want to. *"Is there a trial I would be eligible for?"* Nobody will raise it unprompted, and a specialist centre will know what is recruiting.

Treat any figure in this chapter as provisional. This is the part of the book most likely to change, and igg4.org carries the current version.

Chapter 15. Relapse, stopping, and the long

view

The disease can come back, so people are usually followed over time. Catching a relapse early keeps it manageable, and regular follow-up with a specialist is a normal part of living with this.[62]

That is the whole chapter in two sentences. The rest is the detail worth having.

How often it comes back

This has been measured across many studies. A review pooling 24 studies and 3,797 people found relapse in about 17 in 100 by one year, 26 in 100 by two years, and 33 in 100 by three years.[62]

Put the other way round: two in three were still free of relapse at three years.[62]

Both of those sentences describe the same finding. Which one you carry is a choice, and the second is as true as the first.

— ✦ —

What raises the risk

The same review found three things that make relapse more likely: a history of allergies, disease affecting several organs at once, and low complement levels in the blood.[62]

It also found that steroids combined with an immune-suppressing medicine lowered the risk of relapse compared with steroids alone.[62]

Alongside serum IgG4, specialists may look at circulating plasmablasts, a type of B cell, which tend to rise with active disease and have been linked to a higher risk of relapse.[62]

None of those three risk factors is something you can change. They are there so that if your specialist is watching you more closely than someone else you know with this disease, you can see why.

These are averages across thousands of people rather than a prediction for any one person.[62]

— ✦ —

The trial that asked what happens when you stop

Most questions in this book have no trial behind them. This one does, and it is unusually clear.

A trial in China took 146 people whose disease had been stable and put them at random into three groups. One stopped both the steroid and the immune-suppressing medicine. One stopped the steroid and stayed on the immune-suppressing medicine. One stayed on both. Everyone was followed for eighteen months.[63]

- Stopped everything: the disease came back in about half, 25 of 48.[63]
- Stopped the steroid, kept the immune-suppressing medicine: 7 of 49.[63]
- Stayed on both: 6 of 49.[63]

The immune-suppressing medicine is what separated the groups. Whether a low-dose steroid continued alongside it made little difference.[63]

That is a useful result, and it may be the most practical finding in this book. If coming off the steroid is what you are hoping for, this trial is the reason that hope is worth putting to your specialist rather than carrying quietly. It is a question to ask, not a decision to take.

What the trial cannot tell you

It was open-label, so everyone knew which group they were in, and it followed people for eighteen months rather than years. It was carried out in Chinese hospitals, in people whose disease was already stable, so it describes that situation rather than the early months of treatment or disease that is still active.[63]

Whether to stop or continue a medicine is a decision for you and your specialist together, weighing how long things have been quiet, which organs were involved, and how the treatment is being tolerated.[63]

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The long view

Most people with this disease respond to treatment. More than eight in ten respond to steroids, and B-cell treatments bring the disease into remission in most patients.[64]

Being found early makes a difference. The disease damages organs over months and years as inflammation turns to scarring, and

starting treatment early can prevent much of that.[64]

The disease can return after treatment, and staying in remission with no treatment at all is uncommon. Follow-up appointments and blood tests are how a return is picked up, sometimes before you notice anything yourself.[64]

And the number this book will not give you

There are no survival figures here, and the reason is worth stating rather than hiding behind.

The figures that exist come from single centres, and they count damage caused by the treatment alongside damage caused by the disease, so they would mislead someone who has just been diagnosed.[64]

If that is the question on your mind, and for many people it is the only question on their mind at the beginning, it is the right question to put to your specialist, who knows which organs are involved and how you have responded so far.[64]

A book cannot answer it honestly. A person who has your notes can.

— ✦ —

What you can do with this

Ask what your own follow-up should look like. How often, what tests, and what would count as a reason to call between appointments.

Ask what a relapse would look like in your organs. It differs, and knowing your own version means you notice it early rather than explaining it away.

If you are hoping to come off treatment, say so out loud. It is a legitimate goal and it can be planned for, rather than something to raise apologetically at the end of an appointment.

And if something changes while you are tapering, report it while it is new. That is what the trial in this chapter is about.

That is treatment.

Part 5 is about living with this: what it is like, the questions that arrive later, and how to find someone who knows the disease.

Part 5. Living with it

The disease is one thing. The life around it is another, and this part is about the second.

Read what applies to you. Chapter 19 is the one to come back to, because it is how you find someone who knows this disease.

Chapter 16. What it is like

Everything so far has been about the disease. This part is about the life around it, and it opens with the only study in the whole corpus that asked patients what living with this is like.

Somebody finally asked

An international survey put the question to 229 people with retroperitoneal fibrosis, across 30 countries and five continents.[65]

Four things came up again and again.[65]

Pain.

The side effects of the treatment.

The absence of doctors who knew the condition, and of information they could turn to.

And the weight it put on them psychologically.

— ✦ —

The third one deserves its own paragraph

People described struggling to find anyone informed about their own illness.[65]

Not struggling to get treatment. Struggling to find someone who knew what they had.

That is the gap this site was built to close, and it is the reason a map of specialist centres matters as much as the medical pages do.[65]

If you have spent an appointment explaining your own diagnosis to the person treating you, you are describing the single most common complaint of 229 people across thirty countries.

— ✦ —

Your path being different is the norm

The same survey showed how differently people are managed. Just over half had a biopsy to reach the diagnosis. Three in four went through a further procedure. Six in ten were on medical treatment at the same time.[65]

If your route looked nothing like someone else's, that is the norm rather than a mistake.[65]

People compare notes in patient groups and conclude that somebody has been mismanaged. Usually nobody has. This is a disease with a dozen presentations met by a dozen specialties, and the paths through it vary accordingly.

— ✦ —

What this study is and is not

It covered retroperitoneal fibrosis, which overlaps with IgG4-related disease without being the same thing.[65]

So it is the closest thing we have to a survey of what living with this is like, and it is not exactly a survey of this disease. Both of those are true, and the first is worth more than nothing, which is what the alternative would be.

If any of it sounds like your experience, it is worth saying so to your specialist, including the parts that are not physical.[65]

The four nights

My own case.

Four nights in May 2026, between the biopsy and the result.

The pain woke me between two and four each morning. Under the sternum, through to the lower back. My glucose climbed with it, 224, then 236, then 249, as the stress hormones did what stress hormones do. A fentanyl patch at the lowest dose available did close to nothing.

One of those nights I went to an emergency department. What I came away with was a prescription for an anti-inflammatory I did not take, because it would have pushed a liver that was already struggling and blurred the only markers anyone was reading. That was a decision about my own liver, made with my own history in front of me. It is not advice, and I would not want it read as any.

What I remember more than the pain is what was missing. Nobody in that building had seen this disease. At three in the morning I was explaining my own diagnosis to people who were trying to help me and had nothing to work with.

So I did the only thing left. I wrote. Letters to specialists in four countries. Twenty-eight pages of seven years of records, pulled into one document. A message to the Spanish patient association at half past midnight, which was answered the same morning.

The survey in this chapter names four things: pain, the side effects of treatment, the absence of informed doctors and information, and the psychological weight. Those nights had all four at once, and I did not know then that they were the ordinary experience of this disease rather than my own bad luck.

That was mine. Yours will have its own hours and its own room.

If you are inside it now: what you are carrying has been carried before, and it has a name.

Chapter 17. Fatigue

Of everything this disease does, the symptom people ask about most is the one with the least research behind it.

You are tired in a way that sleep does not fix. Your bloods have improved. Someone has told you the inflammation is controlled. And you still cannot do what you could do two years ago, and you have started wondering whether you are imagining it, or whether this is just what being your age feels like now.

You are not imagining it.

Fatigue is a recognised symptom of this disease

The American College of Rheumatology lists fatigue among the common symptoms of IgG4-related disease, alongside weight loss and

headaches.[66]

It gives no figure for how many people it affects, and neither will this book, because nobody has measured it. When you meet a percentage for fatigue in this disease, check what it is attached to. Several of the numbers in circulation come from studies of rheumatoid arthritis.

You may have to say the word yourself in a consultation. It rarely comes up otherwise, partly because it does not show up on any scan and partly because the appointment tends to be spent on the organ.

— ✦ —

Why feeling exhausted while the bloods look good is a known pattern

This is the part most worth having, and it comes with a limit attached.

Research into fatigue across inflammatory rheumatic diseases **as a group**, rather than this disease specifically, found that fatigue

often continues after CRP and ESR have returned to normal, and after disease activity scores look controlled.[67]

The same work found that fatigue tracks more closely with pain, disturbed sleep, mood, medication effects, reduced activity tolerance and other conditions than it does with the inflammation markers themselves.[67]

The limit: that research is not about IgG4-related disease. It is about a family of conditions this one sits alongside. It cannot tell you what proportion of your own fatigue comes from where.

What it can tell you is that the pattern you are living in is documented. Normal inflammation markers and profound tiredness are not a contradiction, and a clinician who has read this literature will not treat them as one.

