Transcript: Webinar – Diphtheria: a recurring clinical and IPC challenge – Joint HIS/BIA/ESGPHM webinar | 19 December 2022

Watch the webinar

During this webinar our audience submitted their questions to our expert panel:

- Dr Rebecca Cordery, Consultant in Communicable Disease Control UK Health Security Agency
- Dr Patrick Lillie, Consultant in Infectious Disease, Hon Senior Lecturer, Hull University Hospitals NHS Trust & Hull York Medical School
- Professor Jim McManus, Executive Director of Public Health, Hertfordshire County Council and President, Association of Directors of Public Health UK
- Dr Daan Notermans, Medical Microbiologist, Dutch National Institute for Public Health and the Environment
- Dr Norman Fry, Head of the National Reference Laboratory for Diphtheria, UK Health Security Agency

Chairs:

Dr Rajeka Lazarus, Consultant in Infection at the University Hospital Bristol & Weston

Dr Surabhi Taori, Consultant Microbiologist, NHS Lothian

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Surabhi Taori 00:08

Okay, so it is one minute past five. So good evening everybody. It is my pleasure to welcome you all to this evening webinar, which is jointly organized by the Healthcare Infection Society, British Infection Association and the ESCMID study group for public health microbiology. My name is Surabhi Taori. I'm a consultant microbiologist at NHS Lothian and for the HIS as well as for the ESGHM.

The topic for today's session is diphtheria a recurrent clinical and IPC challenge. I have been asked to give you a quick overview of diphtheria before we proceed so here goes.

- It's primarily a respiratory or cutaneous disease.
- The respiratory presentation of diphtheria often starts as a membranous pharyngitis with fever and cervical lymphadenopathy, which is described in the textbooks as the classic bull neck appearance.
- When present, the membrane is a thick grey fibrillous and adherent structure. In children pharyngeal diphtheria may extend to the larynx and present with increasing hoarseness and stridor.
- Another entity nasal diphtheria is more mild and sometimes chronic with a clear discharge which can later become bloody.
- Finally, cutaneous diphtheria consists of lesions which started as vesicles which can lead to ulcerate similar to impetigo, these may be covered with the heart bluish green membrane.

With the success of routine immunization, the classical respiratory diphtheria is now rare. The pseudomembrane can often be absent and mild respiratory cases are more common. These, however, can resemble streptococcal pharyngitis which at the moment is another very popular infection. With the success of immunization healthcare systems see less of the infection but then also lose the key expertise in the nuances of its diagnosis and management. And, unfortunately, if healthcare systems are overwhelmed, and vaccine coverage declines, diphtheria is one of the first vaccine preventable infections which tend to re-emerge.

Microbiologically the respiratory and cutaneous disease is caused by species of Corynebacteria, which can produce the diphtheria toxin. These are *Corynebacterium diphtheria*, obviously, but also to animal associated species, known as *Corynebacterium ulcerans* and the less common *Corynebacterium pseudotuberculosis*. The toxin is carried by a bacterial phage it is an exotoxin, which is responsible for the local tissue neck process, or the systemic manifestations. such as peripheral neuritis, or myocarditis.

The non toxigenic strains of *Corynebacterium diphtheria* are not to be completely ignored, as they can cause severe infections such as endocarditis and osteomyelitis. The pathogenic mechanisms of these cases however, is much less understood.

Now, all three organisms which are associated with toxin mediated disease are notifiable throughout the UK and the member states of the EU. A confirmed or probable case necessitates an incident management team.

Recently there has been an increase in reported cases within the UK and in Europe. And today, we have a panel of five people, each an expert in their field, ranging from community public health, microbiology, infectious diseases, and reference laboratory. Before this webinar, audience members

were asked to submit their most pressing questions, which we will ask the panelists to address during the first 40 minutes of the webinar. During the last 15 minutes, we will answer live questions which you are welcome to submit starting now via Slido. To submit questions, please open the Slido app and enter the code #HIS. It is now my privilege to invite the panelists to introduce themselves and may I start, ladies first, Rebecca Cordery.

Rebecca Cordery 04:30

Good evening, everybody. Yes, I'm Rebecca Cordery. I'm a consultant in communicable disease control with the UK Health Security Agency. I'm currently working with the immunization and vaccine preventable diseases division in Colindale. And I'm the joint incident director for the diphtheria incident in the UK.

Surabhi Taori 04:55

Thank you Rebecca Norman Fry.

Norman Fry 05:01

Thanks, so pleased to meet you everyone. So I'm Norman Fry, consultant clinical scientist at UK HSA at the diphtheria reference lab and immunization. So work on diphtheria, pertussis and some of the vaccine preventable bacteria.

Surabhi Taori 05:16

Thank you, Norman. Can I ask down Daan Notermans?

Daan Notermans 05:20

I'm Daan Notermans. I'm a clinical microbiologist I guess the UK would call it a consultant as well. I work at Amsterdam University Medical Centre and at the National Institute of Public Health in the Netherlands where I'm involved in diphtheria outbreak response.

Surabhi Taori 05:36

Thank you Daan, Jim McManus

Jim McManus 05:40

Good evening everybody. My name is Jim. I'm the Executive Director of Public Health at Hertfordshire County Council in England. President of the UK Association of Directors of public Health. I've been involved in advocating for what local directors of public health want to see for asylum seekers and

refugees to national government but outside work, I'm also advising a number of national and international charity organizations on the issues of health care, and migrants and refugees.

