the Patch Tester

Contact Dermatitis | Haptens | Patch Testing

Edition #6
March 2021

”The Patch Tester” is a quarterly e-magazine from Chemotechnique to the Patch Testers of the world.

We bring you the latest relevant news and developments in Patch Testing

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PURPOSE

The Patch Tester is an e-mag developed by Chemotechnique to serve as an information resource for all Patch Testers and other Dermatologists around the world; not just in Sweden, or Europe, or America, but wherever the English language can be read and understood. This sixth issue comprises no less than 68 pages with various different topics and features. Ultimately, we plan for The Patch Tester to become the forum for all of us to communicate and cooperate, in all directions.

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ACKNOWLEDGEMENTS

Production Editors: David Niklasson & Steve Lee

National Baseline update

During the past year the composition of many regional / national series has been updated. Among these series we find the Australian, the British and the Swedish Baseline Series along with the International Series based on a composition from the ICDRG and the American Core Series based on a composition from the ACDS.

The most notable trends in the 2021 series revisions are the continued implementation of the hydroperoxides of Linalool and Limonene in series, as well as omission of MI (M-035B) in favour of MI/MCI in the new 0.215% (in aqua) concentration (C-009E).

	AC-1000	ABS-1000	GB-1000	IS-1000	SS-1000
ADDED	H-031B H-032B L-003 B-010B D-036 J-002 P-036 P-039 S-015 L-004 C-009B	C-036 G-001 I-002 D-002 T-049 A-011 P-022 B-005 S-001 S-011 P-019B	D-065 L-004	P-005 Mx-30 Mx-03C C-009E	C-009E Mx-05C C-017A
REMOVED	C-009A D-049E	P-019A T-010 B-026 N-001 B-024 C-033 B-023C E-019C T-030 B-043 B-042		M-035B T-010 H-021B M-003A	M.035B C-009B Mx-05A C-017B

Interview with David Alsheimer-Niklasson

Who are you?
My name is David Alsheimer-Niklasson,
Business Development Director
at Chemotechnique MB Diagnostics AB

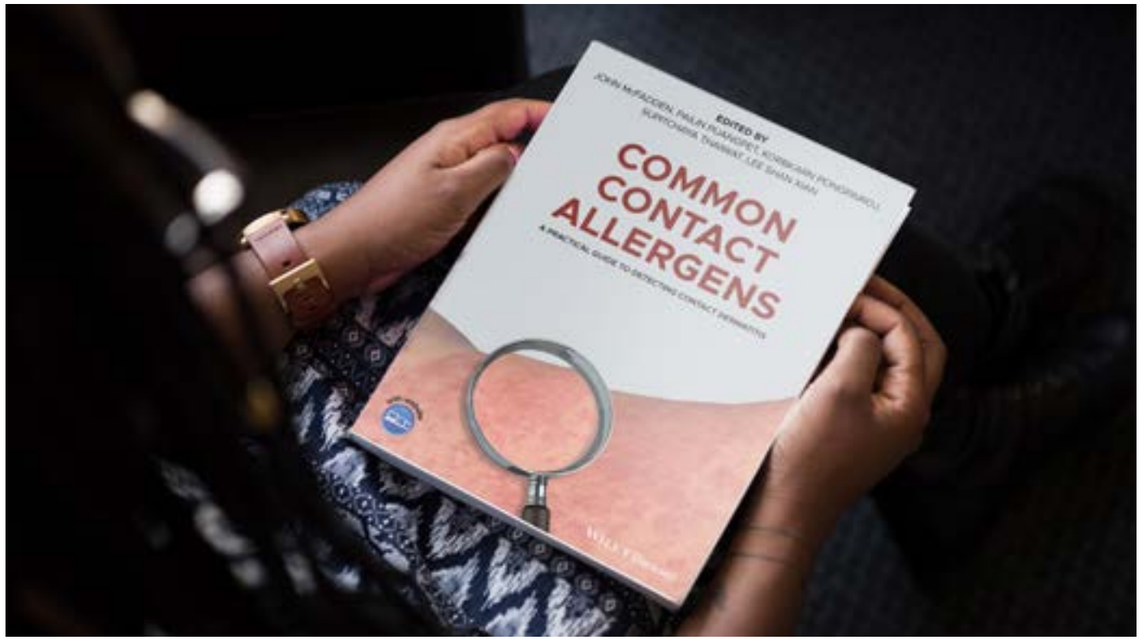
How did you first come into contact with patch testing?
Growing up in a family with a father who was very much committed to patch testing, Bo Niklasson CEO of Chemotechnique, I have been patch tested more times than I can possibly count. Although being tested with different versions of the prototype IQ Chambers at an early age, it wasn't before I was in my teens I was properly introduced to patch testing while interning at Chemotechnique during the ESCD in Geneva 2000.

When did you join the company?
Although I spent summers in my youth earning extra money working within the Chemotechnique order department it wasn't until as late as 2016 I rejoined the team at Chemotechnique on a new project in development – this time working in close collaboration with my sister Helena who had joined the company a year prior, to work with regulatory affairs.

What is the most fascinating aspect of patch testing?
The first order of business I set myself when joining the company was to get a basic understanding through learning as much as possible about the haptens and the underlying mechanisms of contact allergies. Having a background in neither medicine nor biochemistry but rather marketing and Industrial design, I quickly found the concept of patch testing and contact allergies extremely fascinating.

The result of my aspiration to understanding contact allergies has led to me insisting that a page or two outlying the basic correlation between haptens and ACD is found in most Chemotechnique printed material. The reason why is simply because I find the complex nature of contact allergies much too fascinating to be restricted to the realms of physicians with specialised training. I believe that if there would to be a broader general awareness regarding the existence of contact allergies, many more cases of ezcemas on "sensitive" skin would get proper diagnoses.

Business development – where do you see the future of patch testing?
With my background in industrial design and product development, my hope is that increased awareness of contact allergies ultimately will encourage or even force manufacturing companies to opt-out of using in their products those chemicals that function as haptens causing allergic contact dermatitis - hopefully resulting in fewer cases of allergic contact dermatitis. In the meantime, I will however strive to increase the accessibility of patch testing as much as possible so that fewer cases of contact allergy remain undiagnosed.



Win a signed "Common Contact Allergens" book!

Dear Reader,

The Patch Tester e-Mag has now been running for 16 months and is now into its 6th edition.

We have received many *ad hoc* positive feedback and comments on the e-Mag, but we would now like to receive more detailed feedback, both positive and constructive negative, to help guide us in the future development of this service from Chemotechnique.

To encourage this feedback from you, we are offering to three respondents a copy of the book **Common Contact Allergens: A Practical Guide to Detecting Contact Dermatitis** signed by co-author (and Chemotechnique CEO) Bo Niklasson.

The books will be awarded to the 1st, the 10th and the 100th respondent before the cut-off deadline for receipt of responses on Friday 28th May 2021. The winners will be notified by email.

How to participate:

Fill out **this questionnaire (link) (.zip)** and mail it to david.niklasson@chemotechnique.se.
In order to be eligible you also need to be on the "**The Patch Tester" mailing list (link).**

One application per respondent.

Polyethylene Glycol (PEG)

with reference to COVID-19 mRNA Vaccines manufactured by Pfizer/BioNTech and Moderna

In summary, polyethylene glycol (PEG) or macrogol, is a polyether compound. It is widely used as an additive in pharmaceuticals, cosmetics and food. Different types of macrogol exist according to their molecular weight from 300 g/mol to 10,000,000 g/mol. Anaphylactic reactions to macrogol are rarely reported. However, in recent years more reports have appeared in the literature with macrogol-induced hypersensitivities due to drugs, personal hygiene products, dental products, lozenges and lubricants.

Most recently, PEG has become known as an ingredient in two of the leading and currently available COVID vaccines and it is speculated that it may be the cause of some of the adverse reactions that have been experienced by the ever-increasing number of vaccinated persons around the world.

What is PEG?
Polyethylene glycol is a polyether compound derived from petroleum. PEG is also known as polyethylene oxide (PEO) or polyoxyethylene (POE), depending on its molecular weight.
The structure of PEG is commonly expressed as H−(O−CH2−CH2)n−OH.

For further information on PEG (link)

Medical Uses of PEG
Macrogol, also known as polyethylene glycol (PEG), is used as a medication to treat constipation in children and adults. It is also used to empty the bowels before a colonoscopy. It is taken by mouth. Benefits usually occur within three days. Generally, it is only recommended for up to two weeks.

Macrogol is used as an excipient in many pharmaceutical products.

Lower-molecular-weight variants are used as solvents in oral liquids and soft capsules, whereas solid variants are used as ointment bases, tablet binders, film coatings, and lubricants. It is also used in lubricating eye drops. Use appears to be safe during pregnancy.
It is classified as an osmotic laxative. It works by increasing the amount of water in the stool.

Macrogol came into use as a bowel prep in 1980 and was approved for medical use in the United States in 1999. It is available as a generic medication and over the counter. In 2017, it was the 162nd most commonly prescribed medication in the United States, with more than three million prescriptions.

Typically, it is formulated together with electrolytes. When attached to various biopharmaceutical medications (which are proteins), macrogol results in a slowed clearance of the carried protein from the blood. This makes for a longer-acting medicinal effect and reduced toxicity, and it allows for longer dosing intervals. It also reduces the proteins' immunogenicity.
Macrogol is also used to fuse B-cells with myeloma cells in monoclonal antibody production.

Health effects of PEG
PEG is considered biologically inert and safe by the FDA.

However, a growing body of evidence based on plasma samples from 1990–1999 shows the existence of a detectable level of anti-PEG antibodies in approximately 72% of the population, who have never been treated with PEGylated drugs,
Due to its ubiquity in a multitude of products and the large percentage of the population with antibodies to PEG, hypersensitive reactions to PEG are an increasing concern.
Allergy to PEG is usually discovered after a person has been diagnosed with an allergy to an increasing number of seemingly unrelated products, including processed foods, cosmetics, drugs, and other substances that contain PEG or were manufactured with PEG.

When PEG is chemically attached to therapeutic molecules (such as protein drugs or to nanoparticles), it can sometimes be antigenic (a molecule which stimulates an immune response), stimulating an anti-PEG antibody response in some patients. This effect has only been shown for a few of the many available PEGylated therapeutics, but it has significant effects on clinical outcomes of affected patients. Other than these few instances where patients have anti-PEG immune responses, it is generally considered to be a safe component of drug formulations.

Contraindications of Macrogol (PEG)
When administered orally as a laxative, complications can be intestinal perforation, bowel obstruction, ileus, inflammatory bowel diseases, and toxic megacolon.
The doses of PEG/macrogol as an excipient are too low to have relevant contraindications.

Adverse Effects of Macrogol/PEG
Oral macrogol is generally well tolerated.
Possible side effects include headache, bloating, nausea, allergies, and electrolyte imbalance, mainly hypokalaemia and hyperkalaemia. Hyperkalaemia is not an effect of macrogol itself but of potassium salts which are usually part of macrogol formulations. With excessive use, it can cause diarrhoea.
Side effects may also include increased bowel gas, abdominal pain, and nausea.
Rare but serious side effects may include an abnormal heartbeat, seizures, and kidney problems.
Allergy to macrogol is rare, and usually appears as an allergy to an increasing number of seemingly unrelated products, including cosmetics, drugs that use it as an excipient, and peri-procedural substances such as ultrasound gel.

Mechanisms of Anaphylaxis
Concerning the mechanism of anaphylaxis mediated by PEGs, different mechanisms have been proposed. Our case supports the assumption of cross-reactivity between PEGs of different molecular weights and polyethylene glycol analogues.

As has been shown by several authors of clinical papers, the positive intradermal test suggests an IgE-dependent mechanism, although no control tests have been performed on healthy individuals to rule out non-specific reactivity. However, even after a 1:10 dilution, a positive intradermal test has been observed. Other methods besides an oral challenge test to confirm the diagnosis may be by basophil activation test or western blot to show specific IgE binding.

In conclusion, cases of immediate-type PEG hypersensitivity are reported with increasing frequency; therefore, awareness of PEG's allergenic potential should be raised, and better product labelling should be discussed.

For further information on the clinical uses of Macrogol (PEG) (link)

PEGylation
The process of PEGylation is to attach macrogols to biopharmaceutical drugs with the purpose to slow down their degradation in the human body and increase their duration of action, as well as to reduce their immunogenicity.

PEGylation is the act of covalently coupling a PEG structure to another larger molecule, for example, a therapeutic protein, which is then referred to as a PEGylated protein. PEGylated interferons alfa-2a or alfa-2b are commonly-used injectable treatments for hepatitis C infection. Other examples for PEGylated proteins include PEGFILGRASTIM, which is used to treat neutropenia, and PEGLOTICASE for the treatment of gout.

All commercially available PEGylated pharmaceuticals contain methoxypoly (ethylene glycol) or mPEG.

PEGylation by attaching the strands of the polymer PEG to molecules, most typically peptides, proteins, and antibody fragments, can improve the safety and efficiency of many therapeutics. It produces alterations in the physio-chemical properties including changes in conformation, electrostatic binding etc. These physical and chemical changes increase systemic retention of the therapeutic agent. Also, it can influence the binding affinity of the therapeutic moiety to the cell receptors and can alter the absorption and distribution patterns.

PEGylation, by increasing the molecular weight of a molecule, can impart several significant pharmacological advantages over the unmodified form, such as improved drug solubility, reduced dosage frequency, without diminished efficacy with potentially reduced toxicity, extended circulating life, increased drug stability, and enhanced protection from proteolytic degradation.

Interestingly, PEGylated forms may also be eligible for patent protection. There is for example ongoing litigation between Moderna and Arbutus BioPharma over a particular mRNA vaccine.

A PEGylated lipid is used as an excipient in both the Moderna COVID-19 vaccine and the Pfizer–BioNTech COVID-19 vaccine. Both RNA vaccines consist of Messenger RNA, or mRNA, encased in a bubble of oily molecular lipids. Proprietary lipid technology is used for each vaccine. In both vaccines, the bubbles are coated with a stabilising molecule of polyethylene glycol.

There is an ever-increasing list of pharmaceuticals with PEG or PEGylation that have been approved by the FDA over the past 30 years, including in veterinary medicine. ADAGEN (pegademase bovine) manufactured by Enzon Pharmaceuticals, Inc., US was the first PEGylated protein

approved by the U.S. Food and Drug Administration (FDA) in March 1990, to enter the market. It is used to treat a form of severe combined immunogenicity syndrome (ADA-SCID), as an alternative to bone marrow transplantation and enzyme replacement by gene therapy.

Since the introduction of ADAGEN, a large number of PEGylated protein and peptide pharmaceuticals have followed and many others are under clinical trial or under development.
Sales of the two most successful products, PEGASYS and NEULASTA, exceeded $5 billion in 2011.
So, the clinical value of PEGylation is now well established.

For further information on PEGylation (link)

Related Topics

1. A recent publication discussing the implication of PEG as the cause of the first case of anaphylaxis to a COVID-19 vaccine is to be found in the Literature Review section of this issue of The Patch Tester.

2. A recent publication by EAACI (European Academy of Allergy & Clinical Immunology) together with ARIA (Allergic Rhinitis and its Impact on Asthma) entitled “COVID-19 Pandemic: Practical considerations on the organization of an allergy Clinic – an EAACI/ARIA Position Paper” is to be found in the Hot Topic section of this issue of the Patch Tester. Although this article for Allergists is unlikely to be in the reading list of Dermatologists, there is much valuable information and many insights that would assist the Dermatologist in their own clinics and clinical practice.

Patch Test for PEG
Polyethylene glycol 400 (PEG 400) is a Patch test hapten available from Chemotechnique as P-034.

The **Chemotechnique Hapten Information Sheet** on Polyethylene glycol 400 is available for download from the Chemotechnique website (link)

It states the following information, for the professional.