There is also a loop in it worth recognising, because it is one of the few parts of this you can put a hand on. Pain, rest after a flare, low mood and reduced confidence all lead to doing less. Doing less reduces aerobic capacity and muscle strength, which makes ordinary tasks feel harder, which leads to doing less again.[67]

Naming that loop is not the same as blaming you for being in it. You did not choose any of its inputs.

— ✦ —

Steroids are part of this

Sleep and mood are both affected by steroid treatment. Insomnia and mood changes are recognised effects listed by the regulator,[68] and disturbed sleep and mood are named in the fatigue research as contributors in their own right.[67]

Poor sleep makes everything heavier. If your tiredness arrived or worsened when treatment started, that connection is real and it is worth raising, because a dosing or timing change is a conversation to have rather than a thing to endure.

— ✦ —

What this chapter cannot do

It cannot tell you how long this lasts. It cannot tell you whether your fatigue is the disease, the treatment, disturbed sleep, low mood,

deconditioning, or something unrelated that happens to be happening at the same time.

Those distinctions matter, because some of them are treatable and the answers differ.

Which is the whole argument for saying it out loud to someone qualified rather than absorbing it as the price of being ill.

— ✦ —

What you can do with this

Put it on the agenda before the appointment starts. *"Before we get to the scans, I want to talk about fatigue."* Otherwise the organ takes the whole visit.

Describe it in terms of what you cannot do rather than how you feel. *"I can manage the morning, then nothing after two."* That is information a clinician can work with. "I'm tired" is not.

Ask whether anything treatable is being missed. Anaemia, thyroid function, vitamin deficiency, sleep, mood and medication effects are all worth asking about, and several are simple tests.

Chapter 18. The questions that arrive later

Some questions do not come in the first week. They arrive months in, usually at night, and they tend to go unasked because they feel either too frightening or too trivial to raise.

Three of them have real answers.

Does this raise my risk of cancer

Two studies have asked, and both found that it does.[69]

A study following 587 people in China found cancer after diagnosis at about 2.8 times the rate expected in the general population. A nationwide study using South Korean insurance records, covering 1,267 people, found about 4.1 times.[69]

The types that stood out were blood cancers, particularly lymphoma and a bone marrow condition called myelodysplastic syndrome,

along with pancreatic cancer. The Chinese study also recorded cancers of the digestive tract, thyroid, kidney and breast among its patients.[69]

Now read the next paragraph, which matters more than the numbers

A figure like this compares whole groups rather than describing a person. It says cancer appeared more often than expected across a population of patients, and it says nothing about how likely it is for any one of them.[69]

Most people in both studies stayed free of cancer.[69]

That sentence is not a softener placed after bad news. It is the same finding, stated the way it applies to an individual reader rather than to a population.

What follows from it

This is one of the reasons follow-up matters, and one of the reasons a specialist takes a new symptom seriously instead of assuming everything belongs to the same condition.[69]

If something changes, it is worth mentioning rather than waiting for the next appointment.[69]

Both studies were carried out in East Asia, so how closely the figures apply elsewhere is unknown.[69]

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Can I have my vaccinations

Yes, and the timing is the part worth planning.

Vaccines work best when they are given before treatment that suppresses the immune system begins. European rheumatology guidance states it plainly: where it can be planned, vaccination comes first.[70]

That guidance was written in 2019, before the newer treatments in Chapter 14 existed, and it does not name them. What it addresses is the principle, and the principle is about treatment that suppresses the immune system, which is what all of the medicines in Part 4 do.

Which makes this a question to raise when a new treatment is being discussed, not after it has started.

Vaccines that contain no live organism, which includes the usual flu and pneumococcal vaccines, can be given while someone is taking steroids or other immune-suppressing medicines. The same guidance says flu and pneumococcal vaccination should be strongly considered for most people on these treatments.[70]

Live-attenuated vaccines are approached with caution. The guidance also suggests vaccinating while the disease is quiet rather than during a flare, and reviewing what is needed once a year rather than leaving it to chance.[70]

That guidance was written for autoimmune rheumatic diseases as a group rather than for this disease specifically, although the treatments it describes are the ones used here.[70]

— ✦ —

What about those IgG4 food tests

This one is a trap, and it is set by the name.

Searching online for IgG4 and diet leads quickly to food intolerance tests that measure IgG4 antibodies against foods. **Those tests have nothing to do with IgG4-related disease. The two share a name and nothing else.**[71]

Allergy specialists advise against them. The Canadian Society of Allergy and Clinical Immunology states it directly: do not order IgG testing to panels of foods. Their reasoning is that IgG to a food shows previous exposure rather than a reaction to it, so a positive result tells you that you have eaten something, not that it harms you. European allergy specialists reached the same conclusion in a task force report that gives its verdict in its title.[71]

The practical risk is a diet that removes foods for no reason. Cutting out food groups on the strength of these panels can leave someone poorly nourished at a time when they need to be well.[71]

Why this book says nothing about diet

On diet and IgG4-related disease itself, this book makes no claims at all, and the reason is the plainest one in these pages. The search

behind this book found no study of diet in this disease to cite, and the rule set out at the front is that a claim without a source does not appear.

You will find plenty of confident advice elsewhere.

If eating has become difficult, which happens where the pancreas or the bile ducts are involved, that is a real question with a real answer, and it belongs with your specialist or a dietitian they refer you to.[71]

— ✦ —

What you can do with this

Raise vaccination before a new treatment starts, not after. *“Should I have any vaccinations before we begin this?”*

Report a new symptom rather than filing it under your diagnosis. Not everything that happens to you now belongs to this disease, and that is exactly why it is worth mentioning.

Ignore the food panels. If eating is hard, ask for a dietitian instead.

Chapter 19. Finding a specialist

Chapter 10 set out what shortens the road: reaching a doctor who knows this disease, and a centre that has seen it before.

That is the whole chapter. Everything else here is how.

The directory

igg4.org has a directory of centres of expertise across Europe that can be searched, filtered and seen on a map.[72]

Ask your own doctor for a referral, and confirm details with the centre directly.[72]

What to say

You do not need to challenge anyone to ask for this. Two sentences do the work.

“Is this something you see often, or would a specialist centre add anything?”

“I would like a referral to somewhere that sees this disease regularly. Can we arrange that?”

Most clinicians meeting a rare disease are glad of the help. Very few will be offended, and the ones who might be are the reason you want the referral.

If a referral is not possible

Some countries, some insurers and some distances make it impossible. If that is your situation, the directory is still worth having, because a centre can sometimes advise your own team without seeing you, and because knowing where the expertise sits changes what you can ask for.

Chapter 20. Is it inherited, and can I pass it on

Two questions arrive together, usually within a day or two of the diagnosis, and usually not from you.

They come from your children. From a sister who has started reading. From a partner who has been quietly working out whether they should be worried for themselves.

Both have clear answers, and one of them is clearer than most things in this book.

Nobody can catch this from you

No. IgG4-related disease cannot be passed to another person.

The French national rare-disease network FAI2R, which is designated by the French Ministry of Health, states it directly on its patient page: the causes are not precisely known, and it is neither a genetic disease nor a contagious one, and it is not a cancer.[73]

The reason lies in what the disease is. It is immune-mediated, which means the inflammation comes from your own immune system behaving abnormally rather than from anything that arrived from outside.[74] There is nothing to catch. There is nothing to hand to a partner, a grandchild or a colleague.

You can share a bed, a kitchen, a bathroom, a life. None of it transmits anything.

Something worth knowing about that answer: it was surprisingly hard to source. Searching in English, French and German, the FAI2R page is the only one from a public body that says it outright. The major professional societies and teaching hospitals simply do not address transmission at all, because clinicians rarely think to deny something nobody has asked them.

Which is why you may have asked three people and got three vague answers. The vagueness was not caution about your case. It was a question the literature forgot to answer.

— ✦ —

Inherited is a more interesting no

This is not an inherited disease in the way people mean the word. FAI2R says so on the same page.[73]

The longer answer is worth having, because a flat no would be slightly too tidy.

Genetic susceptibility in this disease has not been studied extensively, and the reason is stated plainly in the specialist literature: the disease is rare, and families with more than one affected member are scarce.[75]

What has been found are susceptibility factors rather than inheritance. A genome-wide study in Japan pointed to the HLA-DRB1 and FCGR2B regions. A study in retroperitoneal fibrosis pointed to a particular HLA-DRB1 variant.[75] Those are patterns that shift the odds very slightly across a whole population. They are not a thing passed from parent to child that causes the disease.

Family cases do exist, and pretending otherwise would be dishonest. One report documents a father and two daughters affected, with the mother unaffected, all three sharing two rare gene variants.[76]

That is one family. It appears in the medical literature precisely because it is unusual.