Surabhi Taori 06:13

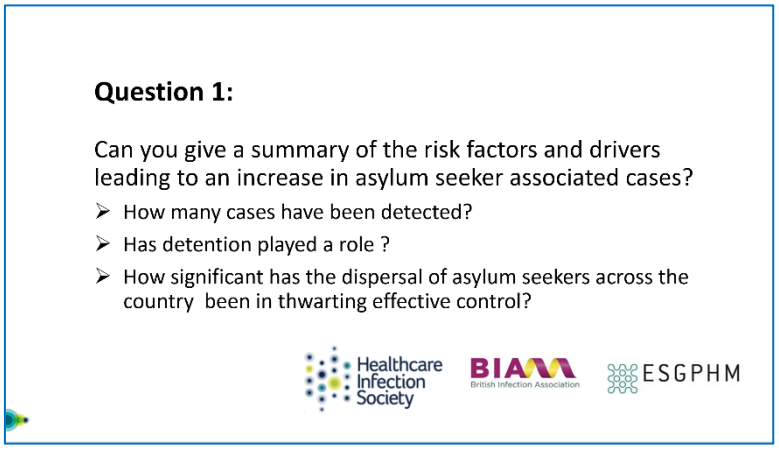
Thank you, Jim. And last but not least, Patrick Lille

Patrick Lille 06:17

Yeah. Thank you very much. So I'm Patrick Lille. I'm a consultant in infectious diseases at Hull teaching hospitals, and I do a lot of our refugee and asylum seeking infection work, both TB and recently diphtheria.

Surabhi Taori 06:34

Thank you all before we start with the questions, just a reminder that we have five questions with sub questions. They've all been selected from those submitted by the audience. We have approximately 37 minutes for questions and please forgive me if I interrupt you in the interest of time. So without further ado, shall we go on to the first question.



Okay, can you give a summary of the risk factors and drivers, leading to an increase in asylum seeker associated cases? The sub questions how many cases have been detected? Has detention played a role and how significant has been the dispersal of asylum seekers across the country importing infection control? That's that's a big question and if it's okay, I'd like to start with Jim.

Jim McManus 07:31

Oh, yes, thank you. So I'll focus on the policy changes if I may. I think there have been several factors that have seen an increase. So some of you may not have seen but in the UK context, Her Majesty's

Chief Inspector of Prisons did an unannounced inspection in July[1], which was published in November of the short term, holding facilities for people arriving principally by boat so that was Manston, Jet Foil and one other and what they found was that there were no clear infectious disease protocols. The isolation and treatment and screening processes were insufficient. And they didn't necessarily have information on who had which infections. And as you know, the Immigration Minister at the end of November announced that people would start to be screened and vaccinated. So there is very definitely an issue of people mixing very close quarters on their journey not being screened. And then the reception centres not being able to pick them up. And then a number of people were dispersed across the United Kingdom, from Manston and various other places who were either infected and ill or infected and asymptomatic and spread the infection. So that's, that's one angle to it. There are clearly others that people are more better qualified to answer than I am.

Surabhi Taori 09:08

Thank you Jim. Patrick, you've been dealing with the cases pretty much first line. So would you like to give us your view?

Patrick Lille 09:16

So I suppose from our point of view, a lot of these people are coming from areas where there is essentially no effective vaccination program going on. So the cases we've seen can't recall any vaccinations, let alone effective. And they've all come via quite a circuitous route, and have you as as Jim says, have been in crowded conditions, crammed in, they're coming from areas where there was a lot of infection per se, including diphtheria. So I think you've got people who've got chronic skin infection, as we know, there's a lot of Group A strep and *Staphylococcus aureus* in amongst all this as well, which I'm sure is contributing. So I think it's very multifactorial in the drivers of why we're picking it up now.

Surabhi Taori 10:06

Everybody's avoiding the question of numbers. Rebecca would you like to add to that?

Rebecca Cordery 10:11

Yeah, so I can give you a little bit of information about the numbers that we've had. So to date this year in 2022 we have had 62 cases of toxigenic *Corynebacterium diphtheriae* reported, we have seen we saw the odd case through the summer, but then the detections picked up in October and November. So we had 18 cases reported in October and then 32 in November. Predominantly, we're seeing these in young males. The median age is 16 and a half years.

And as, as my colleagues have said, on the panel, the majority of these young individuals are from countries where diphtheria may be endemic but actually they've also traveled for many weeks had quite a long arduous journey across across Europe to reach the UK, so have actually spent many weeks

[1] https://www.justiceinspectorates.gov.uk/hmiprisons/inspections/short-term-holding-facilities-at-western-jet-foil-lydd-airport-and-manston/

in settings where they have mixed greatly and with other young individuals, so actually, we feel the majority of these individuals are likely to have acquired their infection prior to reaching the UK. Around a half of the individuals are presenting with skin lesions so cutaneous diphtheria or colonized in the lesions and wounds that they that they may have, we see quite a large proportion of these individuals, clearly from the difficult journey they've had they arrive often with quite a lot of skin lesions and wounds. And so, as I said, that's that's quite a common presentation. We've seen a couple of cases of the more severe respiratory diphtheria, which required antitoxin treatment and the majority of cases that we've had reported to us has been detected in the obviously in the SouthEast of England, but we have seen some cases now reported and picked up more widely across the country.