Art.No	P-034
Formula	H(OCH2CH2)nOH
Conc (% w/w)	100%
Series	INS
MW	400
CAS	25322-68-3

Synonyms:
PEG-2M; alpha-hydro-omega-hydroxypoly(oxy-1,2-ethanediyl); carbowax 200; Carbowax PEG 400; Carbowax PEG 8000; emkapol 200; Ethoxylated 1,2-ethanediol; Ethylene glycol 8000 polymer; gafanol e 200; Macrogol; PEG; PEG 1000; PEG 200; pluriol e 200; polydiol 200; Polyethylene glycol; Poly(ethylene glycol) 100; Poly(ethylene glycol) 1000; Poly(ethylene glycol) 10000; Poly(ethylene glycol) 1500; Poly(ethylene glycol) 200; Poly(ethylene glycol) 2000; Polyethylene glycol 20,000; Poly(ethylene glycol) 300; Poly(ethylene glycol) 3400; Polyethylene glycol 400; Poly(ethylene glycol) 4000; Poly(ethylene glycol) 600; Poly(ethylene glycol) 6000; Polyethylene Glycol 8000; Poly(ethylene glycol) 900; polyethylene glycols; Polyethylene gylcol; Poly Ethylene Oxide; Polyglycol 1000; Polyox WSR-301; Polyoxyethlene; Polyoxyethylene; Polyoxyethylene 1000; Polyoxyethylene ether;

Uses:
Polyethylene glycol is a condensation polymers of ethylene oxide and water with the general formula H(OCH2CH2)nOH, where n is the average number of repeating oxyethylene groups; typically from 4 to about 180.

The low molecular weight members from n=2 to n=4 are diethylene glycol, triethylene glycol and tetra-ethylene glycol respectively, which are produced as pure compounds. The low molecular weight compounds up to 700 are colourless, odourless viscous liquids with a freezing point from -10 degrees C (diethylene glycol), while polymerised compounds with higher molecular weight than 1,000 are wax-like solids with melting point up to 67 degrees C for n 180.

The abbreviation (PEG) is termed in combination with a numeric suffix which indicates the average molecular weights.

One common feature of PEG appears to be that it is water-soluble. It is soluble also in many organic solvents including aromatic hydrocarbons (but not aliphatics).

They are used to make emulsifying agents and detergents, and as plasticisers, humectants, and water-soluble textile lubricants.

The wide range of PEG chain lengths provide identical physical and chemical properties for the proper application selections directly or indirectly in the field of the following applications:

- Alkyd and polyester resin preparation to enhance water dispersibility and water-based coatings. Anti-dusting agent in agricultural formulations.
- Brightening effect and adhesion enhancement in electroplating and electroplating processes.
- Cleaners, detergents and soaps with low volatility and low toxicity solvent properties.
- Coupling agent, humectant, solvent and lubricant in cosmetics and personal care bases.
- Dimensional stabiliser in wood working operations.
- Dye carrier in paints and inks, heat transfer fluid formulation and defoamer formulations.
- Low volatile, water soluble, and non-corrosive lubricant without staining residue in food and package process.
- Mould-release agent and lubricant in fabricating elastomers. Paper coating for anti-sticking, colour stabilising, good gloss and free flow in calendaring operations. Plasticiser to increase lubricity and to impart a humectant property in ceramic mass, adhesives and binders.
- Softener and antistatic agent for textiles.
- Soldering fluxes with good spreading property.
- Polyethylene glycol is non-toxic, odourless, neutral, lubricating, non-volatile and non-irritating and is used in a variety of pharmaceuticals and in medications as a solvent, dispensing agent, ointment and suppository bases, vehicle, and tablet excipient.

The **Chemotechnique Patient Information Sheet** on Polyethylene glycol 400 is available for download from the Chemotechnique website (link)
It states the following information, for the patient:

Polyethylene glycol PEG400 refers to a polymer of ethylene oxide with a molecular mass below 20,000 g/mol, in this case 400. This chemical has many industrial, foods, cosmetic and medical applications. It is added to skin lotions, creams, jellies, soaps and toothpastes. It is the basis for many laxatives and bowel irrigation preparations. It is also used as a lubricant in tire manufacturing; plasticizer for sponges and synthetic leather; a paper softener; anti-curl agent; and an intermediate in resin manufacturing. Further research may identify additional product or industrial usages of this chemical.

What else is Polyethylene glycol 400 (PEG 400) called? This chemical can be identified by different names, including: Polyethylene oxide (PEO); Methoxypolyethylene glycol (mPEG);

Some commercial names (trademarks) include Carbowax and Carbowax Sentry, Alcox, Breox, Lutrol. Some medical and consumer brand names include MiraLAX, GoLYTELY, Fortrans, TriLyte, SoftLax. This may not be a complete list as manufacturers introduce and delete chemicals from their product lines.

Management of Dermatology Clinics in the COVID-19 pandemic

From the various publications on managing a clinic in the current COVID pandemic, two articles have been selected for presentation here. The first publication refers to managing a Dermatology Clinic and the second refers to managing an Allergy clinic. Whilst the latter may seem to be somewhat off-target, that publication is extremely authoritative and comprehensive, and contains many pearls of wisdom, and useful insights, (including on Atopic Dermatitis and Urticaria) and good advice that is applicable also for dermatologists in their own clinical practices.

COVID-19 and dermatology: A comprehensive guide for dermatologists

by D.H. Fahmy et al.
in **Journal of the European Academy of Dermatology and Venereology, Vol 34, Issue 7, pp 1388–1394, 19 May 2020.**

Cutaneous manifestations of COVID-19 are also found with several other types of viral infections. A recent Italian study of 88 COVID patients showed that 20.4% of the patients demonstrated cutaneous manifestation in the form of erythematous rash, urticaria and chickenpox-like vesicles, presenting mainly in the trunk with little or no itching. Furthermore, the authors reported that those skin lesions were not correlated with disease severity. Similarly, Henry et al. reported that COVID-19 patients may present with urticarial eruption without any respiratory symptoms (cough or fever). As perhaps an extreme example, a COVID-19 patient was misdiagnosed as dengue in Thailand, because the principal presentations were skin rash with petechiae and low platelet count.

Cutaneous Manifestations of COVID-19

Galvan Casas et al. performed the first prospective study to classify the cutaneous manifestations of COVID-19 into five major clinical patterns:

1. Pseudo-chilblain (19%)
2. Other vesicular eruptions (9%)
3. Urticarial lesions (19%)
4. Maculopapules (47%)
5. Livedo or necrosis (6%)

With such conditions, dermatologists should pay particular consideration to patients presenting with viral-like skin rash, in order not to miss COVID-19 cases.

The skin is considered a part of the immune system as it acts as a shield against different environmental stimuli. Therefore, compromising the integrity of this barrier by for example lacerations, scratching, needling, or pre-existing infections or diseases of skin, wounds and burns may facilitate the invasion by micro-organisms. As a consequence, dermatological patients may be at higher risk of SARS-CoV-2, either due the loss of the skin integrity by dermatological diseases or the immuno-suppressive therapy used in the management of some dermatological diseases.

Many patients may take advantage of the COVID quarantine period to do some cosmetic procedures, thinking that the quarantine period is an appropriate opportunity for healing and down-time of the skin following elective surgery. However, it should be noted that fractionated ablative laser resurfacing may result in narrow columns of dermal injuries, which could theoretically increase the risk of potential infection. Additionally, micro-needling (especially home-based procedures) may carry a high risk of infection and viral auto-inoculation.

Recommended Measures
Since the start of COVID-19 pandemic, many measures and protocols have been taken to reduce the risk of spread of infection, to flatten the peak of the epidemic curve and to prepare the different healthcare facilities to the expected surge of COVID-19 patients.

Based on experience from China, there are specific recommendations:

1. Only urgent dermatological surgeries should be performed.

2. As the majority of the dermatological outpatient visits are elective, it is recommended to cancel all non-urgent visits and only urgent outpatient visits (including surgeries for malignancies) should be performed - provided that adequate protective measures are followed.

3. The capacity of the outpatient clinics should be reduced.

4. Hospital admission should only be reserved for patients with severe skin disease not responding to outpatient treatment.

5. All patients should be screened at the clinic entrance for fever or history of travel to endemic areas.

6. All patients should be wearing masks; however, it is worth mentioning that sometimes the use of masks for patients may be difficult as most of the high-risk carcinomas are located in face region.

7. Doctors should wear mask, goggles, protective suits, head caps and gloves.

8. Practitioners at risk of COVID-19 (60 years or older, immuno-compromised, pregnant or with co-morbidities) should avoid all contact with patients.

In conclusion, COVID-19 has dramatically affected the dermatological practice; however, dermatologists should pay careful attention not to compromise (by cancelling or deferring) urgent and high-risk cases.

Tele-dermatology
One of the medical technologies that has gained much interest during the current pandemic is the tele-medicine that allows the dermatologists to diagnose the patients remotely and prescribe proper treatment, without compromising the social distancing role. There are two types of consultation in tele-dermatology:

1. Synchronous - which includes real-time interaction between the patient and the physician
2. Asynchronous - the patient's data are stored and then reviewed later by the physician.

Interestingly, smart-phone technology (especially WhatsApp) has been proposed to overcome the lack of tele-dermatology equipment in most healthcare facilities. However, it may be limited by the poor video and images quality, and possible medico-legal and privacy issues.

Teaching and other Scientific Activities
The COVID-19 pandemic has also had a great impact on teaching and scientific activities. Remote teaching of medical students and residents through online lectures, seminars and case discussion is safer compared with the classic methods during this critical time.

Immunomodulators / Immunosuppressants use during the COVID-19 pandemic
Immunosuppressants are mainly used in the dermatological practice for the management of autoimmune and inflammatory diseases such as psoriasis, atopic dermatitis, systemic lupus erythematosus, dermatomyositis, pemphigus vulgaris and pyoderma gangrenosum. However, their use during the current pandemic is a matter of debate as a result of the current lack of evidence about COVID-19 risk in immunosuppressed patients.

Conforti et al. suggested that these immunosuppressant drugs may be associated with higher risk of opportunistic infections, as they weaken the immune response. This suggestion was based on previous reports about the increased risk of swine influenza A (H1N1) infection or death in psoriatic patients using immunosuppressant drugs. Therefore, Conforti et al. proposed that the use of biologics should be weighted in endemic areas, with the aim to limit and/or reduce the administration time of these drugs and to stop all immunosuppressants in patients suspected of having COVID-19. Similarly, a consensus of experts' opinion from New Zealand and Australia advised the cessation of all immunosuppressants (except systemic corticosteroids that should not be suddenly stopped or reduced) in COVID-19-confirmed patients for at least 4 weeks, while for patients with influenza-like symptoms, the dose of immunomodulators should be reduced or stopped for a period of 2 weeks.

On the contrary, Bashyam et al. reported that some biologics may even play a protective role and enhance the aberrant immune response to COVID-19. This hypothesis was supported by Bardazzi et al. who reported their experience with the use of biologics for psoriatic patients in Italy during the COVID-19 pandemic. Several other authors reported that a case-by-case evaluation may be more convenient as some of these biologics may not be harmful during the COVID-19 pandemic but even theoretically beneficial and their cessation may be associated with the development of anti-drug antibody.

Generally, the recommendation for the use of immunomodulators should be based on the mechanism of action of each of drug and its associated risk of infection. COVID-19 patients may benefit from IL-17 blockers, especially patients with higher plasma levels of interleukin-17. On the other hand, corticosteroids should be used with great caution as it was associated with delayed viral clearance in SARS and MERS patients, but not with increased mortality. Therefore, routine use of systemic steroids in the management of COVID-19 patients is not recommended by the WHO. The American Academy of Dermatology recommends that patients on biologic therapy without suspicious or confirmed COVID-19, as well as patients considering the initiation of their biologic therapy, should be evaluated on a case-by-case basis and a shared decision (between the physician and the patient) should be considered based on the risk versus the benefit of such therapy, while patients who test positive for COVID-19 should consider postponing or cessation of their biologic therapy.

Similarly, the European Task force on Atopic Dermatitis stated that immunomodulators (including immunosuppressants) should be continued in patients with atopic dermatitis; however, patients should take care of hygienic procedures such as hand washing.

Considering atopic dermatitis patients with positive tests for COVID-19, careful risk assessment should be performed before cessation of immunomodulators as the abrupt stoppage of these drugs

may be associated with exacerbations of the condition and co-morbidities (including asthma, kidney disease and allergy), and topical therapy should be considered during the pause period.

Dermatologic Malignancies

Cancer patients may be at a higher risk for the development of infectious disease with a 3.5 fold increased risk of developing COVID-19 adverse events, including the need for mechanical ventilation and/or death due to their immunocompromised state that is associated to the nature and the aggressiveness of the neoplasm and the anti-cancer treatment. The use of Immune Checkpoint Inhibitors (ICIs) during the current pandemic may represent a matter of concern as a result of the potential overlap between the SARS-CoV-2-related pneumonia and the pulmonary toxicity of the ICIs (however, it should be mentioned that this pneumological toxicity is a rare event ranging from 2.5% to 5% in case of ICIs monotherapy to 7–10% in case of combination therapy). Furthermore, the synergism between the ICIs mechanism of action and the SARS-CoV2 pathogenesis may potentiate the pathological effect of COVID19. In this setting, the use of ICIs should be carefully considered on a case-by-case scenario.

Considering squamous cell carcinoma of the skin, the same precautions (discussed before) should be followed if immunomodulators are considered for treatment.

Other Diseases

Patients with rheumatologic skin disease may be at higher risk for COVID-19 either due to the disease itself or its medications. Furthermore, some rheumatological diseases such as rheumatoid arthritis may be associated with new-onset or reactivation of arthritis during the remission following some viral infections (including coronavirus).

Considering sexually transmitted diseases (STDs), the quarantine and social distancing measures may not only affect physical and psychosocial health of the individuals but also the sexual health. These measures may lower the opportunity for casual sex, which in turn might reduce the incidence of STDs such as syphilis, gonorrhoea and chlamydia in the future. It is recommended not to cancel the visits of STD patients (which can be managed by tele-dermatology or virtual clinics) to avoid consequences including the further spread of the disease.

Occupational skin problems among healthcare workers during COVID-19

Several skin complications may result from the prolonged use of personal protective equipment as a result of hyperhydration effect, friction and allergic contact reactions. Skin damage resulting from wearing protective equipment was shown to be 97.0% in a recent study on healthcare workers, including lesions of the nasal bridge (83.1%), hands, cheek and forehead. It is well documented that excessive hand washing with detergents and/or disinfectants may cause contact dermatitis. A consensus of Chinese experts on the protection of the skin and mucous membranes recommended that handwashing or glove decontamination should be limited to the following moments:

1. Before touching the patients or any aseptic procedure
2. After exposure to body fluids, touching the patient or any of the patients' items.

Furthermore, they recommended the use of ethanol for hand hygiene and applying hand cream following each event of hand hygiene. With latex gloves, it is recommended to wear cotton gloves underneath the latex gloves, and to use moisturisers with topical glucocorticoid cream. Similarly, it is recommended to use a properly fitting mask and goggles and apply moisturisers or gel on contact areas.

Other researchers have suggested the use of double protection (benzalkonium chloride paste on the nasal bridge followed by hydrocolloid dressing) before wearing the N95 masks.

Summary of Recommendations

Dermatologists should pay particular consideration to patients with viral-like skin rash (with or without infection), as some COVID19 patients present with skin rash and petechiae.