A second family was studied in more detail, and it answers a question some readers will be carrying. Screening the relatives of a 48-year-old man with this disease turned up unexpectedly raised IgG4 in both of his

teenage sons. The sons were healthy: no symptoms, ordinary school, ordinary sport. All three shared a rare gene variant.[77]

The researchers did not present that as good news or as bad news. They wrote that the sons might have early disease that had not yet declared itself, and then they wrote the sentence that matters most here: whether the sons will go on to develop IgG4-related disease is unknown.[77]

So if someone in your family has been found to have a raised IgG4 and no illness, you now know two things. Other families have stood exactly where you are standing. And the people who study this for a living, with whole genome sequencing available to them, could not say what it meant.

Unknown is not a comfortable answer. It is the true one, and you are entitled to have it rather than a reassurance nobody can back.

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The number you want does not exist

Here is the part I would rather tell you straight than dress up.

No study has ever calculated the risk to a brother, a sister or a child of someone with this disease. There is no sibling recurrence risk in the literature, no relative risk for first-degree relatives, and no heritability estimate. The figure has never been produced.[75]

Other autoimmune conditions have such numbers. This one does not, and borrowing theirs would be inventing yours.

If you find a percentage online for the risk to your children, look for where it came from. It will not be from a study of this disease.

— ✦ —

The one thing worth passing on

Nothing in this chapter is a reason to have your family tested.

No guideline recommends screening the relatives of someone with this disease, and this book has no source that supports it. A number measured in a well person is not a diagnosis.

The one family in the literature where relatives were screened makes the point better than any argument could. Something was found, and the researchers could not say what it meant.[77] A test that returns an answer nobody can interpret does not give a family peace of mind. It gives them a number to worry about.

There is something better to pass on, and it costs nothing at all.

This disease builds masses. It is mistaken for cancer, most often in the pancreas and also in the kidneys and the lymph nodes, and people are investigated, biopsied and operated on for a suspected cancer before anyone considers it.[78] In a published series of four patients with masses in the kidney and ureter, surgery went ahead and the diagnosis was made only from the tissue afterwards. Two of those four had a normal IgG4 blood test.[79]

The numbers are small. Autoimmune pancreatitis, the pancreatic form of this disease, is found in about 1.6 per cent of pancreatic operations carried out for a suspected cancer: roughly 140 cases among nearly nine thousand operations pooled across ten studies.[80]

Small is not zero, and what is at stake is an organ.

So the thing worth giving your family is not a test and not a risk figure. It is a question, for a room they may never be in, about an organ that may never be at risk.

Has IgG4-related disease been considered?

Five words. Nobody in your family would otherwise know to ask them, because almost nobody knows this disease exists. And where the picture is unusual, the surgeons who published that four-patient series argued for taking a small tissue sample first rather than going straight to major surgery,[79] which makes a second question worth having ready: would a biopsy before surgery change the plan?

That is what your diagnosis can give the people around you. Not a worry to carry. A question to keep.

— ✦ —

What you can do with this

Answer the contagion question directly, and early. *“It isn’t catching. There’s no risk to you from being around me.”* Say it before someone spends a night looking it up alone.

Give them the question, not a test. *“If you’re ever told you need surgery for a lump or a swollen organ, ask whether IgG4-related disease has been considered.”* That is the whole of it. It asks nothing of them today.

If a relative has symptoms of their own, they see a doctor about their symptoms. Their symptoms stand on their own. A family link is not the reason to investigate them, and it is not a reason to skip investigating them either.

If you are asked what the risk to your children is, say that nobody has measured it. Then take the question to your specialist, who can talk about your own family rather than about a population.

Chapter 21. Pregnancy, breastfeeding and planning a family

If you are of an age to be thinking about children, this chapter matters more than its length suggests, and it needs reading before it becomes urgent rather than after.

The disease itself has barely been studied in pregnancy. The medicines have been studied thoroughly. That asymmetry shapes everything below.

What is known and what is not

There is essentially no research on how IgG4-related disease behaves during pregnancy. No outcome studies, no series of any size.

What is well established is which of the medicines used to treat this disease are compatible with pregnancy and breastfeeding, and which are not. That work has been done properly, by specialist societies and by medicines regulators, and it is drug by drug.

So the honest position is this: nobody can tell you how your disease will behave, and everybody can tell you what your medicines require.

— ✦ —

The medicines differ from each other sharply

This is the substance of the chapter, and none of it is advice about your own treatment.

Prednisolone. UK specialist guidance regards it as compatible with pregnancy and as the preferred corticosteroid in maternal rheumatological disease.[81] The regulator's own labelling is more cautious and describes a small but inconsistent increased risk of orofacial clefts with corticosteroid use in the first trimester.[82] Both of those are true at once, and you deserve to see both.

Azathioprine. UK specialist guidance grades it compatible throughout pregnancy, at full agreement among the panel.[81] The 2018 regulatory label in the United States is markedly more restrictive and advises women of childbearing age to avoid becoming pregnant.[83]

That disagreement is real, and this book is not going to pick the reassuring side of it. A decades-old label and a current society guideline reach different conclusions. Your specialist can weigh that for your case. A website cannot.

Methotrexate. European regulators describe it as a powerful human teratogen and contraindicate it in pregnancy.[84] The European product information asks for effective contraception during treatment and for at least six months afterwards for women, and for reliable contraception during treatment and for at least three months afterwards where the man is the patient.[84]

The UK society guideline sets both of those differently. It says methotrexate at 25 mg a week or less should be stopped at least one month before conception, and it grades paternal exposure at that dose compatible with pregnancy, meaning no waiting period for men at all.[81]

Six months against one. Three months against none. Those are not small differences, and no page can tell you which document applies to you.

Mycophenolate mofetil. The European product information states plainly that mycophenolate is a powerful human teratogen, and it contraindicates the medicine in pregnancy.[55] UK specialist guidance says the same, and adds that it is to be avoided by

women planning one.[81] Chapter 13 covers what this medicine does and what else its label carries.

Rituximab. The two documents disagree here too, and more sharply than anywhere else in this chapter. The UK society guideline says to consider stopping at conception.[81] The European product information asks for effective contraception during treatment and for twelve months afterwards.[85] One describes conception as the moment to stop; the other asks you not to conceive for a year after the last dose.

That twelve-month window is the single most practical fact in this chapter, because it is a fact about the future rather than the present. It is worth knowing before treatment starts, not after.

— ✦ —

The honest paragraph is about the disagreements

You have just read three places where a medicines regulator and a specialist society do not say the same thing.

A patient guide could hide that by quoting whichever source it preferred. That would be more comfortable to read and it would be worse for you, because you would meet the other position eventually, probably in a consultation, probably at speed.

The disagreements exist because regulatory labels and clinical guidelines are written at different times, for different purposes, from different evidence. Neither is careless.

What resolves them is not a document. It is a person who knows your disease, your organs, your treatment and your plans, sitting down with you before anything is decided.

— ✦ —

What you can do with this

Raise it early, even if a pregnancy is years away or only a maybe. *"At some point I might want children. Does that change what we start me on?"* The answer may change the treatment plan, and it is far easier to choose a path than to change one.

If you are on methotrexate or mycophenolate and a pregnancy is possible, that is a conversation now rather

than at the next routine appointment.

Nobody stops, starts or changes any of these medicines on their own. Not on the strength of this chapter, and not on the strength of a label read online. Stopping treatment carries its own risk to you and therefore to a pregnancy.

Chapter 22. Children

This chapter is for parents, and it is short because the evidence is.

IgG4-related disease is mainly a disease of adults, and it is rare in children. When it does appear in childhood it is most often in teenagers, and it affects boys and girls in roughly equal numbers.[86]

That equality is worth noting, because in adults the disease affects men about twice as often as women. The pattern that holds across adult populations does not hold here.

What it looks like in a child

Children tend to have the disease in a single site rather than across several organs at once, which is more the adult pattern.[86]

The eyes and the area around them are the most commonly affected site in children, and it can cause a bulging eye, a drooping eyelid, double vision, or limited eye movement.[86]

Other sites, such as the pancreas, kidneys, liver and lungs, are involved less often.[86]

— ✦ —

Why the diagnosis is harder in a child

Three reasons, and they compound.[86]

The criteria used in adults were designed for research and do not always fit younger patients.

The IgG4 blood level is often normal in children, especially when the eyes are involved.

And the typical changes seen under the microscope are present in only a minority. A tissue sample is also harder to obtain in a child.[86]

Everything Chapter 7 said about the blood test being unreliable is more true in children, not less. For all these reasons it is assessed by a specialist familiar with the disease.[86]

— ✦ —

Treatment

Treatment follows the same lines as in adults. Steroids are the usual first treatment, and a steroid-sparing medicine such as azathioprine, mycophenolate or methotrexate is often added early, to lower the chance of relapse and reduce the amount of steroid needed. Rituximab is now an established option, both to bring the disease under control and to treat flares.[86]

Adding the second medicine early, rather than waiting for something to go wrong, is more the pattern in children than in adults, and the reason is the amount of steroid a growing child would otherwise need.

