**Medical Insider COPD Podcast, Season 2 Episode 3
Macrolides in COPD: Targeting airway inflammation**

Richard ([00:04](https://www.rev.com/transcript-editor/Edit?token=J5EMtjrB91RQydwxbmtOlGs4hftbD8DVf5ayF85KGWkwm_kLx8hIigbc6gAR2SoZvrUh0prHsyO9zjF6SeFZ5IhfcJY&loadFrom=DocumentDeeplink&ts=4.74)):

This podcast is intended for healthcare professionals outside the United Kingdom and the United States of America only.

Richard ([00:25](https://www.rev.com/transcript-editor/Edit?token=Pdde4uIo9srM3Zz_k2-G7PgTrzOByt04usUkGAhxT7cpcjIrKNn0t6CyJ5R7zWjAYxy032GeILlIOmZP3l4wEi61KjA&loadFrom=DocumentDeeplink&ts=10.7)):

Welcome to the Medical Insider COPD by Boehringer Ingelheim, a podcast offering a breath of fresh air to clinicians treating COPD across the globe. My name is Dr. Richard Russell. I'm a Consultant Chest Physician at Lymington New Forest Hospital in the United Kingdom, and a Senior Clinical Researcher at the University of Oxford. I'm also the Editor-in-Chief of the International Journal of COPD. I'm delighted to be your moderating host for this season of The Medical insider COPD podcast. I'm here to bring you news and insights, right from the source directly to you. So, thank you for joining us today. Be sure to keep your eyes out for the next Medical Insider COPD podcast to ensure you do not miss any of our exciting information.

Richard ([01:00](https://www.rev.com/transcript-editor/Edit?token=rjSlcb4IagJ00Swkc3pcSJ1vu9-WdOTyBc3yv_KLYMiy989p448ByGtW4Aq3bFtDKgI1EXOIsj9S5-rOLLu_Igt4ot8&loadFrom=DocumentDeeplink&ts=62.77)):

Today, we're going to delve into a publication, which I believe is very well worth reading. It's entitled ‘The Impact of Muscarinic Receptor Antagonists on Airway Inflammation; A Systematic Review’. We'll also look at emerging and exciting topic on social media, particularly at the moment, looking at COPD and COVID vaccination. But first, I'm delighted to introduce today's guest, who's going to be here with me today to discuss the role of macrolides and macrolide therapy in COPD. She's Professor Jodie Simpson, a Professor of Respiratory Science and Medicine at the University of Newcastle, New South Wales in Australia. Welcome, Jodie, would you like to tell the audience a little bit about yourself?

Jodie ([01:37](https://www.rev.com/transcript-editor/Edit?token=HlM1Euo3pK4SX50YaOF8P33ILwkEUrrDcwaNL7EwhtG8mzPal79Xy4Xkqw0V1_ju-v3Sdnxhwln-xfcQwAlMzWXLwW8&loadFrom=DocumentDeeplink&ts=102.34)):

Thanks so much, Richard, and it's great to be here to talk with you today about macrolides in COPD. I am a Professor in the Research Center for Healthy Lungs at the University of Newcastle in Australia. And my research predominantly looks at airway inflammation and a number of different airway diseases, particularly COPD and asthma and bronchiectasis, and examining, I guess, the inflammatory mechanisms of those diseases and also potential therapies which might help control inflammation and therefore might produce clinical benefits.

Richard ([02:10](https://www.rev.com/transcript-editor/Edit?token=9ajGgB-ssjC9wkSRwORM7p71vAH7cW5okTu4uXvI5ZH5Fa3ejPWkNQLJk-EJ_Gez0Rz5JF73GaPyK-GjbL06JRTbrkA&loadFrom=DocumentDeeplink&ts=135.56)):

So, you're working in a really interesting crossover field here between science and also clinical medicine. Maybe you can unpack for us a little bit about how we treat people with COPD and focus for a moment perhaps on bronchodilators.

