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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Asthma CSI: Behind the Cytokine Curtain, Part 1: Asthma HQ

Announcer
You're listening to *Asthma CSI: Behind the Cytokine Curtain*, sponsored by Amgen and AstraZeneca.

Part 1: Asthma Headquarters

[The sound of boots on wet pavement is heard as Doc, a seasoned asthma investigator, makes her way toward Asthma Headquarters]

Doc (inner monologue)
Another rainy day in the Big City as I head toward the familiar confines of Asthma Headquarters, a special investigation unit for cases of severe airway inflammation. More than 25 million people suffer from asthma across the U.S., and approximately 1.3 million have severe asthma.[1] They're the reason I do what I do, and why my colleagues and I keep working to tackle the toughest mysteries of asthma pathogenesis, detection, and management.

Normally this daily walk to work is my chance to reflect on things, but today, my mind's on the call that came in early this morning. Word from the top is that we've got a new case to solve, and it's a real doozy…

[Doc enters Asthma HQ and shakes the water off her coat. She approaches the front desk where Phil, a lobby attendant, is typing on a computer]

Phil (distractedly)
Welcome to Asthma HQ. Where can I direct– *[realizes]* Oh hey, Doc! Good to see you! Elevator's out again.

Doc
What a surprise. Anyway, what's the latest, Phil? Has my team come in yet?

Phil
You betcha. The Professor went straight upstairs, muttering something like "environmental triggers that activate the immune system are a major underlying cause of asthma inflammation and associated symptoms"[2]…but hey, what do *I* know, right? Now as to your lab tech, Cipher, well, let's just say I haven't seen *her* leave since my last shift...*last* Monday.

Doc (inner monologue)
That sounds like Cipher, all right. Probably up to her ears in some new experiment or tech buildout down in that maze of a lab. There's nothing she can't find for me on airway mechanics, inflammation, and remodeling, but she might just lose her way out of a paper bag. I wouldn't change anything about her.

Doc
Thanks, Phil. I'll check in on the Professor first.

Phil
Great! I'll ring his office to let him know you're coming.

Doc (calling over her shoulder)
You never stop trying, do you, Phil?

[Phil laughs]

Doc (inner monologue)
Professor hasn't answered an office call in 15 years. He says phones are a distraction from the finer points of asthma research. I can't say I blame him; this chronic[3] disease is complex[4] enough. But thanks to him, I'm always getting the inside scoop on all things asthma, whether I'm asking or not.

[Doc knocks and opens the Professor's office door]

Professor
Ah, if it isn't Doc. Come in, you're right on time. Do you know just how *important* identification and proper treatment of patients with severe asthma is?

Doc
Yes, since you told me yesterday, I'm pretty confident I d-.

Professor (interjecting)
Great! I'll tell you again. Severe asthma patients represent *50%* of the overall healthcare cost in asthma, including frequent hospitalization and emergency room visits.[5] *50%!*[5] And uncontrolled patients that continue to exacerbate are at the highest risk of experiencing future emergency room visits or hospitalization.[5]

Doc
That still makes sense, Professor.

Professor
Yes, it does! Alright, your turn. How about telling me about the most common indicators of severe and *uncontrolled* asthma?

Doc
We're a little short on time.

Professor (chuckling)
There's always time to learn! Care to indulge me?

Doc (inner monologue)
I can never seem to wiggle out of Professor's daily pop quizzes. I'm not sure I want to, either. He keeps me on my toes

Doc
Well, indicators of severe and uncontrolled asthma might include daytime symptoms, such as cough, chest tightness, and shortness of breath, but also nighttime impacts like waking due to asthma symptoms more than twice a month.[1] Another indicator is the need for acute reliever use more than twice a week.[1]

Professor
Very good! But you left out activity limitations due to asthma, which is another indicator, as well as exacerbations requiring oral corticosteroids or serious exacerbations requiring hospitalization.[1] You don't want to leave out any considerations for patients who might have severe and uncontrolled disease.

Doc
Thanks, I'll keep that in mind. But right now we've got a reported case of severe airway inflammation on our hands, and I need some top-shelf thoughts I can take with me to scene of the crime.

Professor
Well, let's start with the essentials then: asthma is a highly *heterogeneous* disease that is triggered by a variety of insults and includes a range of phenotypes, varying biomarker profiles, and-[6-11]

Doc (interjecting)
- and multiple drivers of airway inflammation.[6-11] I'm right there with you, Professor.

Professor
Yes, you more than anyone *clearly* know that managing asthma is challenging because airway inflammation is complex,[4] heterogeneous, and dynamic. But! You *also* need to keep in mind that asthma patients have multiple and overlapping phenotypes or drivers of inflammation that can change over time.[6-11]

Doc
Overlapping phenotypes and changing drivers of inflammation.[7] Good to know. That could make things tricky in this case if the cellular suspects keep changing.