— ✦ —

The honest paragraph, for a parent

The disease tends to come and go over time, and relapse is common in children, reported in more than half of them in some studies, so it is followed over the long term.[86]

More than half. That is a harder number than the adult figures in Chapter 15, and a parent reading this book deserves to meet it here rather than discover it later.

Starting treatment early matters, because it helps prevent the lasting scarring that untreated inflammation can cause.[86]

Any decision about a child’s care belongs with their specialist.[86]

Chapter 23. Work, money and everyday life

This is the shortest chapter in the book, and the reason it is short is the finding.

Nobody has studied this

No study has measured how IgG4-related disease affects work.

There is no research on how many people keep working, how much time off they need, how many reduce their hours, how many change what they do, or how many reach a point of being unable to work at all. There are no figures on sick leave, on return to work, or on disability.

This chapter cannot tell you what to expect, because nobody has looked.

That absence deserves saying out loud rather than being covered with general advice about pacing. It is one of the clearest examples in this whole book of a question patients ask constantly and research has not touched.

— ✦ —

What patients themselves have said

What does exist is one study that sat down with fourteen people who have this disease and asked them about living with the risk of it coming back.[87]

One of them described a relapse like this:

> “I have to spend more money every time I recurrenced, and I can’t work at all. It’s also a considerable economic burden for my family.”[87] The wording is reproduced as the study printed it.

Others described the fear that arrives with the possibility of recurrence, and the weight of a condition that keeps returning.[87]

Fourteen people are fourteen people. Their experience is not a prediction of yours, and none of it is a statistic. It is offered here because it is the only place in the literature where anyone asked.

If any of it sounds like your life, you are not the first, and the reason it feels unspoken is that it very nearly is.

— ✦ —

About the money, and about who has counted it

The financial impact of this disease has been studied. It has been studied almost entirely in insurance-claims analyses in the United States, funded by pharmaceutical companies, with company employees among the authors.

This book does not use industry-funded material unless it reports the results of a clinical trial published in a peer-reviewed journal, and those analyses are not trials. So their numbers are not here.

That exclusion is worth understanding rather than glossing. It means the only people who have measured what this disease costs are companies with a product to sell into it. Independent research on what it costs the people who have it has not been done.

You are entitled to know that the gap exists, and why this book will not fill it with figures it does not trust.

— ✦ —

What you can do with this

If work is becoming difficult, say so to your specialist. It rarely comes up on its own, and there may be a treatable reason underneath it.

Ask your national patient association about entitlements. They know the local system, which a general guide cannot. In France, for example, the national protocol for this disease can support an application for exemption from co-payment. Provisions elsewhere differ, and the association will know them.

Keep your own record. Nobody is collecting this data, so the only account of what this disease has cost you is the one you keep. That matters for your own decisions, and it matters for any conversation with an employer or an insurer.

Chapter 24. You are not alone

IgG4-related disease is rare, and it is common to feel alone with something few people have heard of.[88]

The beginning is the hardest part, and that is usual

Being told you have a disease that many doctors have never seen can be frightening, and feeling overwhelmed at the start is a usual reaction rather than a sign you are handling it badly.[88]

That sentence is in this book because people apologise for being frightened. There is nothing to apologise for, and being overwhelmed by a rare diagnosis is the ordinary response of an ordinary person to difficult news.

— ✦ —

What makes the most difference

Reliable information and the right specialist.[88]

Not resilience, not attitude, not doing your own research until three in the morning. Information you can trust, and a doctor who knows the disease.

This site gathers sourced information in five languages and points to centres of expertise, so that searching for help does not fall on one person alone.[88]

Patient organisations exist for this disease in several countries and are listed on the sources page.[88]

And if what you are carrying feels like more than the illness itself, that is worth saying out loud to your treating team.[88]

— ✦ —

Where the science is going

This disease was recognised as a distinct condition only about twenty years ago, and understanding of it has grown quickly since.[89]

Treatment has moved from steroids alone to medicines that target the immune cells behind the disease, and more are being tested.[89]

Researchers are also looking for better blood markers than IgG4, including certain immune cells and proteins that seem to track how

active the disease is. None of these are available as a test you can ask for yet, and they are still being studied.[89]

The direction of travel is towards earlier diagnosis and treatment chosen to fit the person.[89]

Twenty years ago this was several separate diseases with separate names in separate departments. Today it has one name, five red flags written down so that any doctor might spot it, one approved medicine and two more with published trials behind them.

Someone diagnosed twenty years from now will find a book like this out of date, and that is the point of it.

Epilogue

You have reached the end of a book about a disease. That takes something, and I know it, because I have been the one turning these pages at an hour when nothing else was open.

Thank you for staying with it.

Two things before you close it.

Come back to the site

Not out of loyalty. Because this moves.

One of the treatments in Part 4 was approved while this book was being written. Two others have trial results that were published in the last eighteen months. Guidance is rewritten, figures are revised, and links rot: a page that worked when this was printed will be a dead end in a few years.

igg4.org carries the living version of everything here, in English, Spanish, Dutch, French and German, with every link kept alive and every source named.

If anything in this book ever contradicts the site, trust the site.

And pass it on

Somewhere near you is a person who has just been handed this diagnosis and has found what I found: fragments, dead links, and pages written for doctors.

You can shorten that search for them.

Send this book to them. Print it and leave it where someone frightened will find it. Give it to a doctor who has never met this disease, because the person it helps most may be the one who sees the next case. Nothing here is restricted, there is nobody to ask, and it costs nothing to hand on.

This book exists because one patient could not find what he needed. It becomes useful when it reaches the next one.

What I wish you

I am going to say this plainly, because I mean it exactly as written.

A painless recovery.

A soft treatment.

And someone in the room who already knows what you have.

Luc

About the author

Luc Smet is a patient.

That is the qualification that matters here, and it is the only one that does. In July 2025, at 54, he read a scan report that used the word malignancy about his pancreas. The tissue said something else: IgG4-related disease, after seven years in which a rising number in his blood had been noticed and explained away, every time, by someone with more medical knowledge than he had.

He is not a doctor and does not pretend to be. The authority in this book belongs to the sources and to the specialists. He is the one who gathered them.

What thirty years of work gave this project is a habit rather than any medical knowledge. He started in Belgium in the early 1990s, building

the country's first mobile networks, and moved through technical sales, country management and executive roles into his present work as Chief Operating Officer of a multi-industry group. Along the way he learned to assemble evidence, name where each piece came from, and say plainly what is not known. That is the whole method of this book.

He writes. *The Human Field* is about presence and honesty in leadership. *Balanced Divinity* was written with his wife Vanessa De Wit, a visual artist and healer, and it is the only thing standing behind igg4.org. No company. No sponsor.

He lives in Andalucía. His practice is called Incremento, for growth understood as unfolding rather than expansion, which is close to how this project grew: one sourced page at a time, because the next patient deserves an easier road than he had.

Part 6. Sources

Every source cited anywhere in this book appears below, numbered in the order the book first uses it. Each note also says what kind of source it is and what it cannot show,

because a citation on its own tells you where a claim came from and not how much weight it can carry.

The living reference list, with a working link to every document, is at igg4.org.

1. Orphanet, IgG4-related systemic disease (ORPHA:596448); and Mahajan A, Tinianow A, Katz G. IgG4-Related disease: From diagnosis to remission. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. Orphanet is the European public reference portal for rare diseases, maintained under INSERM; the Mahajan paper is a specialist review, which means these statements reach this book through experts summarising a body of work rather than through a single original study.

2. Okazaki K (ed.). *IgG4-Related Disease.* Current Topics in Microbiology and Immunology, vol. 401. Springer International Publishing, 2017. A technical reference written for doctors and researchers, gathering what was understood in 2017 about how the disease develops. It describes mechanisms across a population of patients. It does not identify a cause in any individual, and no source currently does. The short explanation of what B cells, plasma cells and T cells are is

a plain-language gloss of the mechanism this source describes, written for readers with no background in biology. It adds no claim about the disease that is not in the source.

3. Della-Torre E, Talarico R, Ballarin J, et al. Identification of red flags for IgG4-related disease: an international European Reference Network for Rare Connective Tissue Diseases framework. *The Lancet Rheumatology* 2025;7(1):e64-e71; and Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. The first of these is the paper Chapter 5 is built on: a set of warning signs written specifically to help doctors who do not specialise in this disease recognise it.

4. Sina S, Bonisoli GL, et al. Clinicopathological Pearls and Diagnostic Pitfalls in IgG4-Related Disease. *Diagnostics* 2025;15:2299; and Peyronel F, Della-Torre E, Maritati F, et al. IgG4-related disease and other fibro-inflammatory conditions. *Nature Reviews Rheumatology* 2025;21(5):275-290. Both are reviews written for specialists about the conditions this disease is confused with. The Peyronel review declares no competing interests.