Jodie ([02:22](https://www.rev.com/transcript-editor/Edit?token=VWGr6cuABiuGf_fTrpBsmEDULpiTmX3R5FIUkWoQL8Lw5CcifsQTGzFqGHD-39t9LVqyJuApukAY7RtpCDlHAUw6hQA&loadFrom=DocumentDeeplink&ts=149.13)):

Well, sure. And I think it's important to say before we talk about macrolides, that for the vast majority of patients out there who suffer with COPD, they'll be able to use bronchodilator therapy quite effectively to manage their symptoms and prevent exacerbations. But like with most conditions, there are that group of patients who continue to have persistent symptoms and exacerbations or attacks of COPD. And for those patients, we need to really look at the mechanisms what's causing those persistent symptoms and new ways we can improve treatment and management. And I think that's where macrolides really fit in. So, bronchodilators are a very effective therapy and an important main stay in COPD. But for those patients who have ongoing problems with COPD that macrolides offer, I guess, an opportunity to add on a therapy that might help.

Richard ([03:20](https://www.rev.com/transcript-editor/Edit?token=qpuq0U6dH4P6KPHhhtvT2uv0OU5GgguCaSZrgFVtCeyr_wq8oxxH-fK1ItNFVAda34J1C7BqPQ0UbTdU_uEBhJQg9Wk&loadFrom=DocumentDeeplink&ts=206.34)):

That's really important. And actually interestingly that queues into the paper, I'm going to be discussing, which is maybe looking at some novel roles of muscarinic receptor antagonists as anti inflammatories, but you're really saying here, yes, we've got to bronchodilate people to actually open up their lungs to actually improve their symptoms, improve their lung function and quality of life, but there's inflammation underneath there, which may be different. Can you unpack maybe some of the varieties of inflammation that we see?

Jodie ([03:46](https://www.rev.com/transcript-editor/Edit?token=Jbuj0ofYarAC9oh7WwpW1SMhs6SrIHCxV7IrQ7LSmS1KpNroz2RkbitXpyuOtiPjbBjoEMtuV5bG1w3GFu48Y9cp-VA&loadFrom=DocumentDeeplink&ts=232.56)):

Yeah, absolutely. And certainly we know that, opening up the airways is a key part in the process of managing COPD, but there is also other things going on with airway inflammation, which can contribute to, closing the airways, but it also contributes to other things such as mucus hypersecretion, and cough and other symptoms that patients experience. And I guess we know that in COPD, inflammation's quite, the patterns are quite different, so not everyone has the same pattern of inflammation. So, no two patients that sit in front of their doctors necessarily would have the same inflammation. This is why we need to start measuring inflammation so that we can apply targeted therapy.

Jodie ([04:27](https://www.rev.com/transcript-editor/Edit?token=DnrLhuaRTx3ZTM6umin37BiWK_QQRkMC9AfySxrUcj9tA7SCz7kas49zb8cmxmfp70D6_L508hKgCaTUD96qX4o4nrM&loadFrom=DocumentDeeplink&ts=273.94)):

But as an example, I guess, traditionally we've always thought of COPD as a neutrophilic condition. So, we kind of classify people in that classical smoking neutrophilia pattern, but we know now that COPD is much more diverse and certainly there's been some great work looking at eosinophilic COPD. So, we know that there are around a third, I think of patients who have eosinophils airways, who also have COPD. And so, this really draws us into this need for measuring inflammation in patients with COPD and then trying to target that therapeutically.

Richard ([05:05](https://www.rev.com/transcript-editor/Edit?token=rA1DCS-XaiDzgXe-mK9DX7HeZM7q0U4Tbz9JPPhEbrqjpgW5rzjQgoeVEIfjN3nPICqAa5_ixnOhX5Y9elzAfIXccDA&loadFrom=DocumentDeeplink&ts=315.6)):

And does this difference in inflammation occur both in steady state and at exacerbation?

Jodie ([05:09](https://www.rev.com/transcript-editor/Edit?token=3JbsYzgGBx8cqk404e34NlpkTYLl5bilCDZj7XMCI7BM8Hkv0HvKTBz0XGgapm8y2wcxwWORtpbMiqnNx83t6toM52A&loadFrom=DocumentDeeplink&ts=320.86)):

Yeah, it does Richard. And what you often see is you can see a change in the pattern with exacerbations, and that can be related to the trigger or what's caused the exacerbation. So, you might have a patient who at steady state is eosinophilic and then maybe is exposed to bacteria or a viral infection who may then have an abundance of neutrophils in their airways or vice versa. So, someone who's classically neutrophilic who may then have some exposure to allergen or other triggers who cause a transient eosinophilia.