1. Non-urgent outpatient visits should be deferred.
2. Fever screening at the clinic entrance in endemic areas using a contact-free forehead thermometer (if feverish, refer to specialised fever clinic).
3. Patients should stick to wearing masks (if possible).
4. Physicians should stick to personal protective equipment.
5. Dermatological surgeries should be restricted to urgent cases (including malignancies).
6. All cosmetic complaints should be postponed.
7. Hospital admission should be limited to patients with severe skin disease not responding to outpatient treatments.
8. Consider tele-medicine and virtual clinics for follow-up and consultation of non-emergency patients.
9. Consider remote teaching through online lectures and seminars.
10. It is recommended to perform a case-by-case evaluation considering the risk and benefit for each patient before stopping biologics during the current pandemic.
11. In patients with confirmed COVID-19, immunomodulators should be stopped until the patient tests negative.
12. The recommendations should be based on the mechanism of action and the risk of infection for each drug.
13. Corticosteroids may be associated with delayed viral clearance but not increased risk of mortality so they should be used with caution.
14. Dermatologists should be careful that COVID-19 may be associated with new-onset or reactivation of arthritis during the remission period of rheumatoid arthritis.
15. It is recommended to use tele-dermatology to continue the consultations of sexually transmitted diseases to avoid the further spread of these diseases.
16. Cancer patients may be at higher risk for development of infectious disease.
17. Immune checkpoint inhibitors should be used with caution in patients with advanced melanoma (due to the lack of evidence regarding the susceptibility of patients using immune checkpoint inhibitors to SARS-CoV-2 infections).
18. Avoid excessive hand washing (just limit it to the moments before and after contact with the patient or patients' items).
19. Use ethanol for hand hygiene and apply hand cream to avoid dermatitis.
20. Wear cotton gloves below latex gloves and use moisturisers with topical glucocorticoid cream.
21. Use properly fitting masks and goggles and apply moisturisers or gel at contact and pressure areas.
22. For N95 masks, use double protection of the nasal bridge (Benzalkonium chloride and hydrocolloid dressing).
23. Avoid dermoscopy for all COVID-19 confirmed patients (except if urgently indicated).
24. Avoid dermoscopy for highly dangerous sites for infection spread as hands, nails, face, eyes and mucous membranes.
25. Sterilise the dermoscope before and after use using 70% alcohol.
26. Consider using disposable dermatoscopic lens or transparent adhesive tape.
27. All patients should be asked about respiratory symptoms, travel history to endemic areas or dealing with a confirmed COVID-19 patient.
28. All physicians should be wearing proper personal protective equipment and keep the distance with the patient as much as possible.
29. Special care of hand hygiene.

As always, for further information, please read the original article.

EAACI/ARIA Position Paper on Practical Considerations on the Organisation of an Allergy Clinic in COVID-19 Pandemic

by O. Pfaar et al.

in **European Journal of Allergy and Clinical Immunology,**
First accepted for publication on 12 June 2020.

Editor's Note:
This article has been accepted for publication by EAACI and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record.

Although this article is the most recent version, it has not yet been published on the EAACI website at www.eaaci.org as a Position Paper.

This free access full article by 30 authors from 17 countries, and comprising 82 pages and 143 references, can be seen and can be **downloaded as a PDF file (link).**

Due to the extreme length of 82 pages of the original article, only a brief and truncated review can be presented here. For full information, please read the original article.

Background
The Coronavirus disease 2019 (COVID-19) has evolved as a pandemic infectious disease transmitted by the severe acute respiratory syndrome coronavirus (SARS-CoV-2). Allergists and other health care providers (HCPs) in the field of allergies and associated airway diseases are in the front line, taking care of patients potentially infected with SARS-CoV-2. Hence, strategies and practices to minimise risks of infection for both HCPs and treated patients have to be developed and followed by allergy clinics.

Method
The scientific information on COVID-19 was analysed by a literature search in Medline, PubMed, as well as national and international guidelines from the European Academy of Allergy and Clinical Immunology (EAACI), the Cochrane Library and the Internet.

Results
Based on diagnostic and treatment standards developed by EAACI, on international information regarding COVID-19, on guidelines of the World Health Organization (WHO) and other international organisations as well as on previous experience, a panel of experts including clinicians, psychologists, IT experts and basic scientists, along with EAACI and the "Allergic Rhinitis and its Impact on Asthma (ARIA)" initiative have developed recommendations for the optimal management of allergy clinics during the current COVID-19 pandemic. These recommendations are grouped into nine sections on different relevant aspects for the care of patients with allergies.

Conclusions
This international Position Paper provides recommendations on operational plans and procedures to maintain high standards in the daily clinical care of allergic patients, whilst ensuring necessary safety in the current COVID-19 pandemic.

Until the publication of this paper, there has been no clear advice on how to manage allergic patients with co-morbid COVID-19 or non-SARS-CoV-2 infected allergic patients during the ongoing pandemic. The European Academy of Allergy and Clinical Immunology (EAACI) in alliance with the global initiative “Allergic Rhinitis and Its Impact on Asthma” (ARIA) has published several recommendations and assessments in the field of allergic diseases, for example allergic rhinoconjunctivitis (ARC), allergic asthma and others regarding pharmacotherapy, Allergen Immunotherapy (AIT), biological treatment and others.

As allergists and other healthcare providers (HCPs) with a focus on allergic diseases are frequently treating patients with manifestations of atopic disease in the upper and lower airways, they are on the front line in caring for patients potentially infected with SARS-CoV-2. As such, the clinical setting in an allergy outpatient clinic or hospital must ensure optimal care for the patients as well as sufficient prophylactic measures to minimise risks of infection for both the medical personnel and the patients requiring treatment. Therefore, clinical procedures in allergy clinics and outpatient practices must be optimised and standardised, within the contextual considerations regarding national regulations.

The aim of this Position Paper - prepared by EAACI in collaboration with ARIA - is to provide allergy clinics, specialised centres and practices with practical recommendations on measures for daily practice and optimal care for allergic patients during the current COVID-19 pandemic.

These recommendations are grouped into nine sections as elaborated by experts including clinicians, psychologists, information technology experts and basic scientists in the field of allergy. These recommendations are conditional and should be adapted regularly on the basis of evolving clinical evidence.

In the published paper, each of these nine sections – as illustrated below - is then explored in some considerable detail. For further information on each of these nine sections, please read the original article.

Section 1 COVID-19: General considerations for HCPs
Key Conclusion: Protective measures should be taken following the general recommendations from the European Centre for Disease Control and the World Health Organization and current rules must comply with the national responsible government agencies.

Section 2 COVID-19: clinical course in allergic patients
Key Conclusion: Viral infections, including infections with Coronaviruses, are associated with aggravation of allergies such as asthma exacerbations. Limited knowledge is available on the differences in the course of COVID-19 infection in allergic compared to non-allergic patients and further clinical evidence is needed.

Section 3 Care of allergic patients: preclinical setting and triage of patients
Key Conclusion: Many clinics and medical offices already use remote health care tools to triage and manage patients after-hours and as part of usual practices. These measures can ideally be used to prioritise and triage allergic patients on the basis of the severity of the allergic disease, the need for in-person consultation and the differentiation of allergic symptoms from clinical symptoms of COVID-19.

Section 4 Challenges and Chances of Information Technology
Key Conclusion: Digital health solutions, especially the use of telemedicine, has been previously proposed as a useful tool to provide medical advice remotely when physical presence is impossible or should be limited to a strict minimum such as in the current COVID-19 pandemic. However, certain limitations of this technology need to be considered and special emphasis should be placed on data-security and protection.

Section 5 Clinical setting
Key Conclusion: General hygiene rules should be followed, especially in the preclinical and clinical setting. The entrance, which is the first point of contact, further patient traffic organisation as well as the triage of allergic patients should be organised to minimize the risks of viral infection. Moreover, the organisation of staff should be optimised, and regular training of procedures should be provided. Any physical contact with the patient should be minimised, and effective preventive measures should be carried out for any further examination and diagnostic procedures.

Section 6 Specific considerations in diagnostic procedures in allergic patients
Key Conclusion: Specific considerations in a clinical setting are necessary for the diagnostic procedures of different allergic diseases during the current pandemic. As SARS-CoV-2 spreads primarily through respiratory aerosols, airways but also other allergy-related organs are affected, and preventive measures should be ensured. These comprise ENT exams (including endoscopy), bronchoscopy, nasal or bronchial allergen provocation tests, tissue-sampling, lung function tests, skin testing and blood-sample collection, drug provocation tests, oral food challenges and oesophageal exams.

Section 7 Specific considerations in the management of different allergic diseases
Key Conclusion: Though avoidance measures during the COVID19 pandemic are similar in different allergic diseases, specific aspects should also be followed in optimal care for allergic rhinoconjunctivitis, asthma, atopic dermatitis, chronic rhinosinusitis, drug allergy, food allergy, urticaria and venom allergy. Different recommendations can be provided for patients with suspected SARS-CoV-2 infection or diagnosed COVID-19 disease versus non-infected individuals or patients having recovered from COVID-19 infection. After recovery from COVID-19, allergy care has to be resumed, but an interdisciplinary consultation is recommended before any further diagnostic or therapeutic procedure.

Section 8 Socio-psychological considerations for allergic patients and optimal care during and after the pandemic
Key Conclusion: Socio-psychological mechanisms play a major role in terms of symptom development, symptom exacerbation and perception in allergic patients. Besides, the general population is highly sensitive to the perception of people showing respiratory symptoms during the COVID-19 pandemic. This increases the risk of stigmatisation of patients with allergies, further increasing the psycho-social stress of patients. Therefore, optimal medical and psychological care for patients with allergies during the COVID-19 pandemic is essential.

Section 9 Considerations for performing non-COVID-19-related clinical trials
Key Conclusion: Clinical trials to combat the COVID-19 pandemic currently have top priority. However, a number of non-COVID-19 trials are also essential and should be continued if they can be conducted in a safe manner. Safety measures and new guidelines need to be established for participants, and research/laboratory staff dealing with non-COVID-19 related clinical trials to ensure the continuation of essential and critical non-COVID-19 trials.

Editor’s Note:
The two sections of most interest to dermatologists, and where there is likely to be the greatest overlap in patients and clinical conditions and clinical recommendations, are section VI on diagnostic procedures and section VII on management of conditions. These two sections are therefore shown below in greater detail, but not full detail.

Specific considerations in diagnostic procedures in allergic patients
The following sections overview the specific considerations for diagnostic procedures in different allergic diseases in a clinical setting during the current pandemic.

The indication and the urgency for these tests should be taken into account and can be confirmed, for example by an initial visit performed via telemedicine. Contraindications for skin tests, provocation tests and lung function tests can be clarified, and this can help to avoid unnecessary in-person consultation with patients during the COVID-19 pandemic.

ENT examination, nasal provocation testing, and sampling procedures
SARS-CoV-2 spreads primarily through respiratory aerosols, and higher viral loads have been detected in nasal swabs compared to other locations. Thus, rhinoscopy, nasal endoscopy, nasal provocation testing, smell- and taste testing and samplings are high-risk procedures.

Nasal provocation tests should be avoided, whereas rhinoscopy, endoscopy and nasal samplings should be limited to patients with an urgent need for examination. A tower with camera, screen and light source can maximise the examiner-patient distance during endoscopy. The use of anaesthetic spray can be replaced by a soaked pledget, thus avoiding virus atomisation. The examiner should wear the adequate personal protective equipment recommended for HCPs: FFP2 or FFP3 face mask, goggles or disposable face shield covering the front and sides of the face, clean gloves, and clean isolation gown.

Aerosols can be generated during spirometry, bronchoprovocation testing, fractionated exhaled nitric oxide (FeNO) measurement and other lower airway sampling procedures. Therefore, routine lung function testing and related procedures should be generally suspended during the current pandemic. In cases of extreme need, the personnel should use personal protective equipment and follow the other safety measures as described above.

Skin testing should be generally suspended during the current pandemic. Nevertheless, exceptions can be considered after a careful/proper risk-benefit assessment or may be replaced by laboratory tests. When collecting biological samples or conducting skin testing, the personnel must use the recommended personal protective equipment and also follow the standard precautions (SP) when handling clinical specimens, all of which may contain potentially infectious materials. In this case, a laboratory gown and a single-use waterproof apron may replace the isolation gown. After collection, samples should be placed in a leakproof primary container, and inserted into watertight secondary packaging with absorbent material. This package should be placed in a rigid outer packaging with appropriate labelling. Sample processing should be performed following biosafety level 2 (BLS-2) practices, the current standard in clinical laboratories.

Aerosols can originate from centrifugation, pipetting, vortexing, mixing, decanting liquids, loading and spilling samples or cleaning up spills. Therefore, these procedures should be performed inside a biological safety cabinet and using centrifuge safety cups and sealed rotors.

Work surfaces and equipment should be appropriately decontaminated and laboratory waste should be handled as biohazardous agents. The inactivation of serum samples suspected to be contaminated with SARS-CoV-2 should be carried out by following the procedure recommended by WHO for serum samples for ELISA-based analysis.

Research procedures involving virus isolation and propagation in cell culture should be conducted in a BSL-3 laboratory. The appropriate minimum containment measures for research procedures other than virus propagation (e.g., flow cytometry) are currently unclear. The addition of a virus-neutralising agent to research samples might be considered to ensure safe processing under BSL-2 conditions.

Cough, sneezing or rhinorrea may occur during drug provocation tests. Therefore, these procedures should not be generally conducted during the current pandemic. Nevertheless, exceptions can be considered after a proper risk-benefit assessment. Examples of these include chemotherapy with oncologic patients, perioperative drugs or radiocontrast media in subjects needing urgent procedures, or antibiotics in infected individuals without any alternative effective drug.

Oral food challenges may induce respiratory symptoms with aerosol-generating potential, together with vomiting and diarrhoea. Importantly, the virus can persist in gastrointestinal fluids for a longer period than in the respiratory specimens. Therefore, oral food challenges should be avoided during the current pandemic, as they lack urgency.

The diagnosis of eosinophilic esophagitis requires a gastroscopy-guided oesophageal biopsy. The performance of a gastroscopy is not recommended during the current pandemic, due to the possible persistence of virus in biological fluids. In the case of extreme need (e.g., frequent food impaction), a proper risk-benefit assessment should be conducted.

In conclusion, specific considerations in a clinical setting are necessary for the diagnostic procedures of different allergic diseases during the current pandemic. As SARS-CoV-2 spreads primarily through respiratory aerosols, airways but also other allergy-related organs are affected, and preventive measures should be ensured. These comprise ENT exams (including endoscopy), bronchoscopy, nasal or bronchial allergen provocation tests, tissue-sampling, lung function tests, skin testing and blood-sample collection, drug provocation tests, oral food challenges and oesophageal exams.

Specific considerations in the management of different allergic diseases.
According to WHO, patients at risk of or with diagnosed COVID-19 should continue their treatment for any other disease (this includes allergic disease) in line with current guidelines. Special consideration should be given to the interference of drugs with COVID-19 or vice versa.

It is generally recommended that patients should have a supply of the medication they need for at least a 14-day quarantine. Where more stringent or lengthy measures of isolation are enforced, consideration must be given to availability of medicines and potential substitutes for current treatments if particular medications cannot be obtained.

Patients should have an action plan to ensure that these issues are covered.

Telemedicine visits cannot replace all personal consultations, notably those mandatory for the administration of subcutaneous allergen immunotherapy (SCIT). Nevertheless, prior to the consultation, questions identifying actual contraindications can be clarified by a telemedicine consultation.

Many of the biologics used for the treatment of allergic diseases (e.g., Omalizumab, Benralizumab, Mepolizumab and Dupilumab) are registered for self-application if the patients are adequately trained in the injection technique and in the assessment and management of allergic side effects. During telemedicine visits, injection techniques may be rechecked, and patients' questions answered regarding the treatment.

Peak flow protocols can be discussed during a telemedicine visit, and treatments can be adapted. In general, patients can be instructed on allergen avoidance measures and treatment modalities. They can show the drugs they have at home and can be instructed on the use and especially on the application techniques of inhalers and topical nasal sprays.

Patients suffering from anaphylaxis may be trained to use adrenaline auto-injectors for self-administration; this improves safety and may also improve the patient's quality of life.

As a general rule, patients with severe allergic disease who are on biologicals and have a SARS-CoV-2 infection should pause the biologicals. Proper management and background controller treatment (topical steroids or other controller medications as recommended by current guidelines) should be continued as prescribed. If resolution of the disease is established (e.g., via a negative SARS-CoV-2 test) at a minimum of 2 weeks post onset/positive testing, the re-administration of the biological should be reinitiated.