Surabhi Taori 12:15

Thank you all. Norman would you like to add anything to this from the reference lab perspective?

Norman Fry 12:21

Oh, yeah, thanks. I mean, just a few words on the testing. So we we since April 2014 we run a real time PCR as a frontline to detect toxin gene and then anything that's toxin gene positive goes on to get the definitive elec test, which is an immunization test which demonstrates that the organism really does express the toxins, so obviously, we've been quite busy. I don't know if you want me to talk about any of the typing stuff here. But some of this kind of leads into other questions, but I'm happy to expand here or later.

Surabhi Taori 13:05

And I think it'd be great for our audience to know if you know the cohort of patients or samples that you're seeing is anything which is adding more inflammation.

Norman Fry 13:18

Okay, so, so we now we are now doing routinely doing whole genome sequencing on the isolates that we do get and like many other of our colleagues in other reference lab laboratories, there has been a lot of sharing collaborative work to, to look at the data. So there are there are a couple of studies that have been published already and the ECDC have also published on their site some reports. So we know there are at least four different sequence types. So for the audience, multi-locus sequence typing is one of the typing methods you can use. This is based on seven genes you assign each gene an allele and you get like a string of numbers, which is allelic profile, and that generates a single digit sequence type number. So our colleagues in Switzerland and Germany have published a couple of papers and the ECDC have summarized. So there are there are four major sequence types that we've seen. And we've also seen these in the UK. So this kind of just points to the fact that it's not you know, when I think of people describing an outbreak, I think of a single point source, single clone, a single strain. So this is not that scenario. So we know that they have at least four different strains. We are seeing these come from a varied kind of travel route with a mixed history and we've seen these four times in the UK. Thanks.

Surabhi Taori 15:02

Thank you all. This was a great overview. Shall we go on to the next question?

I think this naturally goes to Daan.

Daan Notermans 15:31

Yes, well, ECDC provides regular reports, updates of reports, the latest report, mid December, they mentioned 10 countries, including Switzerland and UK that have reported cases. So that's not all European countries. And I guess UK is one of the countries that has the larger numbers same as Germany and Austria and I guess Austria is in number of inhabitants a smaller country, but it might be more on the beginning of the route into the EU of many asylum seekers. So that may be a reason why they've detected so much.

But I guess of course, some differences in countries in which asylum seekers which what is the origin of the asylum seekers and which routes they take to reach the countries. So that might explain some of the differences. And I guess in different countries, there can be differences in the kinds of diagnostics that are available. In the Netherlands, we didn't have that many cases. So far we've had five and they were all from from Syrian background. And I'm not sure whether that relates to more refugees coming from Syria than from other countries. We did match them too with the whole genome sequencing to isolate from other countries. So they are part of the outbreak. And indeed, as Norman pointed out, there's different types circulate and so it's not just one point source. So it's probably from different original countries that the strains are circulating and they are probably mixing somewhere on the route that these refugees are taking inside and outside of Europe.

Surabhi Taori 17:59

Okay. My question to both Daan and Norman, are there any strains that are linking to countries? Or is it all getting mixed up in the journey?

Norman Fry 18:13

I mean, it's an interesting question, so I think the, the, the ability to sequence can give you an indication of the origin of the strain but obviously, we are at the mercy of what's in the database and who submitted what sequences so some of these strains, I think, let me see one of them, I think 698. So we actually characterize for our Greek colleagues several years ago, which was a fatal case in Greece. So, so that the, the origin of the original strain, you can use sequencing to perhaps give a give an indication of where it first arose. But obviously, you can have multiple sites in the country so yes, potentially, we can trace a route back, but it's only as good as the data and having available isolates so I would say the big gap for us is really what's going on in Afghanistan, which is obviously a challenge to get some some hard data and isolates out of there

Surahbi Taori 19:26

And that is that a similar experience with ECDC?

Daan Notermans 19:31

As far as I know, but I haven't seen all data from ECDC I think they're they're still busy collecting all data and I guess they will come up with a report at some time. Of course, there are several countries in Asia, North Africa or wherever diphtheria is endemic, it's happening a lot, especially the war torn countries. There's a big outbreak starting in 2017, in Yemen on this tree of diphtheria, it has been published already on that outbreak. So that could be the origin of some of the strains. But in many other countries diphtheria is still endemic.

Surabhi Taori 20:19

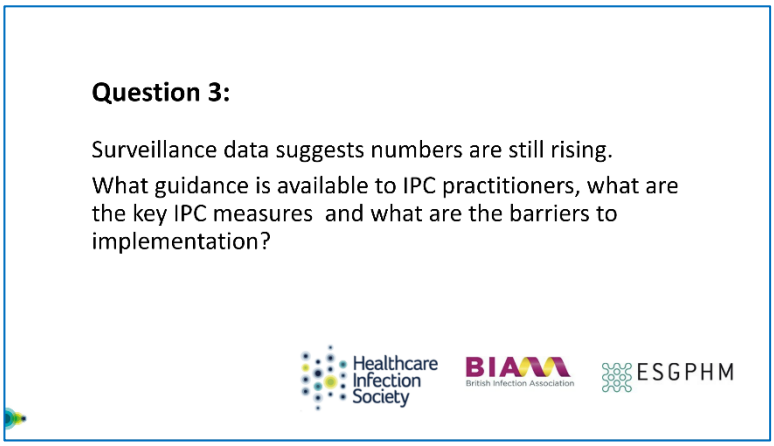
Thank you, Daan. Jim, would you like to add?