Richard ([05:45](https://www.rev.com/transcript-editor/Edit?token=Q0nhlnpz74EVpxF3wF2raSxLzw15n1_c8Xapx6xlYHLsa30PgQgylQAtvGyUm9saq6c-DEiqoCbt05lhwzt8INg4BWw&loadFrom=DocumentDeeplink&ts=356.48)):

It's interesting in the asthma literature at the moment, it seems that researchers are trying to divide up the symptomatic control of asthma from the inflammatory control of asthma. Do you think we should be doing that in COPD as well? Or do you think this is one continuum and we need to look at the whole thing?

Jodie ([06:01](https://www.rev.com/transcript-editor/Edit?token=LuyqyF2QbQLZvoP9lJOE7fDJJUakBYMyzzteQCBuJQjYLNi243rXAFLHzYhbTuuJsQojK4uBdMK4-KN0UWC2tEEnKO8&loadFrom=DocumentDeeplink&ts=374.5)):

Oh, I think that's a really tricky question to answer simply. I think, I guess my, my mantra is that we need to measure inflammation and until we do that systematically and in large numbers, we can't answer that question of where that, where if there is a division between symptoms and inflammation, I expect them, it may not be so clear. And I suspect it's not clear in asthma either, but I guess as you know, COPD is a big problem. We're always trying to find ways to partition people into a group that would be able to do something to help them.

Richard ([06:35](https://www.rev.com/transcript-editor/Edit?token=MEd4thQM6jRANZQDkDq5PFIUxaG_hJRzLkwyPbKdDNd9JuFiwTqfDgvBZnXAajC_-Z_Ai3diB2TiUIWllPzw2WfDZxQ&loadFrom=DocumentDeeplink&ts=408.47)):

I, I think I agree with you. I think it's probably going to be impossible to do that. And I suspect very few patients will be very purely one thing or the other as we've often found.

Jodie ([06:43](https://www.rev.com/transcript-editor/Edit?token=A2WuGhFa9TF7ryyapsOmVw5lHClqLRHAMUVGxukImfNliNwqCfriTYBFmMEwiJgbmgQyVCSGDlDD02Th4YNrwoGRdq8&loadFrom=DocumentDeeplink&ts=417.19)):

Yeah. I think that's really unlikely. And, and I think that's where the importance of, you know, studying all patients with COPD and not narrowing the COPD studies down where we pick out patients who just meet that classical definition.

Richard ([07:00](https://www.rev.com/transcript-editor/Edit?token=rCtBNUpdq85XU4WXqJyOJzfCOHUKGTVvejPkYYfCXlvzBbcN2zVOd-P0qQ-Tco2Y3bURU17hh47IOyy3bYInruXSYgo&loadFrom=DocumentDeeplink&ts=432.16)):

Okay. Let's come on now to talk about the biomarkers we can actually use in practice. You've mentioned eosinophils, so how should we use blood eosinophils and sputum eosinophils. Can you unpack that for us?

Jodie ([07:08](https://www.rev.com/transcript-editor/Edit?token=_LzpkBSWDStspxl5pPHzHMJguoJFOxLBfH-AiuG5NsrI2T3_sjZkvFMPD91HkdtQmFoXFlws_seqFvOn8Cbk3bceeu4&loadFrom=DocumentDeeplink&ts=442.92)):

Well, I think eosinophils, sputum eosinophils, particularly, but blood eosinophils do offer us a reasonably good surrogate for measuring airway eosinophils. So certainly, in COPD collecting a sputum sample is reasonably easy, but obviously the necessary technology after that collection of the sample is being able to do the sputum cell counts, which seems to be a barrier in some places and so blood eosinophils offer a good alternative. And I think that allows you to get a picture, at least a snapshot in time of what is going on, in the airways.