Importantly, self-identified and physician-diagnosed (via skin prick test, blood test, provocation testing) triggers of asthma exacerbation and allergies (seasonal, food allergies, etc.) need to be understood for each patient. Targeted messages to patients who have a known allergen sensitivity may be a meaningful way of connecting with patients during a time of limited in-person clinic visits (e.g., reminder alerts that the spring season has arrived). Educational outreach messages or tele-visits can include instructions on allergen avoidance, indoor air purifiers, proper medication use (e.g., reviewing the appropriate use of inhalers with spacers). Food scarcity during pandemic operations may adversely impact food-allergic families and strategies for planning and stocking safe foods should be discussed. Medication supply should also be addressed in conversations with patients to plan for adequate controller and rescue medication with the possibility of substituting or switching medications as needed.

Atopic dermatitis
AD is one of the most common skin disorders. The lifetime prevalence varies between 0.2% and 25% worldwide, the most affected area being the northern part of Europe. The disease most often starts in early childhood and persists into adult life in up to 50% of affected patients.

Co-morbidities with other atopic diseases including asthma, allergic rhinitis and food allergy are common. Most cases with mild to moderate atopic dermatitis can be controlled on topical treatment. However, in the severe cases, systemic immune-modulating treatments including immuno-suppressive therapy is needed.

Conventional systemic immuno-suppressive treatment, such as Cyclosporin, may interact with the human body's defence mechanisms against viral disease, while Dupilumab, which is registered in many countries for the treatment of moderate to severe atopic dermatitis, selectively interferes with type 2 inflammation and is in general not considered to increase the risk for viral infections.

It is well known that viral and bacterial infection may complicate and exacerbate atopic dermatitis including infections with *Staphylococcus aureus* (impetigo), poxvirus (*Molluscum contagiosum*) and *Herpes simplex* virus (eczema herpeticum). Severe and untreated atopic dermatitis is a known risk factor for disseminated viral skin disease.

In the current SARS-CoV-2 pandemic, the European Task Force on Atopic Dermatitis (ETFAD) recommends the continuation of all immune-modulating treatment since exacerbations of any underlying diseases can have a large negative impact on the patient's immunity. However, patients at risk are advised to strictly follow the recommendations issued by the local health authorities in each European country. The British Association of Dermatologists (BAD) has specifically addressed potential issues regarding the COVID-19 infection of patients undergoing immune-modulating treatment. Other countries will follow.

A thorough hygienic procedure is recommended with hand washing and disinfectants. Non-irritant soap substitutes should be used following the same instructions as those for regular soap. Moisturisers should be applied afterwards.

In the case of COVID-19-infected atopic dermatitis patients, inter-disciplinary risk assessment should be carried out and, in accordance with current guidelines on active infections and systemic therapy, the immune-modulating therapy may or may not be paused afterwards. If any systemic treatment is paused, it is important to optimise the topical treatment. Furthermore, if the paused systemic treatment also has an effect on co-morbidity such as asthma, then the co-morbidity also has to be treated by other drugs.

According to a letter from Italy regarding 245 patients on therapy with Dupilumab, only two developed COVID-19. An abnormal course of COVID-19 was not observed in these 2 patients. More clinical data are needed for this specific treatment.

Urticaria
Urticaria is characterized by the development of wheals (hives), angioedema or both. Acute urticaria is defined as the occurrence of wheals, angioedema or both for less than 6 weeks. Chronic urticaria is defined as wheals, angioedema or both for 6 weeks or more.

Viral infection has been found as a potential trigger - and sometimes as the main etiologic agent - in causing acute or chronic urticaria.

In Italy, 88 patients with COVID-19 were studied by a group of dermatologists. 20% developed cutaneous symptoms including erythematous rash and urticaria. It was concluded that the skin manifestations related to the COVID-19 infection are similar to those occurring during common viral infections.

In France, among 103 out- and in-patients with confirmed COVID-19 infection, two had urticaria.

In a study from China, 1.4% of the COVID-19 patients reported an underlying urticaria. However, skin symptoms during the infection were not described.

The manifestation of urticaria could appear before the onset of fever or respiratory symptoms. As a consequence of these observations, the manifestation of acute urticaria could be an indication to test for SARS-CoV-2.

According to the guidelines, second-generation H1-antihistamines are the base of urticaria treatment and should be continued during the pandemic. If urticaria cannot be controlled on antihistamines in four-fold dose, Omalizumab is recommended as an add-on treatment. Omalizumab is registered for self-administration after patients have received training on the injection technique and on the assessment of allergic side effects. Only the first two injections need to be administered in hospital, due to the risk of anaphylaxis. Therefore, especially during the COVID pandemic, treatment at home is favourable. The efficacy of the treatment can be evaluated and patients' questions regarding the treatment may be reviewed by telemedical visits. This is currently recommended by the BAD.

As for all COVID-19 infected patients, inter-disciplinary risk assessment should be performed and, in accordance with current guidelines on active infections and systemic therapy, the immune-modulating therapy may or may not be paused afterwards.

As always, for full information, please read the original article.

Anaphylaxis to the first COVID-19 vaccine: Is polyethylene glycol (PEG) the culprit?

by Lene H. Garvey and Shuaib Nasser
in **British Journal of Anaesthesia, 17th December 2020.**

The day after the world watched the first person receiving the coronavirus disease 2019 (COVID-19) vaccine on December 8, 2020, reports of three cases of suspected allergic reactions in connection with the vaccine emerged from the UK. Two were reports of anaphylaxis in healthcare workers, with onset within minutes of vaccination, and responding well to treatment with epinephrine. Both recovered fully and were reported to have severe allergies to foods and drugs, respectively. The third case was less severe and did not require epinephrine.

Immediate-type life-threatening reactions to vaccines are exceedingly rare; they are reported to occur in 1.3 cases per million doses. Therefore, two cases of anaphylaxis on the second day of a vaccination campaign with a new vaccine require further scrutiny. The first important task is to confirm that these cases were indeed anaphylaxis. If anaphylaxis is proved likely, the cause of the reaction should be identified.

The active ingredient is rarely the cause, and the focus should be directed at the many excipients usually present in vaccines. A recent review of the literature showed that rare cases of immediate hypersensitivity reactions to excipients have been described for adjuvants/preservatives; antimicrobials; and a single case of a reaction to polysorbate 80, a polymer with structural similarities to polyethylene glycol (PEG).

Hypersensitivity reactions to vaccines containing gelatine and egg had only been described in patients with previous known hypersensitivity to gelatine and egg. In fact, large studies have shown a very low risk of immediate reactions to ovalbumin in influenza vaccines in patients with allergy to eggs, and the recommendation to these patients is that the risk of anaphylaxis is no higher than for non-allergics. The COVID-19 vaccine from Pfizer/BioNTech recently introduced in the UK, USA, and other countries is a messenger RNA (mRNA)-based vaccine (tozinameran, BNT-162b2) using lipid nanoparticles to facilitate the transport of mRNA into cells. The vaccine contains a number of excipients and lipids, one of them based on PEG-2000. This is currently the only excipient in the vaccine with recognised allergenic potential. The severity and rapid onset of the two reported reactions to the vaccine further increase suspicion towards PEG.

Allergy to excipients is often overlooked because of a lack of knowledge about their allergenic potential. However, allergy to PEG, also often called macrogol, has been reported with increasing frequency over recent years. Patients have usually had repeated systemic allergic reactions/anaphylaxis before diagnosis. A typical history is of severe allergic reactions to several classes of drugs, for example, penicillin, laxatives, injected corticosteroids, or antacids, all containing PEG.

Symptoms are of rapid onset, usually within minutes, and typically result in severe generalised pruritus, urticaria, angioedema, hypotension, or difficulty in breathing. Reactions are more severe with higher doses and with higher-molecular-weight PEGs.

Polyethylene glycol is an ingredient in many laxatives, in about 30% of tablets and is used as a

surfactant in many injectable formulations, where a prolonged effect is needed, such as in depot steroids. More recently, the technology of PEGylation has been introduced to enhance drug delivery in many areas of medicine. No reactions to PEG in vaccines have been reported, but PEG has not been a commonly used excipient in vaccines until now.

The mechanism of sensitisation to PEGs is unknown, but from the cases described in the literature and the author's personal experience with a total of 18 patients with PEG allergy, there is no reason to believe that existing inhalational or food allergies predispose to PEG allergy. However, PEG allergy may be suspected in patients with very severe reactions to drugs where the cause is unconfirmed, or patients with repeated immediate-type reactions to several structurally unrelated drugs or other products containing PEG.

The potential benefit of an effective COVID-19 vaccine is far reaching and a potential solution to a substantial threat to global health. The risk of hypersensitivity and ultimately anaphylaxis is present for all drugs, including vaccines, although usually low and is offset by the benefits of the drug.

Randomised clinical trials of the Pfizer/BioNTech COVID-19 vaccine in >22,000 individuals receiving the active treatment were independently reviewed by the US FDA (Food and Drug Administration) and were then presented at an advisory committee meeting for emergency approval of the vaccine on December 10, 2020. The FDA found a small signal towards more hypersensitivity cases in the vaccine group, but none of the reactions were immediate, severe, or requiring epinephrine.

Exclusion criteria for the clinical trials of the vaccine included individuals with known hypersensitivity to vaccines, or with a history of allergy, hypersensitivity, or intolerance to the COVID-19 vaccine or its excipients according to the registration of the trials on ClinicalTrials.gov. At the FDA advisory committee meeting, the cases of anaphylaxis in the UK were discussed at length. The advisory committee voted 17 to 4 in favour of granting Pfizer emergency approval for the vaccine, which was granted on December 11, 2020. The FDA requested that a warning be added to the product information that medication to treat immediate-type hypersensitivity reactions should be available where vaccinations take place. Also, the FDA advised that the vaccine should be contraindicated in patients with a severe allergic reaction to the first dose of vaccine, or with known hypersensitivity to any ingredient/component of the vaccine. Finally, a stringent surveillance system is to be initiated to monitor adverse effects of the vaccine, with monthly reporting.

In the UK, based on the anaphylactic reactions reported, the present advice from the UK Medicines and Healthcare products Regulatory Agency (MHRA) is that 'any person with a history of anaphylaxis to a vaccine, medicine or food should not receive the Pfizer/BioNTech COVID-19 vaccine'. This is very likely to be overly cautious, but understandable, to maintain public confidence in the vaccine until more detailed information about the reactions is available. The individuals who have expeienced allergic reactions to the vaccine in the UK should be urgently investigated to determine the mechanisms behind the reactions and the potential involvement of PEG. The reported history of previous severe allergies should be scrutinised, and their causes determined. Once details are available, it is very likely that more specific recommendations about at-risk groups can be made to modify the rather broad current MHRA recommendations.

As a rule, allergy to foods, single drugs, or insect venom does not predispose to allergy to other drugs or vaccines. Tryptase measurement taken 0.5 to 2 h after the reaction should help determine if this was indeed anaphylaxis. As in all allergic reactions occurring in a hospital setting, other potential allergens, such as disinfectants (e.g., chlorhexidine) and latex, should be excluded.

Investigations for allergy to PEG currently include skin testing, but *in vitro* tests may be in the pipeline. As systemic allergic reactions have been reported in connection with skin prick testing in PEG-allergic patients, the development of a reliable *in vitro* test is urgently needed.

In conclusion, allergic reactions to vaccines are exceedingly rare, and there is no reason to believe that this has changed. PEG has not been used previously as an excipient in vaccines with this potential for wide dissemination, but even if PEG is concluded to be the cause, then allergy to this excipient is also very rare. As soon as a plausible explanation for the suspected vaccine reactions has been found, clear recommendations can be made for a safe vaccination strategy.

At this stage, it is important that events such as these do not lead to misinterpretations and detract from global implementation of the vaccine. The fact that these severe reactions have appeared early in the implementation of the vaccine should remind us all that anaphylaxis is a rare risk of drug administration, including vaccines. Anaphylaxis has a good prognosis when diagnosed and treated promptly and correctly. Vaccination centres should be made aware of the risk of anaphylaxis and have trained staff and equipment immediately available to treat anaphylaxis. If such precautionary measures are taken, combined with continued close surveillance of potential hypersensitivity reactions, then the benefits of the COVID-19 vaccine clearly outweigh the risks, and we can finally start hoping for an end to the COVID-19 pandemic.

As always, for full information, please read the original article.

First case of DRESS syndrome caused by hydroxychloroquine with a positive patch test

by Araceli Castro Jiménez, et al,
in **Contact Dermatitis, Vol 84, Issue 1, January 2021, pp 50-51.**

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, (formerly known as drug-induced hypersensitivity syndrome) is an acute, idiosyncratic, and potentially life-threatening drug reaction, characterised by fever (>38.5 degrees C), skin eruptions, and haematological abnormalities. The most frequently involved drugs are anticonvulsants, sulphonamides, allopurinol, and antibiotics, while hydroxychloroquine has been rarely reported as a causative agent.

The patient had been treated in the previous 2–3 weeks for bilateral pneumonia as manifestation of suspected, but not confirmed, COVID-19, with hydroxychloroquine 200 mg and lopinavir-ritonavir 200/50 mg/12 hours and azithromycin 250 mg/ day for 5 days.

Laboratory tests showed leucocytosis with eosinophilia and elevated transaminases. An abdominal ultrasound was normal, and no atypical lymphocytes were found. Bacterial cultures and viral serologies, including SARS-CoV-2, were negative except for IgG for cytomegalovirus, parvovirus B-19, Epstein–Barr virus, chickenpox, and measles, which were all positive.

After 8 weeks, patch tests were performed with lopinavir/ritonavir, hydroxychloroquine, and azithromycin (each 20% aq. and pet.), which were positive for hydroxychloroquine only, on day 4. Therefore, DRESS was diagnosed in accordance with RegiSCAR group criteria, and an atypical DRESS according to SCAR-J's criteria, caused by hydroxychloroquine.

Hydroxychloroquine has been used as an anti-malarial. Nowadays, it is used in autoimmune diseases such as lupus and rheumatoid arthritis. The growth of many different viruses can be inhibited in cell culture by chloroquine and hydroxychloroquine, including SARS-CoV-2. Therefore, it had been prescribed to our patient with suspected COVID-19.

Hydroxychloroquine is considered to be safe and side-effects are generally mild and transitory. The most common adverse effect of hydroxychloroquine is a skin rash; however, in our patient, DRESS syndrome caused by hydroxychloroquine was diagnosed, based on patch testing that proved useful for identifying the causative drug in this patient.

In conclusion, the first case of DRESS syndrome due to hydroxychloroquine was identified with a positive patch test.

Paediatric contact allergy: A comparative study with adults

by Waranya Boonchai et al,

in **Contact Dermatitis, Vol 84, Issue 1, January 2021, pp 34-40.**

Background
Paediatric allergic contact dermatitis is increasing. The patch test allergens included in paediatric baseline series vary globally. The worldwide prevalence of paediatric reactions to allergens needs clarification.

Objectives
Identify the prevalence, associated factors, and culprit allergens for contact allergy among patch-tested Thai children, and compare with those for adults.

Methods
Baseline series patch test results from 2010–2019 were collected for patients younger than 18 years of age into Bangkok Hospital, Thailand.
As a control group, sex-matched adult patients were randomly selected.
The results and characteristics of the two groups were compared.

Results
The median age of 112 patch tested paediatric patients was 16 (range 2–17) years.
Of the children, 35.5% had at least one positive reaction, significantly less than the 56.6% for adults.
The five most common paediatric allergens were:

1. Nickel sulfate (12.1%),
2. Potassium dichromate (8.0%),
3. Methylisothiazolinone (7.1%),
4. Fragrance mix II (6.0%),
5. Carba mix (5.4%).

Although similar, the 10 most common allergens of the groups differed in order.
Positive reactions to cosmetic allergens were significantly less frequent among the children.
Many allergens remained entirely negative.

Conclusions
The prevalence of positive reactions was lower in children, varying by population and region. The top-10 paediatric and adult causative allergens were almost identical. We recommend using the same baseline patch test series for children and adults in our region.

Allergic contact dermatitis (ACD) is a common skin condition that typically develops as a result of prolonged and repeated skin exposure to certain chemical agents. The causative allergens of this condition are determined by patch testing. Even though ACD mainly affects adults, its prevalence in the paediatric population is increasing and has been reported to be as high as 20% among patients younger than 18 years of age. The prevalence of contact sensitisation varies with respect to geographic localisation. Little is known about paediatric contact sensitisation, especially among Asian children generally.