Jim McManus 20:21

I think Daan's right in that the the countries of origin are one of the biggest drivers of infection. So we know that most people arriving in Europe arrive in Spain, Greece or Italy and then make their way on particularly, you know, so it's quite common for people to go to from Italy to Austria. It's quite common for people to go from Spain to England and the largest contributions of migration in 2021 where 18% of asylum applications were from Syria, 16% from Afghanistan, 4% and 5% from Pakistan and Iraq and 3% from Somalia. And Yemen is in a group that that's other so a lot of the people we're seeing at the minute are coming from countries where diphtheria is endemic or is in high prevalence or as I think it was Norman or Patrick who said, the vaccination program isn't up to scratch. That is just going to keep going. I think that's not going to stem until the conflict stems.

Surabhi Taori 21:35

Thank you. All. Shall we head on to the next question?



I invite Rebecca, perhaps to address this first.

Rebecca Cordery 22:10

Thank you Surabhi, yes. So we are still having cases notified to us. And so just to give you a bit of context of what we have been doing so, back in September time, as this situation was, sort of came to the fore. We sent out alerts to clinicians. The key being then active case finding, so early recognition of cases, early diagnosis and treatment, particularly we were worried at that point about clinicians obviously having not seen diphtheria for many years and often many clinicians not having ever seen it. So making sure that you know, it was recognized and that urgent treatment, like diphtheria anti toxin was used appropriately and appropriate antibiotics courses started early.

So that was all in September. And we produced a wealth of resources and translated into quite a lot of languages so that we can sort of support that with with awareness raising, etc. As the case numbers increase that we were detecting, obviously, it's become became difficult for the initial reception centres with the volume of individuals to manage active sort of case management, contact tracing and ensuring that you know, we could do individual level control measures. And so we missed, we sort of moved to a more population based wider control measures and made a recommendation that there'd been mass, antibiotic prophylaxis and vaccination of all new arrivals coming into the reception centres, all those currently in reception centres and those that had been onwardly dispersed since the end of October.

So those those recommendations were put into place and again, with that we produced some additional guidance particularly as to how to manage diphtheria within the asylum seeker population. So the national guidance is well established, but it was more the application of that within these settings. And our IPC colleagues did produce a new chapter that went into that on the IPC recommendations, including PPE, environmental cleaning, waste management, and all of that. So that's all online on the Gov.UK website, as are the materials that support the mass prophylaxis program, so the leaflets, the consent, everything translated into other languages. So hopefully there are a lot of resources there for clinicians to use and for public health practitioners to use and obviously all of those are working documents. So any feedback that we get and as the response changes, we're updating those as we go along. So we're very grateful for feedback on those.

Surabhi Taori 24:54

Thank you, Rebecca. A lot of work since to have gone on in the past few months. Patrick, would you like to add?

Patrick Lille 24:59

Yeah, I think having been to some of the dispersal centres, the one of our local hotels, the environmental contamination from these people, they've got huge numbers of skin lesions in some cases. So I think the mass antibiotic administration, although I know we all don't like it, I think we're gonna have to suck it up for this. Because I don't think there's going to be a way you can get out of this with just PPE and vaccination. I think it is going to have to be a lot of antibiotic prophylaxis. There is gonna be a lot of environmental contamination, you're gonna have to clean these rooms incredibly well. And people are just crammed in, less crammed in than they were clearly, but there's a lot of risk of transmission. I know we haven't seen much but that's probably because of very good early recognition by UKHSA and early intervention. So yeah, I think I just agree completely with Rebecca that the massive antibiotic administration is probably what's going to be the most useful intervention at the present time.

Surabhi Taori 26:04

Thank you. Patrick. Daan would you like to give the European perspective

Daan Notermans 26:11

Well, I guess it's gonna be different in different countries, but the experience in the Netherlands is that the care for asylum seekers is not very well elaborately funded. In the summer, asylum seekers were forced to sleep in the open air because there was not enough space and they're they're moved around a lot. A lot of them have wounds from the journey that they've taken because it's of course, they haven't had an easy journey through Europe or before arriving in Europe. So I guess and we mentioned the vaccination rate that many countries where they come from in war torn countries, vaccination programs are not running well for for many years already in a country like Syria. So I guess it's a number of points where you could intervene. But it's a matter of organization. And money then I guess. Try to vaccinate earlier. Try to identify people with wounds earlier, culture or treat them with antibiotics without culture if you don't have the capacity to culture

Surabhi Taori 27:33

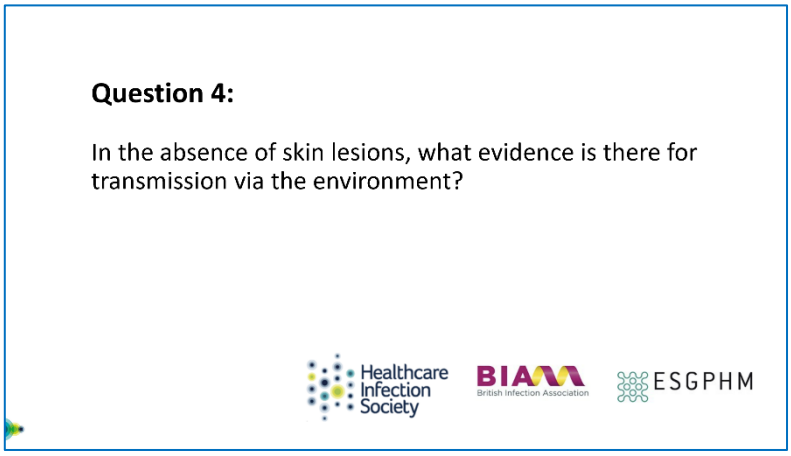
And it may be good to highlight what guidance is available to people in the EU and what would be your key messages.