Jodie ([07:44](https://www.rev.com/transcript-editor/Edit?token=8foE97dAWQZ4xQmKlzoeJ0M8isd341HDtbVJh7UZqtU_ZwUH4KKBSMScJxzWsByi2JpScj6NwWMp6GNDDl0RxLb6A-8&loadFrom=DocumentDeeplink&ts=0)):

I think the GOLD guidelines offer us some helpful cut points for where we might consider using blood eosinophils as a useful surrogate for airway eosinophilia. Certainly, if we're looking at a patient's blood eosinophils and they're higher than 300 cells per microliter, we can have some confidence there that there's likely to be an airway eosinophilia. Perhaps then consideration of therapies to reduce eosinophils might be warranted. Similarly, if the patient's blood eosinophils is lower than 100 cells per microliter, then equally we can have some confidence that it's unlikely that this patient is having an airway eosinophilia at that point in time, and perhaps adding on inhaled corticosteroids maybe not the most beneficial treatment option, and we could consider alternatives or continue monitoring inflammation.

Richard ([08:32](https://www.rev.com/transcript-editor/Edit?token=P1qQJYGD4M2ZBDg8RsVf1dxBGK2bmAx8FrzAHdaBujAj22O9w8y3jn0nv5nd8V4r1Rv7TrSgPTnZlomFKxT5bHTrBQw&loadFrom=DocumentDeeplink&ts=515.24)):

Yeah, you're right. It's a shame that more departments can't have an active and alive sputum lab. And I've used that clinically a few times to great effect in airways disease, but it's obviously impractical and difficult to do. And you need people who can actually not only process the specimens probably, but obviously then look at them, which makes the sputum difficult to do doesn't it, Jodie?

Jodie ([08:52](https://www.rev.com/transcript-editor/Edit?token=7excKnfAZvcguV9QrRpE0jw6F1TuRaYqaqcYiP_k_a8OkSgo63PlY7oq0ilhnX4z2yctEJFwjs0Alp20LIaCI7pR-Ns&loadFrom=DocumentDeeplink&ts=534.6)):

It does seem to present a barrier. I mean, I think in other disciplines, these barriers seem to be able to be overcome, but something in airways disease has prevented sputum cell count doing that. And I guess that's where newer technologies such as artificial intelligence might offer us some future benefits.

Richard ([09:11](https://www.rev.com/transcript-editor/Edit?token=EkEfmc1ORd4oCtZvzVZN1nZMqOKX-R-fGhuj_17dqqSMoWM6CXcqEzXufZwItIoY8v5MFHdC5qlqbkum9l7ISPd-deQ&loadFrom=DocumentDeeplink&ts=553.8)):

Oh, that's very exciting. So, let's move on now to neutrophilic disease. Because again, this is something where sputum can be really helpful and neutrophilic inflammation in COPD and the role of macrolides. Tell us about neutrophilic inflammation and then how macrolides may be working.

Jodie ([09:26](https://www.rev.com/transcript-editor/Edit?token=Z9H8YgGT6Xn9Sol6StQ10D0l2FgYwSkpaJgTMOc5KVRCoreX03xJ47XFrj6VelixA0gSzOi_YttVX7yeyBOlkPPl_Ms&loadFrom=DocumentDeeplink&ts=569.01)):

Yeah, sure. And I think this is the advantage of sputum over blood and that's maybe presenting my bias, but by sampling the airways, we can actually see what the neutrophils are doing as well. And so, we know that there's a group of patients who present with this chronic cough and sputum production, and they tend to have high levels of neutrophils in their sputum, increased total cell counts. And they most often will have a positive culture or be able to have some potentially pathogenic bacteria identified in their sputum samples.

Jodie ([10:00](https://www.rev.com/transcript-editor/Edit?token=NxfJXHi4yNAUwsWKWe3juu-z3Glk7Gl3RZ23ZAU_oI1GVoE55xt4VbUx8rqr64isS6ugl4y42rAN42i9fH1z9p7CXRI&loadFrom=DocumentDeeplink&ts=602.49)):

One of the most commonly identified is some Haemophilus influenzae and those patients tend to not be eosinophilic. So, they, they can have low eosinophils, but irrespective of whether they have eosinophils or not, those patients are, seem to be a particular group that do well when you have macrolides added in as an add on therapy. The big studies in COPD, the Albert study, which looked at azithromycin in COPD certainly showed a benefit for all patients with COPD when you added on azithromycin. So, it's not to say that other patients won't benefit, but certainly in unpacking the literature and looking closely, it does seem to be that clinical profile that are the ones who have perhaps the most to gain.