The baseline series had been adapted from the European and the International baseline series. Both children and adults were tested with the same individual allergen concentrations.

The haptens (Chemotechnique Diagnostics, Vellinge, Sweden) were applied in aluminium Finn Chambers (SmartPractice, Phoenix, Arizona) placed on unaffected skin of the upper back. The patches were removed after 48 hours. Reactions were evaluated on day (D) 2 and D4 after the placement of the patches. No significant patch-testing complications were reported.

None of the children reacted to Compositae mix II, sesquiterpene lactone mix, hydroxyisohexyl 3-cyclohexene carboxaldehyde, diazolidinyl urea, imidazolidinyl urea, lanolin alcohol, p-tert-butylphenol formaldehyde resin, epoxy resin, toluenesulfonamide formaldehyde resin, budesonide, tixocortol-21-pivalate, hydrocortisone-17- butyrate, mercaptobenzothiazole, or N-isopropyl-N-phenyl-p-phenylenediamine.

Therefore, it could be concluded from this study results that patch testing is not an age-specific procedure and can be considered to have diagnostic value in children of any age.

No adverse events were found in this investigation. Patch testing is safe in children using the same allergen concentrations as for adults. However, sensitisation to the allergens in patch testing should be further investigated to determine the long-term safety of patch testing in children.

Globally, the prevalence of atopy among paediatric patients (15%– 20%) is greater than that among adults (only 1%–3%). This has no doubt contributed to the high prevalence of atopy in the paediatric group in the present study (58.9%). The investigators found that either having a history of personal or family atopy, or meeting the Hanifin and Rajka atopic dermatitis criteria, was an important associated factor for a positive patch-test result for the children in the study.

The relationship between atopic dermatitis and ACD in children is controversial. Some studies have identified a correlation between these two conditions, yet other studies have found no evidence in support. In the current research, the investigators found similar proportions for the final diagnosis of ACD in patients with and without a diagnosis of atopic dermatitis. By contrast, another study found that Asian children who underwent patch-testing had a significant degree of concurrent atopic dermatitis, particularly if they presented with a longer-standing and greater severity of dermatitis.

Notwithstanding the diverse reviews and despite ACD being less common among children, children with atopic dermatitis should be referred for patch testing. This is because atopic dermatitis and ACD can occur simultaneously, and external and preventable causes should be ruled out.

The number of patients who had main lesions on their extremities was found to be significantly higher in the paediatric group. This is consistent with the higher-than-usual prevalence of atopy that was found among the children, given that atopic dermatitis usually affects the flexural areas of the elbows and knees. In addition, atopic children are more likely to be recommended to use skincare preparations on their extremities.

On the other hand, facial dermatitis was found less frequently in the paediatric group than in the adult group, which might be explained by their having less exposure to facial cosmetics.

Finally, a history of drug allergies was found to be significantly lower in the paediatric group due to their lower exposure than adults.

The prevalence of the positive patch-test reactions among the paediatric patients was significantly lower than those of the adult patients, who had been matched for sex, race, and season of the year. This can be explained by the children most probably having been exposed to smaller amounts of the allergens, and for shorter periods, than the adults.

The European Union has enacted legislation limiting the use of nickel in objects that might come into contact with the skin; in contrast, Thailand currently has no equivalent regulations. Despite that, the prevalence of contact allergy to nickel among Thai children has been found to be similar to that for European children. This seemingly inconsistent situation can be explained by there being many nickel substitutes nowadays (for instance, plastic, titanium, zirconium, rhodium, sterling silver, and stainless steel). Children may show even less nickel sensitisation in the future.

Currently, there is no consensus about the allergens that should be included in the paediatric baseline patch test series. According to the European Academy of Allergy and Clinical Immunology Task Force on Allergic Contact Dermatitis in Children, the paediatric baseline series was endorsed with the understanding that additional allergens should be added to cater for the specific conditions and exposure patterns in any given region.

In the present study, the same top 10 positive allergens were found with both the adults and the children. This result supports the notion that the current adult baseline series (an integration of the international and European baseline series) can also be used with children. However, 14 of the 32 allergens in our current screening patch-test series yielded a zero-sensitisation prevalence in the 102 children in the study during the past decade, which suggests that the children were not exposed to those allergens during that period. If there is only a limited area of paediatric skin available for patch testing, those 14 allergens could be omitted, provided the patient has no suspected history of exposure to them.

According to the paediatric baseline series recommended by the American Contact Dermatitis Society, a number of paediatric ACD cases in this study might be missed because some recommended allergens are not tested in our patients. The additional allergens that showed high prevalence (such as propylene glycol, bronopol, propolis, and Amerchol L-101) should be considered.

Conversely, potassium dichromate and p-phenylenediamine, which were found as the second and tenth most common culprit allergens in this study, are not included in the recommended American paediatric baseline series. Therefore, selecting additional allergens for patch testing and revising the series for children in different regions is as necessary as for adults.

This report of a rare Asian study in the field provides vital information that will contribute to the eventual development of an international paediatric baseline patch-testing series, a crucial tool for the long-term management of paediatric ACD.

Clinical relevance of positive patch test reactions to lanolin: A ROAT

by Ada Uldahl et al,

in **Contact Dermatitis, Vol 84, Issue 1, January 2021, pp 41-49.**

Background: Lanolin is often included when patch testing for common contact allergens. The clinical relevance of a positive patch test reaction to lanolin markers is, however, still a subject for debate.
Objectives: To evaluate Amerchol L101 as a marker of lanolin allergy and investigate the clinical impact of lanolin-containing moisturisers on healthy and damaged skin using the repeated open application test (ROAT).
Methods: Twelve test subjects and 14 controls were patch tested with Amerchol L 101 and additional lanolin markers. Subsequently, a blinded ROAT was performed on the arms of the study participants for 4 weeks. Each participant applied a lanolin-free cream base and two different lanolin-containing test creams twice daily on one arm with intact skin and on the other arm with irritant dermatitis, induced by sodium lauryl sulfate (SLS).
Results: Eleven test subjects (92%) had positive patch test reactions to Amerchol L 101 when retested and one test subject (8%) had a doubtful reaction. None of the study participants had any skin reactions to the ROAT on intact skin and all participants healed during the ROAT on damaged skin.
Conclusions: Lanolin-containing emollients do not cause or worsen existing dermatitis when performing ROAT in volunteers patch test positive to Amerchol L101.

In 1922, a German report described a patient who developed a “skin reaction” when using a cream containing 6% wool alcohol. There were at the time many similar reports, so lanolin was included in the early baseline series, and has been there ever since.
Due to its emollient properties, lanolin is widely used in medicaments and skin care products, for example, for atopic/dry skin, wound healing, and in nipple care creams. Lanolin is also found in leather softeners and as a lubricant in ball bearings.

Lanolin is derived from the secretions of the sebaceous glands of sheep and the composition may vary depending on the sheep’s breed, geographic location, and methods of extraction, etc. The product named “lanolin” is actually a mixture of substances and much effort has been put into finding the potential allergens. Most researchers state that the allergen resides in the alcoholic fraction, but oxidation with the production of possible haptens has also been found to be of importance. While at the start lanolin may vary in composition, the refining and purifying processes may also differ and, therefore, the end product becomes difficult to define in detail. Thus, the question arises of whether the lanolin chosen for patch tests is representative of the lanolin derivatives encountered in products.

Over the years, manufacturers of lanolin-containing products have refined lanolin and claim the lanolin used today is free from sensitisers and, therefore, no longer a source of lanolin contact allergy. As a result of this notion, the clinical relevance of a positive patch test reaction to lanolin has been questioned.

The primary aim of the study was to evaluate Amerchol L101 as a marker of lanolin allergy.

A second objective was also to investigate through the use of ROAT whether lanolin or lanolin derivatives in commercially sold creams can elicit a skin reaction on healthy and damaged skin, respectively, in those testing positive for Amerchol L101.

Comparison between patch testing with markers of lanolin allergy and additional lanolin derivatives was considered another objective. All participants were initially patch tested with a dilution series of Amerchol L101 (Chemotechnique Diagnostics, Vellinge, Sweden), two dilutions of lanolin alcohol (Chemotechnique Diagnostics) as well as a commercially available cream marketed to contain “pure lanolin”.

Patch testing with the commercially available markers simultaneously, namely Amerchol L101 “as is” and 50% pet., and lanolin alcohol 30% pet., has shown poor concordance, which was also the case in the present study. Additionally, there seems to be no correlation between a positive reaction to the test substances used as markers of lanolin allergy and the lanolin derivatives that were purchased for testing, i.e., those that are actually used in leave-on products. This is consistent with other reported study results and the recommendation of testing with patients’ own products in case of a clinical suspicion of lanolin contact allergy.

Positive patch test reactions to lanolin are often reported to be more common among atopic dermatitis patients. The explanation has mainly been an impaired barrier function and a higher expo- sure to emollients, thus also lanolin-containing ones. The observation made in the present study cannot be explained by overrepresentation of either atopy or atopic dermatitis in the test group since the individuals with atopic constitution did not have slower healing time. The majority of reactions to lanolin preparations are + reactions and reactions stronger than ++ are rare. This is consistent with the clinical experience in the clinic of the study authors and is reflected in the present study results. It is reasonable to expect a faster or stronger elicitation of a contact allergic reaction in an individual with a strong (++/+ ++) patch test reaction as compared to a weak (+) reaction to the relevant allergen.

It is said to be difficult to read patch tests of lanolin-related test substances, and the reproducibility of the positive patch test reaction is low. Studies have shown that in repetitive testing, weak + reactions to contact allergens can alternate with doubtful reactions to the same allergen.

In this study we could reproduce our results with regard to positive or negative reaction when patch testing with Amerchol L 101 “as is” except for a new +reaction in one control and a doubtful reaction in one test subject. However, the strength of the reaction was not reproducible in five of 12 previous Amerchol-positive individuals, which is also quite often the case for other test substances. From the results found in the present study with regard to patch testing with Amerchol as compared to the lanolin derivatives actually used in products tested here, there seems to be no correlation.
It is difficult to explain the discrepancy between patch test reactions with different lanolin markers, the ROAT results as well as finding of more doubtful reactions to the other lanolin markers and the delayed healing time *per se*, including for the cream base in the test subject group. A possible interpretation of the results is that Amerchol allergy is a false-positive, i.e., not a true sign of contact allergy, even though fulfilling the morphological criteria for a positive reaction. This has also been proposed because of the low reproducibility, a higher prevalence of lanolin reactions in children, and doubtful reactions to lanolin being common.

If arguing in favour of lanolin not being a true contact allergen but a marker of unspecific reactivity in the skin, it appears the reactivity provoked by lanolin differs from the reactivity induced by SLS or the sensitivity observed in atopic skin.
Our results support the clinical observation that many patients found to have contact allergic to lanolin or Amerchol L101 seem to be able to use lanolin-containing emollients on healthy skin without eliciting a skin reaction.

Tea tree oil contact sensitisation in children

by Anna Zambello et al,
in **Contact Dermatitis, Vol 84, Issue 2, February 2021, pp 139-140.**

Melaleuca alternifolia is a coniferous tree of tropical regions. The needles contain an essential oil used in “medical” and cosmetic products that contains terpenes (limonene, alpha-pinene, phellandrene) which are potentially sensitisers.
Tea tree oil (TTO) is nowadays increasingly popular in a variety of household and personal-care products, including shampoos, massage oils, skin and nail creams, and laundry detergents. TTO is known to be used for its potential antiseptic, antifungal, and disinfectant action, for example, to treat infections, burns, and pain, with considerable interest in this “natural” antimicrobial agent.
Allergic contact dermatitis caused by TTO has been reported frequently in adults, with positive patch test reactions to TTO varying from 0.1% to 3.5%.
In this study, the authors evaluated the prevalence of contact sensitisation to TTO in 695 children (age: 1-18 years) with clinically suspected allergic contact dermatitis, referred to our paediatric dermatology unit during a period of 5 years (2015-2020). These 695 children were tested with our paediatric standard patch test series, which included TTO 5% pet. and an additional 32 haptens corresponding to the European Baseline Series, supplied by Chemotechnique Diagnostics (Vellinge, Sweden) on Scanpor plaster and Finn chambers for 48 hours. The sites were examined at day (D) 2 and D4, according to the International Contact Dermatitis Research Group guidelines.

Three patients (0.43%), all male, and 9-, 10-, and 13-years-old, had a positive patch test reaction to TTO: Two children tested positive in 2018 (yielding a 1.21% prevalence of contact sensitisation to TTO in that year), and one child was positive in 2019.
All three patients had a + (weak positive) reaction and showed a crescendo or plateau pattern from D2 to D4.
In all three children there was history of atopy: one with mucosal atopy and atopic dermatitis, one with mucosal atopy, and one with a family history of atopy.

In the three patients with TTO sensitization, the manifestations were diverse, with a predominance of desquamation and itching, and dermatitis was localised in visible areas: One child had clinical symptoms on the face and upper limbs; one boy in the periorbital region, hands, and ankles; and one child on the hands, palms, and peri-ungual region.

All three had more than one positive reaction: One child also reacted to lanolin alcohols, *Myroxylon pereirae*, colophonium, and fragrance mix; one child also reacted to *M. pereirae*, neomycin sulphate, cobalt chloride, and nickel sulphate; one boy reacted carba mix.

In all three patients, TTO positive patch test reactions were clinically relevant, as the allergen was traced in topical products containing TTO (detergents and hand cream) used by the children.

The authors conclude that it might be useful to add TTO to the paediatric screening patch test series when investigating contact dermatitis in children with an airborne exposure pattern, above all in those with multiple hypersensitivity.

As always, for further information, please read the original article.

Patch test results with the European Baseline Series and additions thereof in the ESSCA network, 2015-2018.

by Wolfgang Uter et al,
in **Contact Dermatitis, Vol 84, Issue 2, February 2021, pp 109-120.**

ESSCA is the European Surveillance System on Contact Allergies, which includes 48 active departments from 13 countries of Europe.

The ESSCA is a working group of the ESCD. Its objective is the clinical surveillance of contact allergy. The ESSCA Working Group comprises 25 Dermatologists from around Europe.
The ESSCA Working Group is the author of this prestigious and voluminous publication.

For full information, please read the original article.

Clinical surveillance of the prevalence of contact allergy in consecutively patch tested patients is a proven instrument to continually assess the importance of contact allergens/haptens assembled in a baseline series.

The objective of this study was to present current results from the European Surveillance System on Contact Allergies. Anonymised or pseudo-anonymised patch test and clinical data from various data capture systems that were used locally or nationally were transferred to the Erlangen data centre, where they were pooled and descriptively analysed after quality control.

In the 4 years (2015-2018), data from 51,914 patients patch tested with the European Baseline Series (EBS) of contact allergens were analysed.

The four most commonly positive results were:

Nickel	17.6%
Fragrance mix I	6.9%
Methylisothiazolinone (MI)	6.2%
Myroxylon pereirae resin (BoP)	5.8%.

Results with national additions to the baseline series provide important information on substances possibly to be considered for inclusion in the EBS.

Nickel, Chromium & Cobalt
Taken together, and dominated by nickel, the three metals included in the EBS most commonly cause contact allergies. Age-stratified results showed a lower prevalence of nickel allergy in the youngest age group, compared with the quite broadly defined middle age group. This may reflect to some extent a limited decline of nickel contact allergy. However, despite a considerable success of preventive efforts, nickel exposure prevention needs further improvement.

The prevalence of chromium contact allergy is lowest in the youngest age group; however, because chromium is a less ubiquitous allergen, the success of prevention (reduction of hexavalent

chromium in cement and more recently, in leather) should best be reviewed in particularly exposed subgroups, for example, in the building industry and in patients with shoe (foot) dermatitis.

Cobalt, in contrast to the other two metals, does not display any age pattern. Given the general difficulty in identifying clinical relevance for sensitisation to cobalt, it is difficult to identify relevant exposures which need to be addressed by further research and, ultimately, prevented.