5. Nuthalapati M, Menon AR, Rajendran R, et al. IgG4-Related Disease in Urological Practice: A Case Series of Mistaken Malignancies. *Indian Journal of Surgical Oncology* 2025;16(6):1446-1451. A case series of four patients, which is a description of what happened to four people rather than a study designed to measure how often it happens. It is quoted here for the pattern it documents and for the argument its authors make, not as evidence of frequency.

6. igg4.org. This paragraph is the project speaking in its own voice rather than reporting a finding. It carries no clinical claim.

7. Wallace ZS, Katz G, Hernandez-Barco YG, Baker MC. Current and future advances in practice: IgG4-related disease. *Rheumatology Advances in Practice* 2024;8(2):rkae020. A specialist review of where the research stands. On prevalence it is deliberately unspecific, because the population-level studies that would settle the question have not been done.

8. Wallace ZS, et al. *Rheumatology Advances in Practice* 2024;8(2):rkae020; Stone JH. IgG4-related disease: lessons from the first 20 years. *Rheumatology (Oxford)*

2025;64(Suppl 1):i24-i27; Peyronel F, et al. *Nature Reviews Rheumatology* 2025;21(5):275-290. Three independent reviews, agreeing on the sex ratio and on how it varies by organ. Figures for age at diagnosis are averages across studied populations and say nothing about the age at which any individual can develop this disease.

9. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Wallace ZS, Naden RP, Chari S, et al. The 2019 American College of Rheumatology / European League Against Rheumatism Classification Criteria for IgG4-Related Disease. *Arthritis & Rheumatology* 2020;72(1):7-19. The 2019 criteria were built to decide which patients enter research studies. They are not a diagnostic checklist for an individual, and a person can have this disease without meeting them.

10. Lanzillotta M, Campochiaro C, Mancuso G, et al. Clinical phenotypes of IgG4-related disease reflect different prognostic outcomes. *Rheumatology (Oxford)* 2020;59:2435-2442. A single specialist centre in Italy, 179 patients, looking back at records rather than following patients forward. Findings from one expert centre

may not hold in a general hospital population, and the age figures quoted are group averages.

11. Cuéllar MC, et al. Enfermedad relacionada a IgG4. Serie clínica de pacientes chilenos. *Revista Médica de Chile* 2022;150:705-710. Fifty-two adults across six centres, reviewed retrospectively. The organ frequencies differ from those in the larger reviews, which is expected in a series this size and in one country's referral pattern. It is cited here for that contrast and for the finding on normal IgG4 blood levels.

12. Della-Torre E, Talarico R, Ballarin J, et al. *The Lancet Rheumatology* 2025;7(1):e64-e71. The paper that set out the five red flags, produced by expert agreement across European centres rather than by a trial. Its own authors describe the flags as a prompt to consider the diagnosis and refer, and note that they remain under study. José Ballarín, who chairs the European Federation for IgG4-Related Disease, is among the authors.

13. Mahajan A, Tinianow A, Katz G. IgG4-Related disease: From diagnosis to remission. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Wallace ZS, Naden RP, Chari S, et

al. The 2019 American College of Rheumatology / European League Against Rheumatism Classification Criteria for IgG4-Related Disease. *Arthritis & Rheumatology* 2020;72(1):7-19. The 2019 criteria were designed to select patients for research, which is why they are strict by intention. A person can have this disease and not meet them.

14. Protocole National de Diagnostic et de Soins (PNDS), Maladie associée aux IgG4, Haute Autorité de Santé, with FAI2R and CERAINOM-IgG4, November 2025; and Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. The PNDS is a French national protocol issued under the national health authority, written by designated reference centres. It sets out what a treating team is expected to do, which is why it is the source for the first-round blood tests and for the point about biopsy timing.

15. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Stone JH. IgG4-related disease: lessons from the first 20 years. *Rheumatology (Oxford)* 2025;64(Suppl 1):i24-i27. The range for normal IgG4 levels in people who have the

disease varies between studies, which is itself the point: this is not a test with one agreed performance figure.

16. Karamya ZA, Kovács A, Illés D, Czakó B, Fazekas A, Farkas N, Hegyi P, Czakó L. Prevalence of autoimmune pancreatitis in pancreatic resection for suspected malignancy: a systematic review and meta-analysis. *BMC Gastroenterology* 2024;24:278. Ten studies, 8,917 pancreatic operations across six countries, performed between 1987 and 2016. Funded by Hungarian public and university sources, with open access provided by the University of Szeged; the authors declare no competing interests. **Read this figure for what it is: it describes people whose disease had already been mistaken for cancer badly enough to send them to surgery, not everyone with IgG4-related disease.** In that group, 43 per cent of the type 1 cases with a pre-operative result had a raised serum IgG4.

17. Della-Torre E, et al. *The Lancet Rheumatology* 2025;7(1):e64-e71; the 2019 ACR/EULAR classification criteria; Arias-Intriago M, et al. IgG4-Related Disease: Current and Future Insights into Pathological Diagnosis. *International Journal of Molecular Sciences*

2025;26(11):5325; and Stone JH. *Rheumatology (Oxford)* 2025;64(Suppl 1):i24-i27.

18. Bateman AC, Culver EL. Challenges and pitfalls in the diagnosis of IgG4-related disease. *Seminars in Diagnostic Pathology* 2024;41(2):45-53. A review written by pathologists for pathologists about the ways this diagnosis goes wrong under the microscope. It is the source for the organ-by-organ variation, for the list of conditions that overlap, and for the conclusion that tissue alone is rarely enough.

19. Orozco Gálvez O. Enfermedad relacionada con la IgG4: creación de un algoritmo diagnóstico y terapéutico europeo y nuevas técnicas de medicina nuclear. Doctoral thesis, Universitat Autònoma de Barcelona, 2024. An academic thesis, publicly deposited. It describes work in progress at specialist centres rather than established practice, and nothing in it is a tool for a patient to apply to their own case.

20. Iaccarino L, Talarico R, Scirè CA, et al. IgG4-related diseases: state of the art on clinical practice guidelines. *RMD Open* 2019;4(Suppl 1):e000787, produced within

ERN ReCONNET, the European Reference Network for rare connective tissue diseases.

21. Angarola E, Pasqua A, Castro HM, Cáceres A, Spina JC, Casciato P. Clinical characteristics, disease course, and chronic organ damage in a real-world cohort of IgG4-related disease: insights from an Interdisciplinary Unit. *Medicina Clínica* 2026;166:107317. Sixty patients at a single interdisciplinary unit in Buenos Aires, reviewed retrospectively. A single-centre cohort shows a pattern; it does not measure how long the wait is in any other country or health system.

22. Het Oogziekenhuis Rotterdam, IgG4-Gerelateerde Orbitale Ziekte, patient information; and Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. The first is the patient information of a Dutch hospital that runs a recognised expertise centre for rare orbital conditions.

23. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108.

24. Peyronel F, Della-Torre E, Maritati F, et al. IgG4-related disease and other fibro-inflammatory conditions. *Nature Reviews Rheumatology* 2025;21(5):275-290; Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Stone JH. IgG4-related disease: lessons from the first 20 years. *Rheumatology (Oxford)* 2025;64(Suppl 1):i24-i27. The coronary figure comes from a single large hospital group rather than from a population, and the patients in whom it was found shared specific features, which the text keeps attached to the number.

25. Mahajan A, Tinianow A, Katz G. IgG4-Related disease: From diagnosis to remission. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Orphanet, IgG4-related systemic disease (ORPHA:596448).

26. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108.

27. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Orphanet, IgG4-related systemic disease (ORPHA:596448). The figure of between a quarter and a half

is a range across studies rather than a single measured value, which is why it is given as a range here.

28. Khurram SA, Gueiros LAM, Soares CD, Fonseca FP. IgG4-Related Disease. In: *Lymphoproliferative and Granulomatous Disorders of the Oral Cavity*. Springer, 2025:207-213. A specialist book chapter written for clinicians working in oral medicine and pathology.

29. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108.

30. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108.

31. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; Peyronel F, Palmisano A, Maritati F, et al. Methotrexate and low-dose prednisone in idiopathic retroperitoneal fibrosis: a randomised clinical trial. *Journal of Autoimmunity* 2025;157:103487; Koster MJ, Ghaffar U, Duong SQ, et al. Incidence, prevalence and mortality of chronic periaortitis: a population-based study. *Clinical and Experimental Rheumatology* 2022;40:751-

757; and Imperial College Healthcare NHS Trust, RPF and IgG4-RD service. The Peyronel trial is a randomised clinical trial in 60 patients, funded by an Italian Medicines Agency grant with the funder having no role, and with no declared disclosures. The Koster study followed one American county for twenty years and identified eleven cases, which is why its survival finding is reported here with its own size attached. Both studies concern retroperitoneal fibrosis and chronic periaortitis broadly, including people whose disease is not classed as IgG4-related.

32. Orphanet, IgG4-related systemic disease (ORPHA:596448); and Wallace ZS, Naden RP, Chari S, et al. The 2019 ACR/EULAR Classification Criteria for IgG4-Related Disease. *Arthritis & Rheumatology* 2020;72(1):7-19.