Richard ([10:50](https://www.rev.com/transcript-editor/Edit?token=gKDl0m9NhICsG7KVS0nbpKfobH9W_fLKi_ouK8vnMZCAprG8nFGrbyu6BAasUiY91KuWle9_t1M0aEBe-5wTp5WWizk&loadFrom=DocumentDeeplink&ts=649.4)):

How do you think macrolides may be working here? Jodie, is it a direct anti-microbial effect or is there some other anti-inflammatory effect? I know this is an area of controversy.

Jodie ([10:58](https://www.rev.com/transcript-editor/Edit?token=TNqY9LnIQ8EN4KxLa4wSRlnWwdduPLsZ1J6cpb2JntEo_81HLmPRa6zaSoUgUhbBBrd3htmibG891FTQlwwSHI7sF3s&loadFrom=DocumentDeeplink&ts=657.75)):

Yeah. It is an area of controversy, but I certainly think in the literature that I've looked at in the studies we've done and others, it certainly seems that there is a clear anti-inflammatory mechanism for macrolides. So, while there may be that antibiotic effect, we're not using macrolides at the same level that you might treat an acute infection, the same dose. But what we do see is changes in things such as reductions in pro-inflammatory markers, things like IL-1 beta, for example, which we know is an important pro-inflammatory mediator in COPD. We also see reductions in or improvements in things like phagocytosis and efferocytosis. So, they're the processes where our immune cells can actually go and clear out bacteria and clear out dead cells. And that's a really important process in resolving inflammation. So, one way macrolides could be working is by actually improving those mechanisms and improving the resolution of inflammation and improving airway function.

Richard ([11:56](https://www.rev.com/transcript-editor/Edit?token=xzrrOPXPQE7pkRlWcQpLKumPXb-u13l9v7I5fM8WSM1qten6wJbKStBPphaiHCTQh8cQkzkb_NpbLepjXKT3dwjN4Bw&loadFrom=DocumentDeeplink&ts=728.18)):

Is it possible to pick apart the different macrolides in their effects or is it a pharmacokinetic thing why we use the longer acting ones? What do you think?

Jodie ([12:03](https://www.rev.com/transcript-editor/Edit?token=UrefSgFb2yNDp_rY0Lk-RD0nKS1jJlmdtmw5zQhYsvBr_sZgLGcmiXCUBrRjzaXPLzlwceD6XFCtTq8y6-baLwR6KjA&loadFrom=DocumentDeeplink&ts=735.59)):

Yeah, look, I think that's an interesting question and I don't think there's been enough research to look at that closely. It does seem to be a class effect and there's a preference, I guess, for picking things like azithromycin over erythromycin and really more around the side effect profile and the half-life. So, having to dose less frequency and then having those less GI side effects, which are one of the most reported side effects from adding on macrolide therapy.

Richard ([12:30](https://www.rev.com/transcript-editor/Edit?token=7cI5E81Iu1GpatGZniieaSq8aOIIJWoHNnwTD6eYgVn2_SYbynDTP33H2gAqR-7BIn72dRJcZkqZJD4VcwY7axBy8QU&loadFrom=DocumentDeeplink&ts=806.82)):

So, the GOLD strategy suggest macrolides, as you've mentioned, can be an add on therapy. So, would you be happy as a clinician to add on macrolide therapy to someone who's on optimal dual bronchodilatation and also on someone who may be on triple therapy, but still having exacerbations and cough and sputum or maybe neutrophilic disease?