Fragrances

Fragrances are the next most common group of substances or mixtures causing contact allergy. Positive patch test reactions to FM I show a well-known age gradient, possibly owing to the life-long cumulative exposure and steadily increasing risk of sensitisation. It is unclear, at least by just looking at the FM I results, whether the lower prevalence in the younger patients also reflects self-regulatory concentration restrictions concerning FM I constituents in cosmetics taken in the past. A similar pattern is seen for FM II and its main allergenic constituent, hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC). In view of the recent ban of HICC, and the *de facto* ban of *Evernia prunastri* (oak moss) due to the restrictions on (chlor)atranol, a re-design of the mixes could be considered in due time, to adapt these to the currently relevant exposure conditions in Europe. The age gradient of positive reactions to *M. pereirae* (balsam of Peru) is even more marked than that of FM I. This “ill-defined natural fragrance mix” is an apparently important, but also enigmatic allergen, concerning the consequences of a positive patch test for the patient.

MI/MCI

The dramatic increase of contact allergy prevalence to MI and, parallel to this, to the mixture methylchloroisothiazolinone (MCI)/MI 3:1 in the recent past, and the decline since 2013/2014 is well documented and widely known. The fact that MI 0.02 and 0.05% aq. elicited a slightly higher share of positive reactions than MI 0.2% as recommended appears counter-intuitive but should not be overinterpreted: (a) different sub-groups of patients had been patch tested, and (b) the prevalences are not significantly different, if overlapping 95% CIs are considered. The lesser decrease of MI 0.2% aq., as compared with 0.05% aq., during the study period characterised by a marked decrease of MI sensitisation prevalence may have partly contributed to the seemingly similar yield of patch reactions with the two concentrations. The same holds true for formaldehyde, while MCI/MI and methyldibromoglutaronitrile (MDBGN) show a pattern one would expect.

MDBGN

In 2005, the European Union (EU) banned the use of MDBGN in leave-on cosmetic products, and then in 2007 banned it also in rinse-off cosmetic products. The fact that patients up to the age of 30 years had positive patch test reactions to MDBGN in 2015 to 2018 may imply that these individuals were all sensitised to MDBGN in cosmetics by the age of 20 years. Alternatively, or additionally, there may be exposure from rogue cosmetics, unregulated use in medical devices, cosmetic products marketed as medical devices, undeclared exposure, or non-cosmetic sources such as paints, glues, or technical fluids, although such broad exposure to MDBGN is largely unknown presently. From this background, reporting on patients with currently relevant contact allergy to MDBGN is encouraged. A cautionary note is that false-positive reactions particularly to MDBGN 0.5% pet. may occur. As sensitisation to paraben mix and quaternium-15 is now uncommon, the continued inclusion of these allergens in the EBS may be only marginally justifiable. The mixture of MDBGN and 2-phenoxyethanol 1:4 (e.g., Euxyl K 400 as trademark) is still tested to a limited extent by some departments.

Corticosteroids

The EBS contains two corticosteroids assumed to cover different antigenic classes, namely, budesonide and tixocortol pivalate. A Spanish multicentre study involving 3,699 consecutively patch tested patients added six other corticosteroids (methylprednisolone acetonate, mometasone furoate, prednicarbate, clobetasol propionate, betamethasone 17-valerate, and betamethasone 17, 21-dipropionate). Overall, 1.46% (n = 54) showed a positive reaction to at least one of the eight corticosteroids and, among these, 39 to one of the six additional corticosteroids. Interestingly, 24 of those 39 were not positive to any of the two screening markers; hence, contact allergy would have been missed when relying solely on these two markers. In other words, the two EBS markers failed to detect corticosteroid allergy in about 40% of the patients in that study, which probably depends on country- or region-specific exposure/prescription. Of note, the Spanish study used a day 7 reading, which was mostly lacking in the present data, and in the outcome definition, which must be regarded as a shortcoming leading to underestimation of the sensitisation prevalence particularly of the corticosteroids by up to 30%. It is recommended to test with a full series of corticosteroids in case allergic contact dermatitis to these is suspected.

Clioquinol

Clioquinol contact allergy has become a rarity, justifying its recent elimination from the EBS.

Caines

Benzocaine was replaced by Caine mix III in 2019, and at least in the present analysis the detection rate of the latter is higher; however, further patch test studies on Caine mix III are warranted to further assess its diagnostic validity and the clinical relevance of positive reactions.

Neomycin sulphate

Neomycin sulphate is a topical antibiotic rarely used in some countries, while it is a popular, sometimes over-the-counter remedy, in others. Of course, this heavily impacts the prevalence of sensitisation. From this background, the German Contact Dermatitis Research Group decided several years ago to remove neomycin sulphate from its baseline series; however, in other countries, and certainly the United States, it is still an important part of the baseline series.

Rubber compounds

Compared with thiuram mix, sensitisation to the other rubber allergens, including N-isopropyl-N -phenyl-p-phenylenediamine, is relatively rare. Of note, thiurams, including the mix, are considered to detect contact allergy to dithiocarbamates, as corresponding thiurams and dithiocarbamates constitute redox pairs. Positive patch test reactions to the benzothiazoles are almost twice as common in the youngest, compared with the oldest age group, likely pointing to occupational exposure and sensitisation, for example, in the healthcare sector, or perhaps to fashion-related exposures. In general, if (occupational) exposure to rubber additives is suspected to cause allergic contact dermatitis, testing with a dedicated rubber series, pieces of rubber products, or ultrasonic extracts thereof is indicated. Patch testing with rubber constituents has been widely reported, particularly the problem of irritant patch test reactions to 1,3-diphenylguanidine, which has been found, at the same time, to be an important allergen in synthetic rubber gloves.

PPD

The sensitisation prevalence of PPD is largely stable, with a pre-ponderance of females and a weak variation across age groups. Contact allergy to PPD is often related to exposure to oxidative hair dyes. Hence, a much-reduced share of PPD-containing hair dye products and replacement with only partially cross-reacting PPD derivatives recently observed at least in Germany could be expected to contribute to a lessening of sensitisation frequency. The marked cross-reactivity of PPD with TDM, owing to the presence of Disperse Orange 3 in the latter, has been confirmed in the present study data. To avoid unnecessary, possibly strong, or extreme patch test reactions, a TDM without Disperse Orange 3 should be evaluated.

Epoxy Resin

The frequency of sensitisation to epoxy resin largely remained stable over the previous years; contact allergy is mostly observed in patients with occupational dermatitis. This suggests that further efforts to improve occupational hygiene are necessary, especially in (spray) painting and at construction sites or in pipe relining.

Non-EBS substances
Among the allergens still not part of the EBS in the study period, propolis and caine mix III, along with 2-hydroxyethyl methacrylate, have been incorporated in the 2019 version of the EBS.

Propolis
With a sensitisation prevalence of around 3%, remarkably similar between the sexes and with just a slight increase with age, propolis seems indeed a worthwhile addition. Accordingly, propolis had been identified as an emerging allergen in a recent analysis of long-term data from the IVDK. A comparison between results from “IVDK countries” and the remaining countries testing with propolis shows a highly significant difference in prevalences, with a prevalence of 1% in the latter, illustrating the well-known geographical variation of contact allergy to this natural product. Further results are awaited, together with information on clinical relevance and exposure in patients with positive patch test reactions.

Caine mix III
With a prevalence of positive reactions well above 1%, caine mix III also seems a worthwhile addition or rather replacement in the EBS; notwithstanding further studies, for example, comparing mix with break-down results.

2-Hydroxyethyl methacrylate
This had not been consecutively tested in a sufficient number of departments to warrant presentation. However, owing to the massively increased exposure in terms of cosmetic acrylic nail usage, contact allergy to this allergen is expected to escalate.

Compositae
Data suggest that SL mix alone is insufficient as a screen to diagnose Compositae allergy, but the ideal combination is not yet established. Some suggest a combination with Compositae mix II 2.5% pet. and parthenolide 0.1% pet. However, while the original Compositae mix I 5% pet. induced active sensitisation, others feel that the 5% concentration of the Compositae mix II is not sensitising and contains parthenolide 0.1% rather than feverfew extract that was in the Compositae mix I.

Formaldehyde Releasers
The question as to whether different formaldehyde releasers, including quaternium-15, which is a longstanding constituent of the EBS, should be tested in addition to formaldehyde (ideally 2% aq.) has been addressed by another, dedicated analysis and shall not be discussed here. The present results with the different formaldehyde releasers are largely similar to the more detailed, department-wise analysis of 2013/2014 data.

Iodopropynyl butylcarbamate
IPBC 0.2% pet., tested in more than 20,000 consecutive patients, caused over 1% positive, mostly weak positive, reactions and about three times as many doubtful or irritant reactions. However, other studies found a lower sensitisation prevalence (e.g., 0.53%). IPBC liberates iodine, which has also been supported by observing simultaneous contact allergy to IPBC and iodine. Owing to possible endocrine interference, use concentrations are restricted to between 0.02% in rinse-off products and 0.0075% in deodorants/antiperspirants for many years. It would be of interest to further investigate IPBC regarding the clinical relevance of (weak) positive patch test reactions.

Cetearyl alcohol
Similar to propolis, cetearyl alcohol also exhibits significant geographical differences, albeit on a much lower level, presently not justifying inclusion into the EBS.

Sodium metabisulfite
This yields a considerable number of positive reactions and has thus been recommended to be added to the EBS.

Please note that the European Baseline Series as constituted by Chemotechnique comprises the following haptens:

European Baseline Series S-1000
The European Baseline Series consists of haptens based on the experience from many years of studies of frequencies of contact allergy performed by the European Environmental and Contact Dermatitis Research Group (EECDRG).The series can be seen as a basic “standard” baseline series in case no dedicated country-specific baseline series is offered.

Position	Art. no	Hapten	Conc.	Veh.
1.	P-014A	Potassium dichromate	0.5%	pet.
2.	P-006	p-PHENYLENEDIAMINE (PPD)	1.0%	pet.
3.	Mx-01	Thiuram mix	1.0%	pet.
4.	N-001	Neomycin sulfate	20.0%	pet.
5.	C-017A	Cobalt (II) chloride hexahydrate	1.0%	pet.
6.	Mx-19	Caine mix III	10.0%	pet.
7.	N-002A	Nickel (II) sulfate hexahydrate	5.0%	pet.
8.	H-010	2-Hydroxyethyl methacrylate	2.0%	pet.
9.	C-020	COLOPHONIUM	20.0%	pet
10.	Mx-03C	Paraben mix	16.0%	pet.
11.	I-004	IPPD	0.1%	pet.
12.	W-001	LANOLIN ALCOHOL	30.0%	pet.
13.	Mx-05A	Mercapto mix	2.0%	pet.
14.	E-002	Epoxy resin, Bisphenol A	1.0%	pet.
15.	B-001	Peru balsam	25.0%	pet.
16.	B-024	PTBP	1.0%	pet.
17.	M-003A	2-Mercaptobenzothiazole (MBT)	2.0%	pet.
18.	F-002B	FORMALDEHYDE	2.0%	aq.
19.	Mx-07	Fragrance mix I	8.0%	pet.
20.	Mx-18	Sesquiterpene lactone mix	0.1%	pet.
21.	C-007A	QUATERNIUM-15	1.0%	pet.
22.	P-022	Propolis	10.0%	pet.
23.	C-009B	MI/MCI	0.02%	aq.
24.	B-033B	Budesonide	0.01%	pet.
25.	T-031B	Tixocortol-21-pivalate	0.1%	pet.
26.	D-049E	MDBGN	0.5%	pet.
27.	Mx-25	Fragrance mix II	14.0%	pet.
28.	L-003	Lyral	5.0%	pet.
29.	M-035B	METHYLISOTHIAZOLINONE	0.2%	aq.
30.	Mx-30	Textile dye mix	6.6%	pet.

Developing a Cosmetic Series: Results from the ESSCA network, 2009-2018,

by Emma Horton et al,
in **Contact Dermatitis, Vol 84, Issue 2, February 2021, pp 82-94.**

There is considerable variability across European patch test centres as to which allergens are included in local and national cosmetics series. The 18 authors from 6 European countries of this paper propose a standardised evidence-based cosmetic series for Europe, based on up-to-date analysis of relevant contact allergens.

They collated data from the European Surveillance System on Contact Allergies (ESSCA) from 2009 to 2018 to determine which cosmetic allergens produce a high yield of contact allergy. Contact allergens with a prevalence of >0.3% that were considered relevant were included in the proposed series. Rare contact allergens were excluded if deemed to be no longer relevant, or they were added to a supplemental cosmetic series for further analysis.

In the study, the sensitisation prevalence of 39 cosmetic contact allergens were tabulated. Thirty of these allergens yielded >0.3% positive reactions and are therefore included in the proposed European Cosmetic series. Six were considered no longer relevant and therefore excluded. Three were included in a Supplementary European Cosmetic Series. An additional nine allergens were included in either the Core or Supplemental European Cosmetic Series following literature review. In conclusion, they developed a potential European Cosmetic Series based upon the above methods. Ongoing evaluation of new data will be required to establish any change in exposure profiles of cosmetic allergens as well as new and evolving substances.

Many chemicals used within cosmetic products are potent contact allergens. Contact dermatitis secondary to cosmetics is common. It frequently affects the face and can have a significant impact upon quality of life. The appropriate identification of relevant cosmetic is therefore of great importance.
The present analysis included allergens which are part of various “cosmetic series” from centres in the European Surveillance System on Contact Allergies (ESSCA). There is significant variation across Europe with regard to cosmetic series. Some countries have nationally agreed cosmetic series, but individual centres may patch test with different allergens. In addition, recent results suggest that some frequently tested cosmetic allergens have a low yield of positive reactions or are of historical interest only. There is a need to develop an evidence-based cosmetic series to standardise the set of test substances, to improve diagnosis, to facilitate future comparative analyses and surveillance, all whilst maintaining cost effectiveness.

The primary aim of this study was to determine the frequency of reactions to cosmetic contact allergens not already included in the European Baseline Series 2019, which are tested as part of local or national cosmetic series in European dermatological centres. The secondary aim was to propose a European patch test Cosmetic Series.
To achieve the primary aim, the authors analysed the database of the ESSCA in order to determine the frequency of contact allergy to individual cosmetic allergens.
In order to propose a standardised European cosmetic series (the secondary aim), it was necessary to analyse the above information in the context of a literature search. Allergens within the European Baseline Series typically produce a frequency of >0.5% to 1% allergic reactions in those tested.

In order to minimise the risk of missing relevant cosmetic allergens, the authors proposed a threshold for inclusion of 0.3% for a European Cosmetic Series. This threshold does not refer to consecutively tested patients, but to the (often large) subset with suspected cosmetic-related ACD. Proven common contact allergens (based upon an equal to or higher than 0.3% share of positive reactions) qualified for inclusion within their proposed European cosmetic series. Contact allergens that yielded less than 0.3% positivity rate were scrutinised. A PubMed search was performed to highlight relevant publications pertaining to these allergens in order to determine their modern-day relevance. They considered the fact that certain substances may rarely produce contact allergy but are associated with a wide exposure profile; these allergens were still considered for inclusion. They also took into account the fact that exposure profiles may vary, dependent on geographic location; therefore, they have highlighted allergens which provoke a high yield of reactions in certain countries for inclusion in a Supplementary European Cosmetic Series.
In addition, they have reviewed the relevance of cosmetic allergens in sunscreen, hairdressing, and nail aesthetic products. They have recommended inclusion of important contact allergens in these particular groups within the proposed European Cosmetic Series. They have also considered emerging contact allergens with the potential to be of relevance to cosmetic contact dermatitis and have recommended inclusion in the supplementary cosmetic series.

The proposed European Cosmetic Series comprises 34 allergens/haptens, with an additional 6 in the Supplementary Series, making a total of 40 tests. All allergens/haptens are in petrolatum except where indicated.
The original article includes information on some of the individual compounds, and therefore makes very useful reading for the professional patch tester.

In conclusion, the authors propose a core European Cosmetic Series containing allergens of relevance that should be tested in all dermatology patch test centres on patients who present with suspected contact allergy to cosmetics. They have also constructed a separate list of supplementary allergens which are of potential but not definite relevance. These should be tested in all tertiary patch test centres as part of a European Cosmetic Series and their relevance should then be closely observed and evaluated.