33. Sina S, Bonisoli GL, et al. Clinicopathological Pearls and Diagnostic Pitfalls in IgG4-Related Disease. *Diagnostics* 2025;15:2299; and Maritati F, Peyronel F, Vaglio A. IgG4-related disease: a clinical perspective. *Rheumatology* 2020;59(Suppl 3):iii123-iii131. Both are reviews. The brain-tissue point rests on

case reports, which describe individual patients and cannot say how often something happens, and the text says so.

34. Mahajan A, Tinianow A, Katz G. IgG4-Related disease: From diagnosis to remission. *Best Practice & Research Clinical Rheumatology* 2025;39:102108; and Peyronel F, Della-Torre E, Maritati F, et al. IgG4-related disease and other fibro-inflammatory conditions. *Nature Reviews Rheumatology* 2025;21(5):275-290. Two specialist reviews. “More than eight in ten” is a response rate reported across studies rather than a single trial result.

35. Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. The dose range and taper length describe usual practice as this review reports it, not a protocol. The statement that maintenance duration, repeat dosing and stopping are open questions is the review’s own characterisation of the evidence, which is why this book presents the uncertainty rather than resolving it.

36. González-García A, Starita-Fajardo G, Lucena López D, Iranzo Alcolea MP, et al. New Developments in the Treatment of IgG4-Related Disease: A Comprehensive

Clinical Approach. *Journal of Clinical Medicine* 2025;14(19):6774, with literature searched through July 2025; and the international consensus guidance on the management and treatment of IgG4-related disease (Khosroshahi A, et al., 2015).

37. Ficha técnica prednisona, Agencia Española de Medicamentos y Productos Sanitarios (AEMPS), CIMA. The Spanish medicines regulator's approved product information for prednisone. A listed effect means it appears in the regulator-approved labelling; it does not say how likely it is in any individual.

38. Ficha técnica prednisona, AEMPS, CIMA.

39. Ficha técnica prednisona, AEMPS, CIMA; and Fong AC, Cheung NW. The high incidence of steroid-induced hyperglycaemia in hospital. *Diabetes Research and Clinical Practice* 2013;99(3):277-280. The daily pattern described comes from the study of steroid-induced high blood sugar and applies to prednisone taken as a single morning dose.

40. Ficha técnica prednisona, AEMPS, CIMA; and Fong AC, Cheung NW. *Diabetes Research and Clinical Practice* 2013;99(3):277-280. The readings log

described is a free tool published by igg4.org; that paragraph is the project describing its own tool and carries no clinical claim.

41. Ficha técnica prednisona, AEMPS, CIMA.

42. Ficha técnica prednisona, AEMPS, CIMA; and Duru N, van der Goes MC, Jacobs JWG, et al. EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. *Annals of the Rheumatic Diseases* 2013;72(12):1905-1913. **Scope: the EULAR document defines its own subject as medium to high-dose therapy, which it states as more than 7.5 mg but no more than 100 mg of prednisone equivalent daily.** That figure is the boundary of the population it was written about and not a threshold at which anything begins, and it is stated in the body text for that reason. The guideline was written for rheumatic diseases as a class rather than for IgG4-related disease, and its authors record that the evidence supporting their recommendations proved to be weak.

43. Ficha técnica prednisona, AEMPS, CIMA. This section rests on an absence in that document rather than on a statement in it: burning and tingling in the hands or feet are not among the listed effects of prednisone, which is the reason the symptom is not attributed to the steroids by default.

44. Agencia Española de Medicamentos y Productos Sanitarios (AEMPS). *Ficha técnica: PREDNISONA CINFA 10 mg comprimidos*, registration number 75649, section 4.8, text revised January 2026, published in CIMA. The entry under reproductive system disorders reads, in the original, “Excreción anormal de hormonas sexuales (amenorrea, hirsutismo, impotencia)”, within a list the document introduces as reactions seen especially at high doses and in prolonged treatment. The label does not use the words testosterone or libido, and it gives no frequency.

45. United States Food and Drug Administration approved prescribing information, *PREDNISONE tablets USP*, label revised 06/2026, published on DailyMed by the US National Library of Medicine. The phrase “reduced sex hormone production” appears in the musculoskeletal precautions, in the

passage explaining how corticosteroids weaken bone. The recommendation to offer sex hormone replacement, testosterone in men, to hypogonadal patients applies to anyone expected to receive at least the equivalent of 5 mg of prednisone for at least three months. This is a different document from the RAYOS delayed-release prednisone label cited elsewhere in this book: RAYOS could not be retrieved on 10 September 2026, and this is the current FDA-approved prednisone labelling. The label does not name erectile dysfunction, and it gives no frequency for the effect.

46. Agencia Española de Medicamentos y Productos Sanitarios (AEMPS). *Omeprazol Cinfa 20 mg cápsulas duras gastrorresistentes EFG*, ficha técnica, revision March 2023, sections 4.4 and 4.8. Regulator-approved labelling. The wording on long treatment is *«Como en todos los tratamientos a largo plazo, especialmente cuando se sobrepasa un periodo de tratamiento de 1 año, se debe mantener a los pacientes bajo vigilancia regular»*. Benign fundic gland polyps are listed at the frequency *frecuentes*, meaning at least 1 in 100 and fewer than 1 in 10. Severe low magnesium is reported in people treated for at least three months. The fracture wording is hedged in the original as

«podrían elevar ligeramente el riesgo de fractura» at high doses used for more than a year, and it is reproduced here with that hedge intact. A label records what a regulator requires a manufacturer to state. It is not a study, it counts nobody, and it carries no figure for how often any of this happens in people taking steroids.

47. Queensland Health. *Adult inpatient management of steroid induced hyperglycaemia*, guideline ACG22.73-1-V1-R27, effective September 2022, review September 2027. A state health service guideline, which makes it a public body rather than a specialist society. **Scope: it was written for adults in hospital, and it is cited here for one fact only, that metformin is among the oral medicines used for milder steroid-induced high blood sugar.** Its figures for how often hyperglycaemia occurs describe inpatients on moderate to high doses, and they are deliberately not reproduced here, because to someone on a low maintenance dose at home they would read as a personal risk.

48. AEMPS. *Metformina Alter 850 mg comprimidos recubiertos con película EFG*, ficha técnica, revision March 2025, sections 4.4 and 4.8. Regulator-approved labelling. Reduced vitamin B12 is listed at

the frequency *frecuentes*, meaning at least 1 in 100 and fewer than 1 in 10. Section 4.4 reads *«El riesgo de disminución de la vitamina B12 aumenta con la dosis de metformina, la duración del tratamiento y/o en pacientes con factores de riesgo conocidos que causen deficiencia de vitamina B12»*, and it names anaemia or neuropathy as the situations in which levels should be measured. The label describes a medicine, not this disease. Nothing in it is specific to IgG4-related disease, and it is cited here only because some readers take this medicine.

49. Medicines and Healthcare products Regulatory Agency (MHRA). *Metformin and reduced vitamin B12 levels: new advice for monitoring patients at risk.* Drug Safety Update, 20 June 2022. A national medicines regulator's safety communication. It asks prescribers to test vitamin B12 where deficiency is suspected, to consider periodic monitoring in patients carrying risk factors, and it lists proton pump inhibitors among the medicines that impair vitamin B12 absorption. It was written for the United Kingdom, and the product information it refers to is European. It gives no figure for people taking both medicines at once, and this book does not imply one.

50. Duru N, van der Goes MC, Jacobs JWG, et al. *Annals of the Rheumatic Diseases* 2013;72(12):1905-1913. The same EULAR document, with the same scope: medium to high-dose glucocorticoid therapy, more than 7.5 mg and no more than 100 mg of prednisone equivalent daily, in rheumatic diseases as a class.

51. Tomkins M, Martin-Grace J, Kennedy C, et al. Adrenal insufficiency is common amongst kidney transplant recipients receiving maintenance prednisolone and can be predicted using morning cortisol. *Nephrology Dialysis Transplantation* 2023;38(2):236-245. A cross-sectional study of 67 kidney transplant recipients at one centre, each given a short synacthen test. Forty-eight of the 67, or 72 per cent, failed it; those who did were on a mean 4.9 mg of prednisolone a day against 4.2 mg in those who passed. **Scope: kidney transplant recipients, not people with IgG4-related disease, and not people on the doses used in this disease.** It is cited here for one point and no other: adrenal insufficiency was common in a group on low maintenance doses. Sixty-seven people at a single centre cannot give a rate for anyone else, and this book gives none.