Jodie ([12:50](https://www.rev.com/transcript-editor/Edit?token=5fy7fAiZV6pJmrYbIY8F2l-hi_wh3YJACsW5CGCsqWdqs4hb_ZbvobYdO8HSEVoPnToKdi5RCbhsI2nCilJRe6Y1PjE&loadFrom=DocumentDeeplink&ts=827.54)):

Well, I guess as a scientist and reviewing the literature in that way, and certainly from the studies we've done. Yes. I think I would be comfortable with that, but there's certainly some safety things that are important to consider before you add on macrolides. So, the common things that have been reported in the literature are things like QTC elongation and hearing loss. And although their reports on that are variable, I think it's important in an older population, such as those with COPD that we really screen and have a baseline for those things so that we can try and add on this therapy in the safest possible way. And of course, it is an antibiotic. And so, we need to add that therapy on mindfully knowing of the risks of anti-microbial resistance. But again, the evidence really is quite scarce around anti-microbial resistance, following macrolide therapy.

Richard ([13:38](https://www.rev.com/transcript-editor/Edit?token=Ael19PeyvFForxajwyFLXI5IDh4dlDUHXVRCQShsWraZAAhgvLfiCytURirE3Sp21-ejpcBAZSKpLTeO75YJV-U0t5M&loadFrom=DocumentDeeplink&ts=877.88)):

Yeah. And I think the clinical impact at the moment is unknown and you're right. We do need to be cautious. It's interesting. I've certainly found the other thing I do is have a trial period. And it seems to me very clear that patients, when they respond to macrolides, they've got a clinical phenotype maybe of cough, sputum, and as you said, Haemophilus, when you start them on a trial of two or three months trial of macrolide, they either do really, really well or really badly and in a sense of nothing at all. So, it's a good way of actually saying you're a responder and you're not a responder. I think that's very helpful.

Jodie ([14:10](https://www.rev.com/transcript-editor/Edit?token=AODjEh1dOlZhDOWL-GKiQfZcvUe6hUSv8DtNJxccq5XpVZ6zGnjkmbB_AdKjl98OM6hqdFoNwpHHzO5TO0-_uPvjOZ0&loadFrom=DocumentDeeplink&ts=909.25)):

I think so. And it's unfortunate at the moment we aren't able to give that recommendation of, you know, here's how you pick out the patient in clinic who is a responder, but there is more research going on to try and answer those questions. But I think having that trial is relatively safe way to make that clinical determination.

Richard ([14:28](https://www.rev.com/transcript-editor/Edit?token=uCHfy0jnzUJaXF1xO3w8WJwYNz3aofUrHn9Vk-NvPhvD-alxu2yPxtnc6xvBv6NH-w_JG8K609dmJW-7qm0G73KcaME&loadFrom=DocumentDeeplink&ts=929.43)):

Yes, it's helpful. So, Jodie, can you take, give us a few bullet points you want to take away from this discussion to actually help us understand the macrolides as a role in therapy and also where we may go with this.

Jodie ([14:42](https://www.rev.com/transcript-editor/Edit?token=GI7BMWD4gRONWPn3EOdI9toejMmieLhXKoDJ61aI260GMBsfvOorS1VJgTx3Vr0W39lZF0Y7eiKOvnVQYX3Q0tqRfho&loadFrom=DocumentDeeplink&ts=943.33)):

Yeah, absolutely. So, I think macrolides offer an add on therapy in patients with COPD who are experiencing persistent symptoms and exacerbations despite having sufficient bronchodilation. So, considering an add on therapy in those patients, macrolides is a consideration. I would promote measuring inflammation at that point to get an understanding of what is the pattern of inflammation, whether you have that kind of classic neutrophilia, Haemophilus or bacterial pathogen picture, cough and spit, or perhaps you have an eosinophilia, and then you can make that distinction between whether you would go perhaps for a trial of macrolides or something else, or perhaps you want to, you know, you will try macrolides and if you get a response and there's still some residual problems, you can consider as an additional add on therapy, but doing that with a safety view of assessing baseline QTC and other important contraindications for macrolides.

Richard ([15:42](https://www.rev.com/transcript-editor/Edit?token=HC_143rCUQhF4AF9wkJYDnyvQSNHL8ff7H2kAlG1yxEbE8SJu1jSiINT3eXgxMx4wDxSqdeG6sL3FUhRO9HVGkRZapE&loadFrom=DocumentDeeplink&ts=1005.9)):

And, and finally, where do you think we may go with macrolides? What's the next step? What's the next big piece of research that may come out?