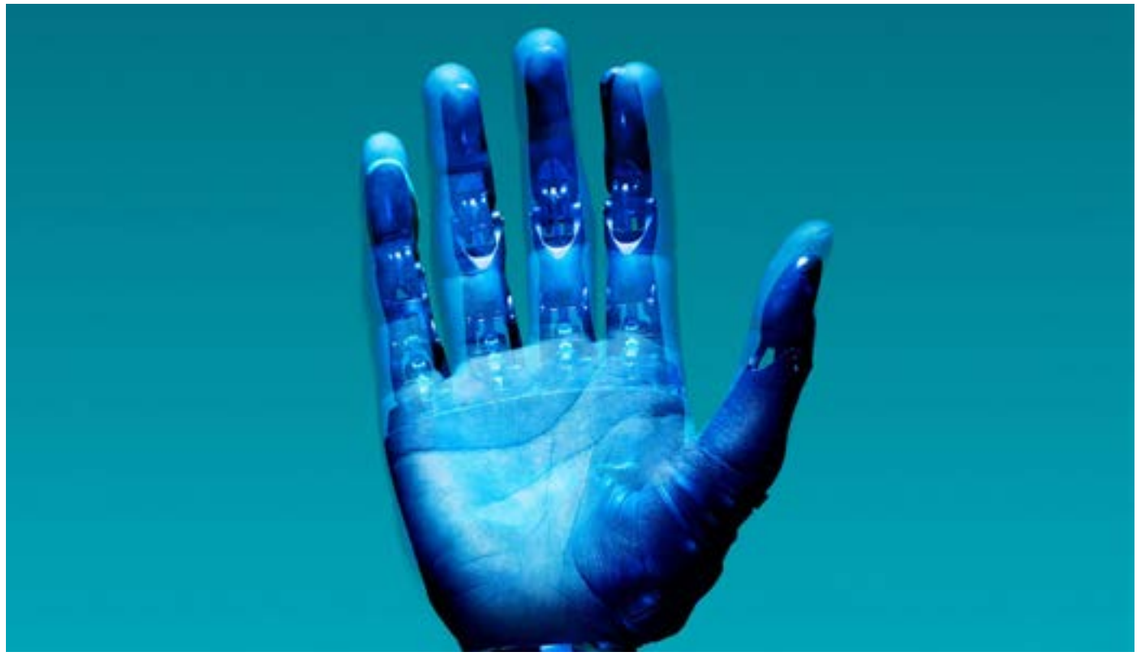
As always, for full information, please read the original article.

Proposed European Cosmetic Series

Type of hapten	Name	%
Preservatives	Benzyl alcohol	1%
	Chloroacetomide	0.2%
	TBHQ (tert-Butyl hydroquinone	1%
	2-Bromo-2-nitropropane-1,3-diol	0.5%
	DMDN hydantoin	2% Aq
	Diazolidinyl urea	2%
	Imidazolidinyl urea	2%
	Iodopropinyl butylcarbamate	0.2%
	Sodium metabisulphite	1%
	Phenoxyethanol	1%
	Sodium benzoate	5%
	Sorbic acid	2%
Antioxidants	Butylated hydroxyanisole (BHA)	2%
	Propyl gallate	1%
	Caprylyl gallate	0.3%
Antiseptics	Methenamine (Hexamethylentetramine)	1%
	Chlorhexidine digluconate	0.5% Aq
	Triclosan	2%
Emollients	Lanolin (Amerchol L-101)	50%
	Cetearyl alcohol	20%
	Propolis	10%
Emulsifier/Surfactant/Vehicle	Sorbitan sesquioleate (SSO)	20%
	Cocamide diethanolamine	0.5%
	Decyl glucoside	1% Aq
	Lauryl glucoside	3%
	Propylene glycol	20% Aq
Special Functions	Hydroabietyl alcohol (Abitol)	10%
	Shellac (natural resin)	20%
Sunscreens	Benzophenone 3	10%
	Benzophenone 4	10%
	Octocrylene	10%
	Butyl methoxydibenzoylmethane	10%
Nail Aesthetics	Tosylamide/formaldehyde resin (TFR)	10%
	Tocopheryl acetate	10%

Proposed Supplementary European Cosmetic Series

	Panthenol	5%
	Triethanolamine	2.5%
	Glyceryl thioglycate	1%
	PTG copolymer	1%
	AA copolymer	1%



Self-Reported Hand Eczema: Assessment of Prevalence and Risk Factors in Health Care Versus Non–Health Care Workers During the COVID-19 Pandemic

by Pourani, Mohammad Reza MD, et al,
in **Dermatitis, Vol 32, Issue 1, January-February 2021, pp 19-21.**

The original article in **Dermatitis** also provides links to other related articles in previous issues of **Dermatitis**; as shown below:

Hand Hygiene Among Health Care Workers During Covid-19 Pandemic: Challenges and Recommendations
Volume 31, Issue 4, pages 233-237 in July/August 2020 by Araghi Farmaz, et al. (link)

Screening for Hand Dermatitis in Health Care Workers
Volume 25, Issue 5, pages 281-282 by Sharon Shin et al, in September 2014

Hand Dermatitis in the time of COVID-19: A Review of Occupational Irritant Contact Dermatitis
By Anna Kersh, et al. on 16th February 2021 (link)

Impact of Gloves and Mask Use on Epidermal Barrier Function in Health Care Workers
Volume 32, Issue 1, pages 57-62, by Trinidad Montero-Vilchez, et al, in January 2021 (link)

Nickel: Intrinsic Skin Sensitisation Potency and Relation to Prevalence of Contact Allergy

by David Basketter

in **Dermatitis, Vol 32, Issue 2, March/April 2021, pp 71-77.**

Nickel remains the most commonly identified contact allergen. However, it has proven difficult to demonstrate significant skin-sensitising activity for nickel in toxicology tests, which typically have indicated a weak skin sensitisation potential. Information indicates that *in vivo* assays are not predictive of dermal sensitisation hazard or potency for nickel due to a human-specific mechanistic route for nickel sensitisation that is lacking in animals.

A similar rationale will apply to *in vitro* alternatives—although these currently have limited ability to determine intrinsic potency. Generally, *in silico* methods are not designed for metal allergens and cannot contribute to the analysis. For ethical reasons, human experimental work has been limited, with a single study suggesting moderate potency. Accordingly, it seems reasonable to conclude that the high frequency of contact allergy to nickel in humans is a function of both its intermediate potency coupled with a high level of dermal exposure, particularly to damaged/inflamed skin.
In the toxicological world of skin sensitisers and predictive tests for their identification and characterisation, as well as the clinical world of contact allergy and the disease allergic contact dermatitis (ACD), no single cause has a longer and more abundant history than nickel. A good deal of this was captured about 3 decades ago in an impressive overview of current knowledge at that time: (Maibach HI, Menné T. Nickel and the Skin: Immunology and Toxicology. Boca Raton, FL: CRC Press; 1989).

Recent publications confirm that nickel, despite legislation in some countries, remains at the top of the list of agents causing contact allergy - for example, approximately 16% (1 in 6) of patch-tested dermatology patients in Germany. The proportion with nickel contact allergy in the general population in Europe is not far short of this figure, at 14.5%. Of course, these high numbers contain a significant cohort who became nickel allergic before the European legislation, the purpose of which was to reduce exposure to metal objects in prolonged contact with the skin. The effectiveness of this legislation has been reviewed recently.

However, the present work focuses on one medical conundrum: the disparity between the frequency with which nickel induces contact allergy (and thereby the elicitation of ACD) versus its relative lack of skin-sensitising potency in predictive tests.
Chemical substances causing skin sensitisation (sensitisers) must make permanent changes to skin protein that can be recognised by the cellular immune system, triggering a response usually termed type IV delayed hypersensitivity. However, there is a question whether, and to what extent, skin sensitisers vary in their capacity to cause this outcome. This is typically referred to by the term “potency,” which refers to the ability to induce allergy. That skin sensitisers do have widely differing intrinsic induction potency is well described in animal models, as well as in humans. The central question addressed is where nickel fits into the potency spectrum; a secondary question considers thresholds. Prompted by this discussion is the question of whether there is a relationship between the potency of an allergen and its elicitation threshold.

Nickel remains a very common human contact allergen and an important cause of ACD. Evidence for this derives from use of nickel sulphate at either 2.5% or 5% in petrolatum in the baseline diagnostic patch test screening trays in North America, Europe, and many other countries. Inevitably, results from the use of various screening series embrace multiple variables, including differing patterns of exposure in these locations, as well as variation in local medical referral practices and the precise details of the diagnostic patch test process, combined with the impact of regional health and safety legislation. For example, whereas nickel has always a relatively high percentage of patients tested, the response to chromate varies, for example, in Europe, due to the use of ferrous sulphate chelating agent in cement, which has sharply reduced the frequency of allergy. That same article notes also the positive impact of European legislation on lowering the frequency of nickel contact allergy, although room for improvement remains (e.g., increased compliance with the legislation and adoption of similar legislation in other geographies) to decrease the prevalence further.

At the end of the last century, the very eminent research dermatologist Prof Jan Wahlberg came to the conclusion: “The basic question of why nickel is such a common cause of contact allergy in the female population, but not a potent contact allergen in experimental animals can probably be explained by exposure conditions. Does anything we have learned since that time alter, or indeed substantiate, this perspective? In the view of the author, the most significant new knowledge that has a bearing on this arises from new insights into the molecular mechanism of nickel allergy.

The recognition that nickel allergy is mediated through a specific toll-like receptor present on human, but not other mammalian, cells was immediately perceived to provide a rationale for the less effective induction of sensitisation in the *in vivo* test systems. Nevertheless, it does not explain the fact that nickel is clearly not intrinsically a strong sensitiser in human predictive tests. Thus, one is left with the obvious conclusion that the common clinical prevalence of nickel allergy is very largely a direct consequence of the extent of human skin exposure.
For full information, please read the original article.

Editor's Note:
The format of The Patch Tester in now expanding to include not only articles from the medical journals "Dermatitis" and "Contact Dermatitis" but also other articles from other sources that are of great relevance to the Dermatologist.

In this case, Nature magazine has published a good review of the safety aspect of COVID vaccines, that is not the traditional scientific/medical article but pitched for a somewhat different audience. As such, it could be useful as a recommendation for reading by a concerned patient.

COVID Vaccines and safety: what the research says

in **Nature, 16th February 2021.**

It is clear that coronavirus vaccines are safe and effective, but as more are rolled out, researchers are learning about the extent and nature of side effects.

As people around the world receive COVID-19 vaccines, reports of temporary side effects such as headaches and fevers are rolling in. Much of this was expected — clinical-trial data for the vaccines authorised so far suggested as much. But now that millions of people are vaccinated, compared with the thousands enrolled in early studies, reports of some rare, allergic reactions are surfacing, and questions are arising about whether any deaths are linked to the shots.

There is no question that the current vaccines are effective and safe. The risk of severe reaction to a COVID-19 jab, say researchers, is outweighed by the protection it offers against the deadly coronavirus. Nature looks at what scientists are learning about the frequency and nature of side effects as huge numbers of people report their reactions to physicians and through safety-monitoring systems, such as smartphone apps.

How many people experience common side effects from COVID-19 vaccines?
For the two available messenger RNA (mRNA) vaccines — one made by Moderna at Cambridge, Massachusetts, and the other developed through a collaboration between Pfizer in New York City and BioNTech in Mainz, Germany - a significant portion of people experience non-serious reactions, such as injection-site pain, headache and fatigue.

According to data from the US Vaccine Adverse Event Reporting System (VAERS), about 372 out of every million administered doses of the mRNA vaccines lead to a non-serious reaction report. This number is lower than would be expected from clinical-trial data, which indicated that at least 80% of people would experience injection-site pain. Researchers running trials monitor patients closely and record every reaction. VAERS, meanwhile, relies on health-care workers and vaccinated individuals to self-report side effects.

So far, reactions to the mRNA vaccines are similar. These vaccines are administered in a two-dose regimen: the first shot triggers an immune reaction, and the second is a 'booster' that strengthens the body's ability to fight the coronavirus. For the Pfizer-BioNTech vaccine, which has been in use longer than the Moderna vaccine and therefore has generated more data, side effects increase with the second dose (see 'Tracking side effects').

In the United Kingdom, three million doses of another vaccine, developed by the University of

Oxford and pharmaceutical firm AstraZeneca, have been doled out. This vaccine, which also requires a two-dose regimen, contains an inactivated cold-causing adenovirus with genetic instructions for making coronavirus proteins to trigger immunity. According to UK safety-monitoring system the Yellow Card Scheme, about 4,000 doses out of every million administered lead to adverse reactions. Again, clinical-trial data suggest that a higher frequency is more accurate: around 50% of participants had injection-site pain, headache or fatigue, according to data reported to the European Medicines Agency (EMA).

Few people have received a second dose of the Oxford–AstraZeneca vaccine because the United Kingdom used its supplies to administer a first dose to as many people as possible, but clinical-trial data presented to the EMA suggest that side effects of the second shot are milder than those caused by the first.

Safety data for shots rolling out in other parts of the world, such as the COVID-19 vaccines in China, are harder to come by.

Preliminary data from clinical trials of the adenovirus-based Sputnik V vaccine in Russia suggest its most common side effects include flu-like symptoms and injection-site reactions.

How does that compare with side effects from an annual flu shot?
At least for the mRNA vaccines, physicians are seeing more side effects than for flu shots, says Helen Chu, an infectious-disease specialist at the University of Washington School of Medicine in Seattle, who directs the Seattle Flu Study. In clinical trials for the Pfizer-BioNTech vaccine, for instance, 75% of participants reported a ‘systemic reaction’, such as headache, fever or chills. In a clinical trial for the common influenza vaccine Flubok Quadravalent, around 34% of participants aged 18–49 had a systemic reaction. Side effects were even less frequent in study participants who were at least 50 years old.

Chu says the mRNA COVID-19 vaccines generate a particularly strong immune response that increases the risk of side effects, although this also means that the vaccines are working. She notes that her second dose of the Pfizer-BioNTech vaccine made her ill. “I got the vaccine, and 6 hours later, I had chills, a high fever, muscle aches and I went to bed for 24 hours,” she says. “Then by 36 hours later, it was totally over, and I was back to normal.” But Chu would rather be temporarily ill from a vaccine than deal with COVID-19, “a potentially mortal disease that could kill me”, she says.

Have investigations linked any deaths to a COVID-19 vaccine?
Although some have questioned whether the vaccines have led to deaths, none have been directly attributed to a COVID-19 jab. After 33 elderly care-home residents in Norway died within 6 days of receiving the Pfizer-BioNTech vaccine, investigations by both the Norwegian Medicines Agency and the World Health Organization concluded that these deaths were in line with normal death rates in this age group and that the vaccine is still safe for older people. India’s Ministry of Health and Family Welfare reported 27 deaths in the country, but none of these have been linked directly to a COVID-19 vaccine either.

It is “extremely difficult” to definitively link a death to the vaccine itself, says Hilda Bastian, a writer and scientist who specialises in validating evidence-based health claims. That is partially because the deaths reported so far have occurred days or weeks after an injection, making it hard to rule out other circumstances. Another reason is that, right now, clinicians are prioritising vaccines largely for a population of older people with underlying health conditions. Most of those who have died after vaccination have been in this group, according to reports from the United Kingdom and the United States.

What do researchers know about the rare, but severe, allergic reactions to the vaccines?
The Moderna vaccine elicits about three anaphylactic reactions per million doses administered, and the Pfizer-BioNTech vaccine triggers five reactions per million doses, according to VAERS data. This is a higher rate than most other vaccines — including annual flu shots, which trigger anaphylaxis for only one out of every million doses administered. For the Oxford-AstraZeneca vaccine, 30 cases of anaphylaxis have been confirmed overall so far, out of a little more than 3 million administered doses (at the time of writing). Vaccine specialists expect that these rates might change as more shots are administered.

Although some people have required hospitalisation, all have fully recovered.

Public-health officials advise people with a history of allergies to any of the vaccines’ ingredients not to get a COVID-19 jab.