Professor
Maybe, but… not if they answer to someone else… hmm, something to think on some more, I think…

Doc (inner monologue)
He trails off and looks out a rainy window, lost in this new thought of his. I wouldn't be surprised if I came back and found him in the exact same spot, still contemplating.

Doc
I'll leave you to it, then, Professor. I'm off to the scene of the crime, the Airway Epithelium.

Professor (comes back to Earth)
What's that? Airway Epithelium? Remember, Doc, that's the first point of contact for viruses, allergens, pollutants, and other environmental insults. Nasty bunch, those. But their exposure makes the epithelium an active player in the pathogenesis of asthma, and the source of an overactive immune response. If you're headed over there, just keep your eyes open and your wits about you.[7-9]

Doc
Always do, Professor. Thanks.

[Doc closes the door behind her and takes the stairs back down]

Doc (inner monologue)
One more stop inside Asthma HQ before I head out to brave the elements. I can faintly hear the drum of the rain pattering outside as I head down to the lab. Or maybe that's just my heart rate catching up to these flights of stairs.

[An opening of Cipher's lab door, closing behind. Various sounds of frothing beakers, electronics, and ventilation machines are heard]

Doc
Cipher, are you in here?

[Cipher responds from another room nearby]

Cipher
In the Spirometry Room. I'll be right there!

Doc (inner monologue)
Cipher's lab should be short for labyrinth rather than laboratory. There are open doorways in every direction, heading to more rooms and even more doorways. Each room houses a different avenue of Cipher's research into the key pathophysiological processes of severe asthma. It's a place I don't mind getting lost in from time to time, but right now, I've got a case to solve and I need all the help I can get.

Cipher (rolls in on a stool)
So what can I do for ya, Doc?

Doc
Phil over in the front lobby says he hasn't seen you come out of this place in a while.

Cipher
Well, that's… relative. What day is it, exactly?

Doc
That… pretty much says it all, Cipher. You must have a lot going on down here.

Cipher
Tons! There's so much to learn about asthma pathophysiology. Airway inflammation, abnormal lung mechanics, airway hyperresponsiveness; it goes on and on. Honestly, there aren't enough hours in the day!

Doc
Well, that's what brings me down here. We've got a case of severe asthma on our hands where any of those processes could be in play,

and I'll need your help identifying inflammatory suspects so we can find out who's responsible.

Cipher
You got it! But fair warning: there are a *lot* of players involved in the asthma inflammatory cascade, from cells to cytokines to alarmins to everything in between.[7-9] There even seem to be multiple *types* of inflammation.[7-9]

Doc
I've heard about that. Professor mentioned that the dominant driver of airway inflammation changes over time.[6,11]

Cipher
Yeah, that's the dynamic, heterogeneous nature of asthma. We even saw evidence of that in the lab, where in a study investigating phenotype stability by sputum analysis, about 50% of patients with asthma changed their biomarker profile after 1 year of follow up.[6-11]

Doc
50%?[9] That's shifty business in the inflammatory chain. We'll need to approach this case carefully. I'm headed to the scene of the crime. How can I reach you onsite if I need to phone a friend?

Cipher
Here, take this earpiece. It'll patch you straight to mine if you need me to dig up anything for you while you're out there.

Doc
Thanks, Cipher. I'll take you up on that. Just promise me you won't get lost down here again. I've never actually seen where all these doors lead.

Cipher
Pretty cool, right? I like to think they're kinda like the branching airways that form the lungs.

[Doc walks back to the door and opens it]

Doc
That's a good one, Ciph. Hope to see you above ground soon …. Cipher? You still here?

[Cipher responds from another room nearby]

Cipher
Sorry, Doc! I've got lots to do today. But give me a ring anytime!

[Doc closes the door behind her and takes the stairs back up]

Doc (inner monologue)
My team is on the case and ready for anything that comes. Now it's time for me to do what I do best: get out there and investigate. My first destination: the Airway Epithelium, where this severe asthma exacerbation started. Someone may have left a molecular calling card at the scene of the crime, and if so, it's my job to figure out who did.

[Doc pauses by an exit door, takes a steadying breath, and steps back outside. The sound of boots walking on wet pavement is heard as Doc moves briskly away from Asthma Headquarters]

Doc (inner monologue)
Asthma culprits, beware… Doc is now on the case.

Announcer
You've been listening to Asthma CSI: Behind the Cytokine Curtain, sponsored by Amgen and AstraZeneca.

Join us next time for Part 2: Scene of the Crime.

For access to additional episodes and information about severe asthma, visit ReachMD.com/AsthmaCSI

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