Daan Notermans 27:43

I guess the documents are available, WHO and ECDC has plenty of documents and otherwise people can look at different national bodies. I'm always impressed by the UK documentation and guidelines or would like to look up UK guidelines for different diseases, so I guess documentation is plenty available.

Surabhi Taori 28:15

Okay, thank you. Shall we head down to question number for then?



And for this, can I invite Patrick first?

Patrick Lille 28:44

Yeah, as far as I'm aware, not a lot. The vast majority of these people do tend to have, if they're diagnosed, are going to have quite a few skin lesions. Clearly you may well get environmental contamination then lots of shedding of skin and kind of pustules and what have you, but in the absence of skin lesions, unless they've got respiratory diphtheria and kind of actively aerosolized and spreading droplets out, I don't think there's gonna be a huge amount but I think the microbiology team of Norman and Daan might have a bit more to say about that. And I will defer to them.

Surabhi Taori 29:25

Okay, so Rebecca, would you like to take this next?

Norman Fry 29:31

I'm just gonna butt in if that's all right?

Oh, well, I was just gonna make the general point that it's actually quite hard to find the evidence for, for transmission via the environment. So I think the, you know, I think one of the messages we want to get out is that it's close contact really. So we're aware of a few family groups with, you know, with

the same sequence type so the typing data only ever goes to support or refute the epidemiology. So it's not a surprise that in a family grouping that you might find, spread and, and also you even if you're fully immunized, you could be an asymptomatic carrier. So although transmission historically in the UK has been quite rare we have, it has been seen, and we published that a few years ago, didn't we? There was a visit to West Africa and we had a transmission, but on the whole, I think transmission is quite rare.

But also maybe if I can just wave the flag for growing bacterial strands. You could get potentially a toxigenic strain from your pet. So I think in terms of contact and hygiene, and washing bedding and all that stuff, then I think good hygiene practice remains the kind of mainstay, but actually, the nitty gritty of demonstrating transmission via the environment is quite hard, but if obviously, it can survive, and it would survive longer in an exudate. So that's the kind of one of the reasons for doing the hot washes and paying attention to the cleaning. Thanks.

Surabhi Taori 31:09

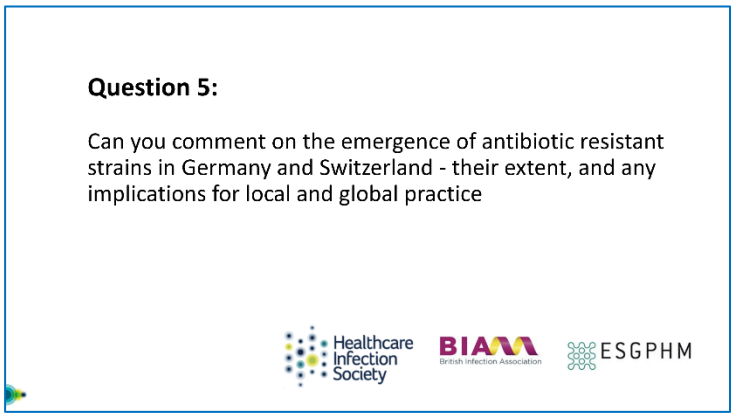
Thank you, anyone else Daan or Jim would like to add?

Jim McManus 31:12

I guess the only thing I'd like to add if I may would be the the kind of given the importance of what our colleagues have said. It raises significant policy issues about putting people in hotels, and also given that many people will also have scabies infestation, the importance of good cleaning, the importance of ensuring that they can get clean clothes and clean bedding becomes ever more pressing. And the importance of ensuring that the hotels are right and the Home Office has a as a very difficult job of sending people out and finding people suitable accommodation. But I think the way that they haven't worked with health systems has actually made things worse. And I know I've gone on record on national media saying the Home Office could have done better and should have done better working with us all. Because actually, in some ways I think this situation has been made worse, not better by the lack of engagement of health professionals from the immigration service.

Surahbi Taori 32:19

Okay, thank you, Jim. Anybody else would like to add? Shall we get on to the next question?



And for this, Daan, can I invite you first? Yes.

Daan Notermans 32:51

Can I go to Norman if he could like summarize experience in the UK, if any implications to clinical practice. Well in your surveyance papers, from Switzerland and Germany they both mentioned a number of cases with macrolides and beta-lactams resistance. The German paper mentioned the ST. 377. And the German paper mentioned it's one group of five, was it five four, I think that our one cluster the Swiss paper mentioned two out of seven from ST 377. But I haven't seen other data that are more Europe wide. I guess that will come when ECDC summarizes all sequence microbiological data, it does show that it can happen. What also has changed eucast has come up with with breakpoints for diphtheria, but they're very new. They came last summer with with epidemiological cut offs, and they came with advice breakpoints in October. So older measurements, I'm not sure to what breakpoints they've been evaluated, although the resistance in the papers is based also on the presence of earned genes. So that's also genetically shown that there's resistance. I think it's important to continue culturing and regularly, to regularly culture and do resistance testing to make sure that strains are still susceptible to macrolides because they are the preferred first line treatment.