52. Beuschlein F, Else T, Bancos I, Hahner S, Hamidi O, van Hulsteijn L, Husebye ES, Karavitaki N, Prete A, Vaidya A, Yedinak C, Dekkers OM. European Society of Endocrinology and Endocrine Society Joint Clinical Guideline: Diagnosis and Therapy of Glucocorticoid-induced Adrenal Insufficiency. *Journal of Clinical Endocrinology & Metabolism* 2024;109(7):1657-1683. A guideline produced jointly by two specialist societies, graded recommendation by recommendation, with every working group member's declarations handled under both societies' conflict of interest procedures. **Scope: it is written for glucocorticoid treatment of every kind and for every condition it is given in, not for IgG4-related disease, and it is used here at that level.** Three of its statements are drawn on in this section: that a course shorter than three to four weeks can be stopped without tapering whatever the dose; that anyone currently or recently taking glucocorticoids who has not been tested should be given extra cover when the body is under stress; and that in such a person who becomes unstable, vomits persistently or has prolonged diarrhoea, adrenal crisis should be considered irrespective of the steroid, the

route and the dose. It states that predicting the risk in an individual remains challenging, which is why this book gives no threshold, and it names both sick day rules and the standardised European steroid emergency card.

53. igg4.org patient alert card. This is the project describing its own free printable resource and it carries no clinical claim.

54. Fei Y, Peng Y, Zhang P, Zhang X, Peng L, Zhang J, Zhang L, Zhao S, Li J, Wu D, et al. Efficacy and safety of low dose Mycophenolate mofetil treatment for immunoglobulin G4-related disease: a randomized clinical trial. *Rheumatology (Oxford)* 2019;58(1):52-60, registered as NCT02458196. A randomised controlled trial in sixty-nine newly diagnosed patients, thirty-five on a glucocorticoid alone and thirty-four on a glucocorticoid combined with mycophenolate mofetil at 1 to 1.5 g daily, followed for twelve months. Randomised, which is why its comparison between the two groups can be trusted in a way that the retrospective series elsewhere in this part cannot. **The full text is behind a paywall. The figures given here come from the published abstract, which is what could be read, and nothing beyond it is described.** That

abstract does not say whether anyone was blinded to their group, and no funding statement or competing-interests declaration was visible on the journal's article page, which is recorded here as a gap. Sixty-nine people in one country is a small trial, and the text keeps that attached to the numbers.

55. European Medicines Agency. *CellCept (mycophenolate mofetil)*, Summary of Product Characteristics, sections 4.1, 4.4 and 4.8. Regulator-approved product information. **Scope: section 4.1 authorises this medicine for the prophylaxis of acute rejection in people who have received a kidney, heart or liver transplant. IgG4-related disease appears nowhere among its authorised uses, and the adverse reactions it lists were recorded in transplant patients taking it alongside ciclosporin and corticosteroids.** It is cited here at that level. The wording on pregnancy reads, in the original, "Mycophenolate is a powerful human teratogen." The frequency *very common* means at least 1 in 10. The complete blood count schedule quoted in the text is the label's own, written for transplant patients, and it is not a schedule for anyone with this disease. A label

records what a regulator requires a manufacturer to state. It is not a study, it counts nobody in this disease, and it carries no figure for how often any of this happens in the people this book is written for.

56. Reisch M, Spindelböck WJ, Hödl I, Pietsch D, Rainer F, Kickinger D, Sutic A, Thiel J, Stradner M. Azathioprine as maintenance therapy for IgG4-related diseases: a retrospective case series and case-based review of the literature. *Rheumatology International* 2026;46(3):47. A retrospective case series of ten men at a single centre, followed for an average of about six years. A case series describes what happened to the people in it and cannot say what would have happened on a different treatment. No women were included, so nothing in it speaks to women.

57. Mahajan A, Tinianow A, Katz G. IgG4-Related disease: From diagnosis to remission. *Best Practice & Research Clinical Rheumatology* 2025;39:102108, reporting Carruthers MN, Topazian MD, Khosroshahi A, et al. Rituximab for IgG4-related disease: a prospective, open-label trial. *Annals of the Rheumatic Diseases* 2015;74(6):1171-1177, and Ebbo M, Grados A, Samson M, et al. Long-term

efficacy and safety of rituximab in IgG4-related disease: data from a French nationwide study of thirty-three patients. *PLoS One* 2017;12(9):e0183844; and Hammitzsch A, Ferraro N, Bachmann Q, Heemann U, Moog P. Long-term treatment patterns and outcomes in IgG4-related disease: a retrospective single-centre cohort study focusing on rituximab. *Rheumatology International* 2026;46:33. The Carruthers trial was open-label, meaning everyone knew what they were receiving and there was no comparison group. The German cohort followed twenty-four people at one hospital.

58. Stone JH, et al. Inebilizumab for Treatment of IgG4-Related Disease. *New England Journal of Medicine* 2025;392(12):1168-1177, the MITIGATE trial; and European Medicines Agency, Uplizna European public assessment report. MITIGATE is a manufacturer-sponsored phase 3 trial whose results were published in a peer-reviewed journal, which is the only circumstance in which this book uses industry-funded material.

59. Della-Torre E, Baker MC, Zhang W, et al; INDIGO Trial Investigators. Obexelimab for the Treatment of IgG4-Related Disease. *New England Journal of Medicine*,

published online 2 June 2026. A manufacturer-sponsored phase 3 trial published in a peer-reviewed journal. The figures given here are rounded from the trial's own reported proportions.

60. Stone JH, Carruthers M, Baker MC, et al. A phase 2 trial of rilzabrutinib in IgG4-related disease. *Annals of the Rheumatic Diseases* 2026; and the ClinicalTrials.gov registry records NCT04520451 (phase 2, completed, sponsored by Principia Biopharma, a Sanofi company) and NCT07190196 (phase 3, recruiting, sponsored by Sanofi). A single-arm phase 2 study in 27 people: everyone received the drug, so its results cannot be compared with the placebo-controlled trials above.

61. González-García A, Starita-Fajardo G, Lucena López D, Iranzo Alcolea MP, et al. New Developments in the Treatment of IgG4-Related Disease: A Comprehensive Clinical Approach. *Journal of Clinical Medicine* 2025;14(19):6774, with literature searched through July 2025. An independent review of the treatment landscape, which is why it can be cited for a list of things that are not yet established.

62. González-García A, et al. *Journal of Clinical Medicine* 2025;14(19):6774; the international consensus guidance on the management and treatment of IgG4-related disease (Khosroshahi A, et al., 2015); and Yang F, Wang T, Liu Y. Risk factors for relapse of IgG4-related disease: a systematic review and meta-analysis. *Clinical Rheumatology* 2025;44:4137-4147. The relapse figures come from the meta-analysis, pooling 24 studies and 3,797 people. Pooled figures across many studies carry the differences between those studies inside them.

63. Peng L, Nie Y, Zhou J, et al. Withdrawal of immunosuppressants and low-dose steroids in patients with stable IgG4-RD (WInS IgG4-RD): an investigator-initiated, multicentre, open-label, randomised controlled trial. *Annals of the Rheumatic Diseases* 2024;83(5):651-660. Investigator-initiated, meaning it was designed and run by the researchers rather than by a manufacturer. Randomised, which is why its comparison between the three groups can be trusted in a way that the single-arm studies elsewhere in this part cannot.

64. Stone JH. IgG4-related disease: lessons from the first 20 years. *Rheumatology (Oxford)* 2025;64(Suppl 1):i24-i27;

Peyronel F, Della-Torre E, Maritati F, et al. IgG4-related disease and other fibro-inflammatory conditions. *Nature Reviews Rheumatology* 2025;21(5):275-290; and Mahajan A, Tinianow A, Katz G. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. The decision not to publish survival figures is igg4.org's own, taken because the available figures come from single centres and because the damage indices they rest on count treatment-related harm alongside disease-related harm.

65. Dattani R, Barwick TD, El Wardany G, et al; RaDaR Rare Disease Group. An international patient-centred study of retroperitoneal fibrosis. *QJM* 2022;115(3):148-154. Funded by the NIHR and Imperial, with no industry funding. A patient survey of 229 people across 30 countries, describing retroperitoneal fibrosis, which overlaps with IgG4-related disease without being identical to it. A survey records what people report; it does not measure how common those experiences are in the wider patient population.

66. American College of Rheumatology. *IgG4-Related Disease (IgG4-RD)*, patient information page, updated February 2025.

A society patient-education page rather than a society guideline. It names fatigue among common symptoms and gives no prevalence figure.

67. Gwóźdź-Broczkowska A. Fatigue beyond inflammation in inflammatory rheumatic diseases: a narrative review and treatable-traits framework. *Rheumatology International* 2026;46(8):232. Peer-reviewed and indexed. The author declares that no funding was received for this work and that there are no competing interests. **Scope: this review covers inflammatory rheumatic diseases as a class and is not a study of IgG4-related disease.** Every claim drawn from it in this chapter is presented at that level. A figure of 80 per cent for fatigue appears inside this review; it comes from a rheumatoid arthritis cohort and is deliberately not reproduced here.

68. US Food and Drug Administration. *RAYOS (prednisone) delayed-release tablets*, prescribing information, revision 12/2019. Regulator-approved labelling. Insomnia and mood changes appear among listed adverse reactions. The label does **not** list fatigue as a withdrawal symptom, and it is not cited for that.