Jodie ([15:50](https://www.rev.com/transcript-editor/Edit?token=8NYtlTlmLrW3JF9_0hmFyJiPVCfTO6Ffy8YEoX5jm0rJjfuco9nTBKqrYRXTTuIKRrGOtLAamI5vdLICuGv1qbRPWjo&loadFrom=DocumentDeeplink&ts=1014.13)):

Yeah, I think that's a good question, Richard. And I guess from a mechanism point of view, I think it'd be really interesting to look at some of the newer work being done in the non-antibiotic macrolides. So being able to understand how we can get that anti-inflammatory and exacerbation prevention happening, but without the anti-microbial resistance problems. So that's, I think one area. And then of course, I think there's a lot of work that needs to be done with understanding dosing and dose holidays and things like that. Because at the moment we have big studies with long treatment durations, but we don't really know the best regime to offer patients

Richard ([16:32](https://www.rev.com/transcript-editor/Edit?token=W86LRTK6t_mu9YSXEHRCSHCJbOC8s6bumtdSdRN5legicSO6fjRcAZxPGZLcVa_nx5gpBw7xOh-9Lxui9fY7aCI0DBU&loadFrom=DocumentDeeplink&ts=1054.9)):

In a moment I'm going to come on to discuss an important paper that's just been published but before I do that, I've got to thank my friend, colleague and Professor Jodie Simpson. Jodie, thank you so much for us today. That's been really helpful unpacking this a world of macrolides, and I'm sure there's much more to come about this.

Jodie ([16:47](https://www.rev.com/transcript-editor/Edit?token=UyDRnrEfNaPunlOZydhI5DmEt_3y7glA6iC6qoXgQTsW9Rjmp1b_YJ2jRrhfh9g_ks-wxXlaPj00IZKlcoCaILelEE8&loadFrom=DocumentDeeplink&ts=1075.4)):

Thanks so much for having me on the podcast today, Richard, I've really enjoyed chatting with you.

Richard ([16:55](https://www.rev.com/transcript-editor/Edit?token=ZKToOlbyYbH1hcrQ6v1cMRJFNDkWnzVKprPHW0xjO_q3fQaFvgou7dHlxmfhyzR1-FIbxe8K94VIukfumMwOTVEwjQc&loadFrom=DocumentDeeplink&ts=1083.8)):

I'm going to unpack for you now an important paper that's just been published in the world. Literature of COPD. This is entitled ‘The Impact of Muscarinic Receptor Antagonists on Airway Inflammation: A Systematic Review’ published by an Italian group led by Calzetta et al. This was published in the International Journal of COPD on the 12th of February this year, volume 16, page 257 to 279. It’s a serious in-depth analysis of the role anti-muscarinics may play on inflammation. We know that long acting muscarinic antagonists are the cornerstone of COPD management, bronchodilatation is essential. They lead to reduction in airflow limitation, reduction in gas trapping, improvement in lung function and therefore symptoms. There's also been shown some effect on exacerbation. The question we don't know is do these drugs have an effect on airway inflammation? Because it's postulated they may well do. So, this group conducted a PRISMA standard literature search of all available antimuscarinics: tiotropium, glycopyrronium, umeclidinium and also aclidinium as well as older medications, such as ipratropium. They found 268 studies and looked at 49, which were eligible for full analysis.

Richard ([18:09](https://www.rev.com/transcript-editor/Edit?token=pOHkSjtCt7sZctPbaLWF1GPour8L6QUz0wbenNl1XdVvtT4yEj-gSH-SrQta67n2VIZBG4uM4ENFPltrUdCP5Vq_0pE&loadFrom=DocumentDeeplink&ts=1155.87)):

These included in vivo as well as in vitro work, animals and human studies. So, what did they find? There certainly were effects on inflammatory pathways and the inflammatory cytokines with reductions in IL-8, IL-1 beta, reduction in the nuclear factor Kappa B pathway activation, and an increase in HDAC activation involved in glucocorticoid action in the nucleus. There's some evidence for the role of aclidinium and glycopyrronium, but most evidence was for tiotropium. Well why is this? Well, tiotropium has been around for the longest and more extensively studied, but also tiotropium has the greatest effect on exacerbation, which may be a mechanism of action here. Tiotropium was also studied in the setting of stimulation with LPS, a marker of bacterial activation, ovalbumin and rhinovirus infection. And also, they looked at neutrophil adherence with some effect. The effects were not large but putting altogether these drugs may have anti-inflammatory properties.