Norman Fry 35:16

Okay, so. So, antibiotics aren't my particular area of expertise, but I can summarize some of our findings. So, so thanks to sharing your data from our European colleagues. We identified one of the resistant strains that the Swiss described so we're very keen that people do do phenotypic testing and get isolates so the recommendation now is for for local labs to screen with penicillin and macrolide. So to date, in the UK we have reports of a few with the resistant profile which is resistant to erythromycin, but fortunately at the moment, there are still alternatives. So I think that's the that's the message that we'd like to get out is that the local lab should screen with penicillin and a macrolide and if resistance is found, then obviously do an extended panel and we in the reference lab are keen to see those and to be flagged about those as well. But at the moment there are still options even if a resistance is seen. So prior to this resistance is thankfully, quite rare. I don't know Rebecca, if you'd like to add anything to that.

Rebecca Cordery 36:44

And no just to say, maybe to add that we are very keen on all cases having clearance swabs when they complete their antibiotic treatment and I think what we need to be particularly aware of is where we've got treatment failures or failures of clearance because clearly that would be an issue and the reference lab and our microbiologist can advise on on alternative courses of antibiotics to go forward with. So we're certainly we're we're monitoring this all of the local lab sensitivity data and also clearance and that will feed into any changes in policy that we need to make going forward or change in the in the control measures but at the minute it's it's a watch and wait situation.

Surabhi Taori 37:28

Thank you, Rebecca. Daan you have your hand up and then

Daan Notermans 37:33

May ask how many of how often do you see clear of swabs positives after treatments? We had we had a discussion in the Netherlands as well as should we implement clearance swabs. We did following European and British guidelines, but we've had quite some discussion and it was difficult to find public data on it

Rebecca Cordery 37:57

At the minute with the particular one that we're the strain that you're concerned about, we haven't seen any failures of clearance on that particular one at the minute but obviously we have people in currently on treatment in the process of clearance swabbing but at the minute we don't have any.

Norman Fry 38:13

If I could just come in, sometimes it's actually compliance that's the issue. So we have we've had treatment failure with with sensitive strains as well. So I think sometimes it's not always you know, there are many layers to the issues. But thankfully the treatment failures are rare.

Surabhi Taori 38:36

Patrick and Jim, would you like to add?

Patrick Lille 38:38

I mean, I think it is also worth bearing in mind that a lot of these people will have co infection with either Group A strep or *Staff. aureus* including MRSA. And therefore, actually, if you're trying to find something, it's ideal if you can get a silver bullet because as Norman mentioned, compliance is a bit of an issue if you are chopping and changing antibiotics left right and centre. That is a bit of a problem. Certainly we have ended up using some of the Netherlands because we know that's going to hit everything and clear what we need it to clear. That's not a great idea on mass treatment clearly for things so but I think it is worth bearing in mind that you may need to broaden your cover to cover everything else that might be present certainly in the active cases. For the kind of prophylaxis in contact, that's a different matter. And so far we've just gone with higher doses of amoxicillin to cover things that there may be problems if you do get people that are penicillin allergic and you have resistant strains.

Surabhi Taori 39:41

Thank you Patrick that was very useful. Jim.

Jim McManus 39:45

Nothing to add, really, other than to say, I think this just emphasizes the importance of getting a screening in pathways right as people move through the asylum seeker system, to wherever they're going to go and more for the sake of their health but also to reduce antibiotic resistance.

Surabhi Taori 40:06

Thank you all that's been very helpful. We now have a few questions submitted by our live audience, after which I might ask each of you to give your key message to our audience today. So I'll go across to each of you but that's after this.

So our first question submitted by sli.do is:

> *In Europe or UK and in countries where immunization is relatively high. Has there ever been nosocomial transmission of toxigenic diphtheria?*

And this is really open for everybody who'd like to volunteer for this. Maybe Rebecca or Norman?

Norman Fry 40:52

Hi, Norman here. I'm not aware of any nosocomial case in the UK. I think. I think as we kind of mentioned before, the issue is kind of close contact so it tends to be in a family setting or if also round an animal is involved. So I'm not aware of any nosocomial case, that I can point to so the answer from for me is no.

Rebecca Cordery 41:21

Me too. I'm not aware of any but I've not been working in the field as long as Norman so I think I would go with his answer.

Surabhi Taori 41:28

Link to that, another question.

> *Do we see the patients with diphtheria being admitted to hospital settings?*

Patrick Lille 41:46

I mean, yes. Dependent upon what's the matter, I think almost certainly for anybody with respiratory diphtheria I would probably want them in hospital initially. Particularly you're going to be giving them antitoxin. I think it's just safer to do it that way. You've got the risk of anaphylaxis, to anti toxins after all, for cutaneous cases, I think it's a bit more dependent upon the extent of them whether or not there's anything else going on, and also how easily they can self isolate. So if people are in a nice, small hotel room on their own, it's not great to be isolated in there and I think it's reasonable in some cases to get them into hospital just to do a once over make sure everything else is okay. So I have a

reasonably low threshold for admitting people for the start of their treatment. And then once people are improving, by all means, get them home.