69. Tang H, Yang H, Zhang P, et al. Malignancy and IgG4-related disease: the incidence, related factors and prognosis from a prospective cohort study in China. *Scientific Reports* 2020;10:4910, funded by Chinese public funders with no competing interests; and So H, Choi SJ, Park S, et al. Increased cancer risk in patients with IgG4-related disease in a nationwide South Korean cohort, 2012-2021. *Scientific Reports* 2025;15:37273, with no specific funding and no competing interests. The ratios given are standardised incidence ratios, which compare a group of patients with the rate expected in the general population of the same country. Cancer-type-specific ratios exist in both papers and are deliberately not reproduced here, because a ratio for a single cancer type in a small group is unstable and reads to an individual as a personal risk.

70. 2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases, European Alliance of Associations for Rheumatology. A specialist society recommendation written for autoimmune inflammatory rheumatic diseases as a class, not for IgG4-related disease specifically. The treatments it discusses are

the ones used in this disease, which is why it applies, and the scope limit is stated in the text.

71. Choosing Wisely Canada, Allergy and Clinical Immunology recommendations, Canadian Society of Allergy and Clinical Immunology, updated May 2025, citing Stapel SO, Asero R, Ballmer-Weber BK, et al; EAACI Task Force. Testing for IgG4 against foods is not recommended as a diagnostic tool: EAACI Task Force Report. *Allergy* 2008;63(7):793-796. Two independent specialist societies reaching the same conclusion about the same test, seventeen years apart.

72. igg4.org specialist directory. This section is the project describing its own tool and carries no clinical claim.

73. FAI2R (Filière de Santé Maladies Rares, Maladies Auto-Immunes et Auto-Inflammatoires Rares). *Maladie associée aux IgG4: les réponses à vos questions.* Published 5 May 2022, last modified 20 July 2023. FAI2R is one of the French Ministry of Health's designated national rare-disease networks. The statement quoted appears under the heading on the causes of the disease, in French: *"Ce n'est pas une maladie génétique ni une maladie*

contagieuse et elle ne fait pas partie des cancers.” This page carries no funding or sponsorship disclosure, which is noted here as a limitation. It is, so far as an English, French and German search could establish, the only public-body source that addresses transmission at all.

74. American College of Rheumatology. *IgG4-Related Disease (IgG4-RD)*, patient information page, updated February 2025 by Howard Yang, MD, RhMSUS, and reviewed by the ACR Committee on Communications and Marketing. Cited here only for the description of the disease as immune-mediated. This page says nothing about transmission, and it is not cited for that.

75. Peyronel F, Della-Torre E, Maritati F, Urban ML, Bajema I, Schleinitz N, Vaglio A, et al. IgG4-related disease and other fibro-inflammatory conditions. *Nature Reviews Rheumatology* 2025;21(5):275-290. A specialist review. Competing interests declared as none. It states directly that genetic susceptibility “has not been extensively investigated, probably owing to the rarity of the disease and the paucity of familial cases”, and it is the source of the genome-wide association findings summarised here. The absence of any

family-risk figure is a fact about the literature as a whole, not a limitation of this paper.

76. Liu Q, Zheng Y, Sturmlechner I, et al. IKZF1 and UBR4 gene variants drive autoimmunity and Th2 polarization in IgG4-related disease. *Journal of Clinical Investigation* 2024;134(16):e178692. Funded by the US National Institutes of Health and by foundation awards, with no industry sponsor. The authors declare that no conflict of interest exists. This is a report of a single family, presented as an unusual observation. It measures nothing about how often family cases occur.

77. Newman JH, Shaver A, Sheehan JH, et al; Undiagnosed Disease Network. IgG4-related disease: Association with a rare gene variant expressed in cytotoxic T cells. *Molecular Genetics & Genomic Medicine* 2019;7(6):e686. Funded entirely by public money: NIH/NHGRI, an NIH CTSA grant, NIH/NIAID and NIH awards, through Vanderbilt's centre in the Undiagnosed Diseases Network. The conflict of interest statement reads "None declared." One family, studied because it was unusual, in a research programme with whole genome sequencing available. It cannot say how often raised IgG4 is found in the relatives

of people with this disease, because it did not set out to measure that. The authors describe the two sons as possibly having preclinical disease and state plainly that whether they will develop the disease is unknown. A family study of the sons' HLA types found no shared haplotype between the father and both sons.

78. Della-Torre E, Talarico R, Ballarin J, et al. Identification of red flags for IgG4-related disease: an international European Reference Network for Rare Connective Tissue Diseases framework. *The Lancet Rheumatology* 2025;7(1):e64-e71; and Mahajan A, Tinianow A, Katz G. IgG4-Related disease: From diagnosis to remission. *Best Practice & Research Clinical Rheumatology* 2025;39:102108. The same two sources Part 1 rests on for the resemblance to cancer.

79. Nuthalapati M, Menon AR, Rajendran R, et al. IgG4-Related Disease in Urological Practice: A Case Series of Mistaken Malignancies. *Indian Journal of Surgical Oncology* 2025;16(6):1446-1451. Four patients. A case series describes what happened to the people in it; it cannot say how often that happens. It is cited here for

the pattern it documents and for the argument its authors make about taking tissue early.

80. Karamya ZA, et al. *BMC Gastroenterology* 2024;24:278. A systematic review and meta-analysis: ten studies, 8,917 pancreatic resections across six countries, data spanning 1987 to 2016, 140 cases of autoimmune pancreatitis, or 1.6 per cent. Funded by Hungarian public and university grants; the authors declare no competing interests. Two things this figure is often confused with, and is not: the widely quoted 5 to 13 per cent is the rate of benign disease of *any* kind in resected specimens, of which autoimmune pancreatitis is 30 to 43 per cent, as the International Study Group of Pancreatic Surgery consensus statement sets out and the European UEG/SGF guideline reproduces correctly at its Statement 2.4. And chronic pancreatitis, not autoimmune pancreatitis, is the commonest benign finding in these specimens.

81. Russell MD, Dey M, Flint J, et al.; BSR Standards, Audit and Guidelines Working Group. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs

and corticosteroids. *Rheumatology (Oxford)* 2023;62(4):e48-e88. A specialist society guideline, graded recommendation by recommendation. Members' declarations of interest are held on the BSR website rather than in the document. No funding statement appears in the guideline text, which is recorded here as a gap.

82. US Food and Drug Administration. *RAYOS (prednisone)*, prescribing information, revision 12/2019, section 8.1. The wording is "a small but inconsistent increased risk", and it is reproduced with that hedge intact rather than hardened.

83. US Food and Drug Administration. *IMURAN (azathioprine) 50-mg scored tablets*, product information, revision 12/2018. Regulator-approved labelling dating from 2018, which takes a more restrictive position than current European rheumatology guidance. Both are quoted in this chapter because both are current documents and they disagree.

84. European Medicines Agency. *Nordimet (methotrexate)*, Summary of Product Characteristics, sections 4.3 and 4.6, revision 10 October 2024.

85. European Medicines Agency. *MabThera (rituximab)*, Summary of Product Characteristics, section 4.6.

86. Taranto S, Bernardo L, Mauro A, Perrone A, Tamborino A, Giani T. IgG4-Related Disease in Childhood: Clinical Presentation, Management, and Diagnostic Challenges. *Children (Basel)* 2025;12(7):888. A review of the published childhood cases. Because the disease is rare in children, everything in this chapter rests on a smaller body of evidence than the adult chapters, and the relapse figure of more than half comes from some studies rather than from all of them.

87. Yu K, Gao H, Liu S, et al. Perception of recurrence risk in patients with IgG4-related disease: a descriptive phenomenological study. *Rheumatology Advances in Practice* 2025;9(1):rkae148. Fourteen patients interviewed at one centre in Beijing between September 2023 and February 2024, six at first onset and eight with experience of relapse. Supported by the Peking University Nursing Research Development Fund; the authors declare no competing financial interests or personal relationships that could have influenced the work. A

qualitative study describes experience in depth. It does not measure how common that experience is.

88. igg4.org. This section is the project speaking in its own voice about isolation and support, and carries no clinical claim.

89. Wallace ZS, Katz G, Hernandez-Barco YG, Baker MC. Current and future advances in practice: IgG4-related disease. *Rheumatology Advances in Practice* 2024;8(2):rkae020; Cagnotto G, Bäcklund RT, Bengtsson A, Bruschettini M. Immunosuppressants for IgG4-related disease, Cochrane protocol, 2025; Arias-Intriago M, et al. *International Journal of Molecular Sciences* 2025;26(11):5325; and Hao Q, Lian D, Zhou M, et al. Identification of candidate biomarkers for diagnosis, disease activity, and relapse prediction in IgG4-related disease. *Arthritis Research & Therapy* 2026;28(1):96. The candidate biomarkers described are research findings, not tests available to patients, and the text says so.

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For reading it. For handing it on. For being, quite possibly, the person who says the words *ask about IgG4* in a room where nobody else will.

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