Richard ([19:06](https://www.rev.com/transcript-editor/Edit?token=9uNR-vHTt7R-HG5yPqn17RSNB7GTk-JSbNH38D0mF-t_YmZrQtIwF0jA4N9dpT9qytvF6HoCrcikU0JTcXp_E3sNGNI&loadFrom=DocumentDeeplink&ts=1215.82)):

So how does this actually work? Well, this may be via blockade of the M3 receptors, and it's certainly true that tiotropium is highly selective for these M3s. So, what do I think? Well, I think this paper and a very thorough analysis of the data that we have allows us to look in depth at the role of these drugs, as anti-inflammatories. The effects are there, they're consistent and a little bit better for tiotropium versus the other medications. It'd be great to have some head to head studies, but more needs be understood about the role of the M3 receptor and anti-inflammatory properties of these medications.

Richard ([19:47](https://www.rev.com/transcript-editor/Edit?token=GR5fwnsWU9hTAROc3rkA0dpgDnXlCUmVpZFNkYivRbhS7OnRRwT0-QBkUsJeE2bx3aMljyr7-HRLlehWzO8x_LdjN_M&loadFrom=DocumentDeeplink&ts=1258.34)):

So, one of the hottest topics in social media at the moment is that of COPD and COVID vaccination. COVID programs are being rolled out across the world. And this is leading to much activity on social media from our COPD patients concerned about COVID vaccination. When will people with COPD become vaccinated? This is a worry for people. What are the effects of the vaccine? Should people with COPD be prioritised? And also, people are then saying after they've had a vaccine, what a great relief it is to actually have the weight lifted off their minds actually worry about the future. Remember many of our patients with COPD have been protecting themselves and shielding for nearly a year or more. We also have evidence from social media of people trying to explain how bad COVID and COPD can be together. And actually, people are talking about how they're relieved when they get the vaccine and how they feel after they've recovered from the disease.

Richard ([20:41](https://www.rev.com/transcript-editor/Edit?token=Dd5QaSmd0C_ZYyTxrJr5JkTlJr-bDlrT4AFle86ivoy_es4DRkejyZmE38WcmX7ZtynFOC2teLQ5EwEV949r7yb-rWc&loadFrom=DocumentDeeplink&ts=1312.68)):

It's interesting also on social media to note the different countries at the moment, are setting different priorities for people with COPD. Ireland, for example, it's just recently moved up the COPD patients to be a priority. And in other countries such as America, it is not simple at all, at the moment. Patients with COPD clearly do want to become vaccinated. People are still scared though, but there's still a clamor on, on social media that people want to be protected themselves, but also understand the need to protect others. And then the other thing that COPD patients are looking forward to, which is great to see is actually perhaps travel again. And finally, one thing on social media I was surprised about, but also quite pleased that people had picked up on was the role of long COVID and do vaccinations protect against long COVID? Patients with COPD are worried about this and also want to be as well as possible going into next winter and the future.

Richard ([21:32](https://www.rev.com/transcript-editor/Edit?token=w3TiZX22wiXugJtps2kG8Qhw64eu39ewe4prULDAAKW6a1g0CFQ8esEsmdBZnxGcKX8PRecJebEaOXDy52LvkdvaMpc&loadFrom=DocumentDeeplink&ts=1370.3)):

So overall COPD patients are certainly understanding COVID and understanding the vaccination. They seem to understand the implications of it, and there was an overwhelming desire to be vaccinated, and we need to encourage our patients in this. So, thank you for joining us today for this edition of Medical Insider COPD podcast. I hope you've enjoyed what we've been talking about with regards to the new papers, social media, and of course, especially Professor Jodie Simpson discussing macrolide therapy in COPD. Please join us again for the next edition of Medical Insider COPD podcast, where we'll be unpacking more new information directly from the source to you.