Surabhi Taori 42:39

Thank you, Patrick. Rebecca.

Rebecca Cordery 42:42

Not much to add on that except just to say that the recommendation is it is any case of toxigenic diphtheria is it has a clinical assessment and we would recommend that that's with an ID clinician, or at least the support of an ID clinician, but where services don't necessarily have one on site. And so that essentially the discussion around whether antitoxin is necessary is taken early. Because, obviously you'd want to get in as quickly as possible with that because essentially, the antitoxin locks up the toxin, and will therefore prevent the long term damage that you can get with the more severe forms of diphtheria. And as we know, the sort of neurological and the cardiac complications can start to occur two or three weeks down the line, can't they and that's what's the antitoxin is trying to prevent so you don't want to see the symptoms of that before you start the antitoxin. So that would be our our plea, is a discussion of a case with an ID clinician and having a low threshold for face to face consultation with one.

Surabhi Taori 43:48

That's great. Thank you all shall we go on to the next slide?

Daan Notermans 43:52

One thing to ask ECDC rapid risk assessment and on sixth of October they do mention one case of a staff member as a reception centre for immigrants who was infected doesn't state more details than that.

Surabhi Taori 44:13

Okay. So there is a potential for nosocomial transmission.

Daan Notermans 44:17

Yeah. Then the the effect of the immunization may wane over time. Normally I say that the advice is to to recirculate every 10 years, which many adults don't do in many countries. Unless they travel abroad to countries where they have to visit to get vaccinations advice beforehand. And then also the the vaccine is directed against a toxin and not against bacteria itself. So especially skin diphtheria can occur even in vaccinated people

Surabhi Taori 44:59

So related to that, what advice are we giving? Maybe - Patrick or Rebecca?

Rebecca Cordery 45:07

The advice given is that all staff who are working in in settings for asylum seekers are to make sure they're up to date with vaccinations as per the UK schedule. But that's particularly pertinent for staff who have been born abroad who might not know what their immunization status was. And so therefore, as for any adult in the UK, you know, they should discuss it with their GP and make sure that they're brought up to date with the UK schedule.

Surabhi Taori 45:37

Thank you Rebecca, Patrick

Patrick Lille 45:39

Yeah, no, I was just gonna say that's exactly what our Occupational Health Service is saying. Clearly if you know you're dealing with a suspected case, then following the UKHSA guidance on PPE is very sensible as well. So that you know exactly what you're doing there.

Surabhi Taori 45:55

Great, thank you all. Next question.

What are the risks of using lots of prophylactic antibiotics in regards to resistance?

Are we seeing resistance from these isolates compared to previous?

Right, maybe Norman, would you like to address this question?

Norman Fry 46:28

Okay, well, maybe I can start but I think I mean, I think it's a balance of risk. So I think I think for us in the UK, we have a very vulnerable group, particularly the teenagers. And we have to remember, this is potentially fatal. So I think it's a balance of risks. That's why we've gone with offering prophylaxis. I think we're all aware in an ideal world, we wouldn't be doing that. It's not an ideal world. So it's a balance of risk, it's potentially fatal. We talked a lot about the cutaneous infections, but some have been respiratory requiring antitoxin. So I don't think we should forget the severity and lethality of the disease. Thanks.

Surabhi Taori 47:10

Thank you Norman, Patrick or Jim.

Patrick Lille 47:13

Yeah, no, I would certainly go along with that. I mean, I appreciate that we don't want to be driving antibiotic resistance, but neither do we want to have uncontrolled outbreaks of diphtheria in very close confined settings because this will cause huge problems. And I am not a microbiologist, I'm an infectious disease physician and we are renowned for saying one thing and doing another, I appreciate, but you know, we're not going to be giving these people meropenem for their prophylaxis, we're going to be giving them either azithromycin or amoxicillin and we're not going to drive huge amounts of resistance in this and on this occasion I think it is the lesser of two evils.

Jim McManus 47:51

Yeah. I find myself in agreement with Patrick I think this is a balance of risk, isn't it? And it also makes me ask the question of how else can we mitigate the risk through good public health practice across the entire asylum pathway? And I think that for me remains a really key thing that despite the commendable efforts of AXA, who I think have made significant strides. I think we've still got work to do in this country. That's not a criticism at all, but just pointing out there's still a lot of work to do because we can't let antibiotics do all the work but equally as Patrick says, We can't not use them appropriately either.

Surabhi Taori 48:42

Thank you all anyone else would like to add?

Daan Notermans 48:44

Yeah. I completely agree. It's, it's a balance of risk. The fear can be very serious. I think it's important to monitor the development or the spread of resistance when you start early treatment of larger groups. So don't abolish culturing because you're administrating antibiotics. So you know, at least, where resistant strains might pop up and might start to spread.

Surabhi Taori 49:15

And Rebecca this is where your your request for clear samples would, would come in as well, to keep a watch.

Rebecca Cordery 49:22

Yes, absolutely. So we tried to, obviously an expert group met to discuss which antibiotic to use and the course etc. And then you know, the recommendations on what to use should we see resistant

strains so I think yes, we just have to work within those recommendations, don't we? For a short period of time whilst we've whilst we have this issue, and then and keep it under review.

Surabhi Taori 49:46

So my question to all of you:

Diphtheria has not been a very common disease in recent times, but it has in the past. Is there any evidence or publications of emergence of resistance as a result of mass antibiotic usage?

Rebecca Cordery 50:07

Not that I'm aware of Surabhi and in fact, in this population, I think this is a control measure that we're using at the moment for a short period of time in the UK. And we're not aware that this is being used in any other European country, so on routes, so I don't think we're repeating doses of vaccine that other countries are giving prophylactically on to these individuals on their route to the UK. And so this should be a short intervention on a time limited basis.

Surabhi Taori 50:37

Brilliant, thank you so much.

Helen, do we have any more questions? Okay, this should be short and easy.

Have all hotel staff been offered diphtheria vaccine?

Jim McManus 50:56

My experience is it's very hit and miss. So no, I couldn't hand on heart say I'm aware of everyone being offered it.

Patrick Lille 51:08

I think as soon as there's a case locally, it goes massively up the agenda and people start getting checked. Whether or not, until there has been that kick up the backside, people do it I would agree it probably is a lot more sporadic.

Surabhi Taori 51:26

And would you recommend that all hotel staff be offered the vaccine?

Patrick Lille 51:32

I think that's a no brainer. It's simple intervention, which is going to potentially even if the number needed to treat is in the hundreds, it's not going to exactly break, blow the budget out of the water. So yeah, I would certainly recommend that everyone is up to date.

Jim McManus 51:49

I'd be inclined if I might butt in , I tend to agree with Patrick because there are in the hotel estates in the UK, a number of people from nations who don't have diphtheria vaccination as a standard as we do. And so in terms of risk to them, it does feel like it's a cheap way of protecting them and getting the benefit.

Surabhi Taori 52:15

That's a very clear message going out. Helen, one more question perhaps?

We still have some time.

> *Although currently the bacteriophage associates with three species, what prevents it from infecting the other species, do we know?*

Who would like to volunteer for this question? Very, very specific question. And I'm assuming only somebody who does research on this would would may be inclined to address it.

Norman Fry 52:51

So I mean, I'm by no means a phage expert. But I think the I would say that phages tend to be specific for species and there are even subtle differences between the phages that in fact, the diphtheria and novel strands. There may be some evidence that they could cross but yeah, I don't have I don't have all the answers, I'm afraid but it's a it's a good question.

Surabhi Taori 53:22

Great, thank you all. We have exactly five, five and a half minutes left.

And can I ask each of the panelists to give us one sentence or one key message which you think the audience should know? And can I start with Rebecca?

Rebecca Cordery 53:40

Just to say thank you for having me this evening. It's been a pleasure.

I think my key message would be that obviously we're going to continue with the mass antibiotic and vaccination prophylaxis for the time being, but actually going forwards, what will be key here is early case finding and diagnosis and treatments.

So for just for us to keep raising awareness amongst clinical colleagues of diphtheria and making sure that it's in differential diagnoses, but to say that we haven't had cases in the wider population of this

in particular, we've not seen cases spread outside of the asylum seeker population in these settings and so for the general public, the risk is low.

Surabhi Taori 54:22

Thank you, Rebecca. Daan.

Daan Notermans 54:27

Well, I completely agree with Rebecca that early awareness and early diagnosis is important. All over Europe, I guess. As of measurements. I think before we start mass treating with antibiotics, we should attempt to raise the vaccination coverage in the refugees as early as possible.

Surabhi Taori 54:53

Brilliant, thank you. Patrick.

Patrick Lille 54:57

No, I would second all of that, and also to say that, just to be aware that diphtheria does seem to go together with the Group A strep and *Staff. aureus* and that please be aware that you may need to be not quite a purist as you might like to be with your prescribing in these cases than to cover everything in that case, but to get local expertise involved soon is a good idea as well.

Surabhi Taori 55:24

Great, thank you Patrick. Norman?

Norman Fry 55:27

Thanks. So although we've been talking about asylum seekers, and *Corynebacterium diphtheria* here, I would just put in a plug for don't forget about *Corynebacterium ulcerans*. And please send isolates of both species to the reference lab as soon as you can. Thanks.

Surabhi Taori 55:43

Thank you, Norman. And last but not least, Jim.

Jim McManus 55:46

So I'm just smiling at Norman's plug for wanting isolates. So firstly, I want to say thank you for this. I've enjoyed immensely listening to the expertise of colleagues on the panel. It's been brilliant, and

thank you for organizing it. I think Rebecca hits the nail on the head for me when she says case finding, particularly when there's so little information, we don't know who's got it, we don't really know who's been exposed. So case finding in a system. I last week I had 2000 asylum seekers in my area. I now have something like 3000 asylum seekers in my area. They're going up. So case finding is really crucial. Big thanks to AXA for the huge work they have done in getting the Home Office and others on board with that, I think that has been really crucial. And obviously vaccination. So we in the health side of this I think have to work together to make sure that the immigration and hotel side is as protected as possible. And with colleagues like this on the call, that gives me hope.

Surabhi Taori 56:54

Thank you, everyone. And my key message to everyone is to have a brilliant holiday season. But before we finish, I'd like to thank our expert panel and the audience for participating and for people behind the scenes who have been moderating the questions and organizing everything. Certificates of attendance will be sent out after the event and a recording and transcript will be available after the event. And of course there are also past webinars which are available on the HIS website. So thank you all and have a brilliant evening.

Norman Fry 57:27

Thanks very much bye Bye