Unlike COVID-19, anaphylaxis is treatable with drugs such as epinephrine if caught quickly, says Paul Offit, a vaccine and infectious-disease specialist at the Children’s Hospital of Philadelphia in Pennsylvania, who participated in the US Food and Drug Administration advisory-committee meetings that led the agency to authorise both mRNA vaccines. “I wish that SARS-CoV-2 could be immediately treated with a shot of epinephrine!” he says.

Most of the people who experienced anaphylaxis had reacted to other substances before. Approximately 80% of people who reacted to the Pfizer-BioNTech vaccine, and 86% to the Moderna vaccine, had a history of allergies, according to the US Centers for Disease Control and Prevention.

The specific cause of the anaphylactic reactions remains unknown, but the US National Institute of Allergy and Infectious Diseases told Nature in an e-mail that the agency has designed a clinical trial to determine the underlying mechanism but did not specify when the trial would begin.

What could be causing the allergic reactions?
Some researchers have had their eye on polyethylene glycol (PEG) as the anaphylaxis-causing agent in the mRNA vaccines. The Moderna and Pfizer-BioNTech vaccines use hollow lipid nanoparticles to store and then deliver their mRNA payload to cells. PEG is linked to the lipids in these particles and, under normal circumstances, helps them to sneak by the immune system. Although PEG-linked molecules are found in a variety of products, such as laxatives and gout medicines, they have been known to cause allergic reactions.

Follow-up studies in people who experienced anaphylaxis could help to determine whether PEG is the culprit, says Samuel Lai, a pharmaco-engineer at the University of North Carolina at Chapel Hill. If blood samples from these people contain anti-PEG antibodies, it could be an indicator, says Lai, but it is as yet unclear how long these proteins remain in the bloodstream after anaphylaxis.

Vaccines that don’t use PEG - such as the not-yet-authorized shot from Johnson & Johnson, which also uses an adenovirus to trigger immunity to the coronavirus - might be a way to vaccinate people with a sensitivity to the polymer, he adds.

Because mRNA vaccines have shown such promise, Ulrich Schubert, a polymer scientist at the University of Jena in Germany, thinks now is the time to invest in developing vaccine-compatible polymers that don’t cause allergic reactions. At the German Research Foundation-funded collaborative research center PolyTarget, where Schubert works, these studies are already in progress. “If we want to be ready for the next pandemic — which will come — we have to start now,” he says.

Suitable test concentration of cobalt and concomitant reactivity to nickel and chromium: A multicentre study from the Swedish Contact Dermatitis Research Group,

by Marléne Isaksson, et al

in **Contact Dermatitis, Vol 84, Issue 3, March 2021, pp 153-158.**

In Sweden, cobalt chloride 0.5% has been included in the Swedish Baseline Series since the mid-1980s. A recent study from Stockholm showed that cobalt chloride 1% petrolatum was more suitable than 0.5%. Cobalt chloride at 1% has been patch tested for decades in many European countries and around the world.

The objective of the study was to assess the suitability of patch testing to cobalt 1.0% vs 0.5% and to analyse the co-occurrence of allergy to cobalt, chromium, and nickel.

Since the 1980s and '90s, the European Baseline Series and many national baseline series have contained cobalt chloride 1.0% pet. In Sweden, cobalt chloride 0.5% has been tested within the Swedish Baseline Series since the mid-1980s, although the dental series has included cobalt chloride 1.0% pet. The reason for using 0.5% was the notion that cobalt 1.0% caused false-positive reactions.

The Swedish Baseline Series is probably the only baseline series that still includes cobalt 0.5% pet. One may wonder why this has persisted for so long when 1.0% pet. has been used almost everywhere else in the world for decades.

This study shows that a significant proportion of cobalt allergy is missed by testing to cobalt 0.5% compared to 1.0%, thus confirming the results in the first Swedish study.

Altogether, 515 patients had either a positive, doubtful, or irritant test reaction to at least one of the following test preparations: cobalt 0.5% and 1.0%, chromium 0.5%, or nickel 5.0%.

- Contact allergy to cobalt was shown in 90 patients (6.6%).
- Eighty (5.9%) patients tested positive to cobalt 1.0%.
- Thirty-seven of the 90 patients (41.1%) with cobalt allergy were missed by cobalt 0.5% and 10 (0.7%) were missed by cobalt 1.0%.
- Allergy to chromium was seen in 2.6% and allergy to nickel in 13.3%.
- Solitary allergy to cobalt without nickel allergy was shown in 61.1% of cobalt-positive individuals.
- Female patients had larger proportions of positive reactions to cobalt and nickel than males.
- Allergy to any of the studied metals was shown in 255 individuals.
- Allergy to chromium was seen in 35 (2.6%) and allergy to nickel in 180 patients (13.3%).
- Thirty-seven of the 90 patients (41.1%) with cobalt allergy were missed by cobalt 0.5% and 10 were missed by cobalt 1.0%.
- Solitary allergy to cobalt without concomitant allergy to chromium or nickel was frequent in this study (54.4%), a finding also seen in earlier studies from Sweden and Germany.
- Female patients had larger proportions of positive reactions to cobalt 0.5% and 1.0% (4.5% and 6.8%, respectively), than males (2.6% and 3.9%). Statistically, the gender difference was only a trend for 0.5% and significant for 1.0%.
- Female patients also had larger proportions of positive reactions to nickel (17.2%) than males (4.9%).
- Female patients had larger proportions of solitary positive reactions to cobalt 1.0% (3.0%) than males (2.1%).
- Female patients had larger proportions of solitary positive reactions to nickel (12.9%) than males (4.4%).
- No case of patch test chamber sensitisation was reported, using Finn Chambers or Chemotechnique IQ Ultra Chambers.

The variation seen for irritant reactions implies that standardisation is warranted, not only for the dose of the patch test, but also when various combinations of morphological features should be classified as irritant or doubtful. In this multicentre patch test study, there was a high standardisation of the patch test methodology.

In a recent publication on how to improve the quality of multicentre patch test studies, 16 factors of possible significance in the patch test results were discussed. Besides listing the 16 factors, a scoring system was also suggested with scores based on the relative importance of each factor for the quality of the multicentre patch test study. In this current study, the highest scores were obtained for all factors except for different patch test techniques, lack of control of occlusion after 48 hours, no calibration of the test reading, and no monitoring. Despite this, the total score was 23, which rendered this study as a high-quality multicentre patch test study.

Since it is still unclear how individuals are exposed to cobalt, at least domestically, it is proposed that more studies are warranted to pin-point cobalt exposure.

The conclusion from this study is that cobalt chloride 1.0% pet. is more suitable for patch testing than 0.5%, and that the Swedish Contact Dermatitis Research Group will recommend that cobalt chloride 1.0% should replace 0.5% in the Swedish Baseline Series.

You are invited to notify us If there is a website you would like to have reviewed in a future issue of The Patch Tester or if there is a society or other website that you would like to have included in these lists.

Dermatology Society Websites

ILDS:	*International League of Dermatology Societies*	www.ilds.org
ICDRG:	*International Contact Dermatitis Research Group*	www.icdrg.org
EADV:	*European Academy of Dermatology & Venerology*	www.eadv.org
ESCD:	*European Society of Contact Dermatitis*	www.escd.org
ACDS:	*American Contact Dermatitis Society*	www.contactderm.org
APEODS:	*Asia-Pacific Envmntl & Occupational Dermatology Society*	www.apeods.org
EAACI SAM:	*European Academy of Allergy & Clinical Immunology*	www.eaaci.org
BAD:	*British Association of Dermatology*	www.badannualmeeting.co.uk
AAD:	*American Academy of Dermatology*	www.aad.org
PDA:	*Pacific Dermatololologic Association*	www.pacificderm.org
APD:	*Association of Dermatology Professors*	www.dermatologyprofessors.org
NDA:	*Nordic Dermatology Association*	www.nordicdermatology.com
GDA:	*German Dermatology Society*	www.derma.de
FSA:	*French Society of Dermatology*	www.sfdermato.org
CDA:	*Caribbean Dermatology Association*	www.caribbeanderm.org
ACD:	*Australian College of Dermatologists*	www.dermcoll.edu.au
NZDS:	*New Zealand Dermatology Society*	www.nzdsi.org
DNA:	*Dermatology Nurses Association*	www.dnanurse.org
DermNET NZ:	*Dermatology Infomation Resource for Patients*	www.dermnetnz.org

Dermatology Meeting Websites

www.eadv.org
www.aad.org
www.dermatologymeeting.com
www.asiaderma.sg
www.dubaiderma.com
www.cairoderma.com

Editor's Note:
In previous editions of The Patch Tester this Website Review section has focussed on the websites of dermatology organisations in various countries. However, for this issue #6 we choose to focus on the pages of two websites, of the BAD and AAD, respectively, that state the position and recommendations of these two societies on the COVID-19 pandemic. Although the BAD information is highly country-specific, for BAD members, there is nevertheless much good and useful information that can be of benefit for dermatologists in other countries.

From the website of the British Association of Dermatologists

COVID-19: Clinical guidelines for the management of dermatology patients remotely

Teledermatology: Advice and Guidance, tele-triage, video consultation and remote working
As hospital services come under increasing pressure and dermatologists are re-deployed to front line services, clinicians need to work differently. Departments will need to rapidly adapt to run significantly reduced services to support dermatology care, both in the short and long term. The focus is to reduce patient travel to GP and Provider organisations while maintaining continuity of care.

This guidance should be used to help dermatology units maintain urgent services, optimise use of medical staff, minimise additional work for GPs, and provide continuity of care with virtual patient management where possible. Dermatologists will need to comply with their own commissioners and organisations guidance in this unprecedented situation; this document aims to provide guidance and share good practice.

Key principles:

1. Streamline skin cancer patients on 2WW pathways, using teledermatology to triage referrals and book patients directly to surgery where possible

2. Manage urgent / on-call patients and in-patient referrals using secure nhs.net email or mobile messaging apps where possible

3. Redirect new patients through Advice and Guidance services where possible rather than referral

4. Manage referred patients by switching face-to-face clinics to teleconsultation +/- video consultation where possible (new and follow-up)

5. Optimise remote access to allow dermatology staff to continue to provide patient care from home if required

6. Facilitate virtual staff team meetings to coordinate patient care

7. Establish patient consent policies for receiving reviewing and storing patient images from health care professionals and patients.

Further information about these key principles is detailed on the following pages.

1. 2-week wait patients

Ensure that booking slots and clinic templates are adjusted to protect 2WW and urgent slots. Consider changing directly bookable 2WW services to Referral Assessment Services (RAS) with images attached, to optimise triage +/- directly book patients to skin surgery. If teledermatology is used for 2WW triage, then patients should ideally have their skin lesions photographed by a GP with dermoscopic training or by appointment with a medical photographer. Patient images are unlikely to be adequate for suspected melanoma / pigmented lesion triage but may allow triage of patients with squamous cell carcinoma direct to surgery. Secure clinical image smartphone apps (e.g., Consultant Connect® and Pando®) can aid clinical image capture in primary care. Triage should ideally be carried out by a dermatology consultant (core member of LSMDT/SSMDT). 2WW triage models are described in Dermatology Outpatient Case Studies December 2019: Using technology to enhance service delivery

2. Urgent / on-call and emergency in-patient consultations

NHSX has produced Information Governance Advice recognising the unprecedented challenges we are all facing during the Coronavirus (COVID-19) pandemic, particularly when there is a need to share information quickly. This advice is endorsed by the Information Commissioner's Office, the National Data Guardian and NHS Digital.

Mobile messaging can be used to communicate with colleagues and patients/service users as needed, including commercial applications such as WhatsApp where there is no practical alternative. Consider what type of information you are sharing and with whom, and as much as possible limit the use of personal/confidential patient information. Commercial medical smartphone apps such as Consultant Connect®, Pando® and Hospify® can support sharing of clinical information securely between health care professionals. Departments may set up a central nhs.net e-mail address or use individual nhs.net mail for photographic images transfer between health care professionals.

3. Advice and Guidance

Dermatology departments should encourage GPs to consider Advice and Guidance (A&G) requests, or other established teledermatology pathways, rather than routine referral where possible. Advice and Guidance services can be provided through the NHS e-Referral service (e-RS) or commercial platforms.

See guidance from NHSD: e-RS features that many help organisations during the Coronavirus (COVID-19) situation: Advice and Guidance

Standard NHS Advice and Guidance services involve GP / Consultant communication rather than patient / Consultant communication. However, a number of platforms are already in use in primary care which can allow patients to send photographic images to the GP securely (e.g., eConsult® and accuRx ®), and these images can be attached to Advice and Guidance requests to reduce patient travel. For patients having images taken in the GP surgery, smartphone apps (e.g., Consulant Connect® and Pando®) can allow easy capture and transfer of images into A&G requests by primary care staff.

Dermatology departments with existing teledermatology Advice and Guidance or other teledermatology services should work with local GPs / commissioners to mobilise these services rather than referrals where possible. Consider working with regional dermatology departments to temporarily open wider A&G services or cross-cover for colleagues. Support for Dermatology departments who do not currently run an Advice and Guidance teledermatology service is available through the BAD or using the NHS A&G toolkit

NHS e-RS Advice and Guidance Toolkit

Although A&G usually involves direct GP and Consultant communication, a wider referrer and provider workforce may be appropriate in the response to COVID-19, including non-Consultant grade doctors and specialist nurses, in order to free up senior front-line staff for acute care.

4. Managing routine referrals

Patients should be offered the opportunity for a telephone or video-consultation at their previously allocated face-to-face appointment timeslot if possible. Trusts may already have an established videoconfer-encing solution such as NHS Attend Anywhere® or accuRx®.

COVID-19 Information Governance Advice encourages the use of videoconferencing to carry out consultations with patients and service users to reduce the spread of COVID 19, using video conferencing tools such as Skype, WhatsApp, Facetime as well as commercial products designed specifically for this purpose. The consent of the patient or service user is implied by them accepting the invite and entering the consultation. Safeguard personal/confidential patient information in the same way you would with any other consultation.

Departments may choose to set up a central nhs.net email for photographic images to be sent through for review by the consultant to assist teleconsultation. Patients should be advised that e-mails sent from personal email addresses to nhs.net are not guaranteed to be encrypted. Voice recognition software (e.g., M-modal®) is available in some Trusts to support clinic letter documentation.

Routine dermatology referrals are likely to decrease during the coronavirus pandemic, referred patients will continue to be added to provider waiting lists, with uncertainty as to when they can be seen. NHS Digital has produced advice on managing routine referrals, monitoring provider worklists and managing cancellations.

5. Providing patient care from home

Members of staff may be away from their usual place of work and isolating for different reasons. Many dermatologists will already have hospital laptops with Virtual Private Network (VPN) access to hospital systems from home. Hardware requests for laptops and issuing of VPN licences is being accelerated in many hospitals – please discuss with your hospital Chief Clinical Information Officer, service manager and IT teams.

Hospital-approved laptops with VPN and smartcard access can allow dermatologists working from home to provide;

- Electronic Advice and Guidance to GPs
- Tele-triage of GP referrals
- Telephone consultations with access to electronic patient records and blood results

Commercial platforms used through NHS contracts enable users to work on non-NHS equipment from home within Virtual Private Networks.

6. Virtual staff team meetings

NHS mail, Zoom®, Microsoft Teams® or Cisco WebEx® are widely used platforms to maintain team communication throughout the COVID-19 pandemic.

7. Patient consent

Photographic consent policies should be discussed with your health care organisation information governance and medical photography teams, as policies may vary across organisations. The following guidance relates to COVID. Consent is required for patient images to be used for patient care, including diagnosis or triage. The consent process;

- informs the patient that there may be a difference between the accuracy of clinical care using photographs as compared to face-to-face clinical assessment
- explains how the images will be used, transmitted and stored in the health care organisation
- obtains wider consent for teaching / publication / research if relevant

Written consent is recommended **(see specimen consent forms) (link)**

UK guidance on the use of mobile photographic devices in dermatology
However, where planned face-to-face consultations have been changed to non-face-to-face consultations then written patient consent may not be possible or practical. Where verbal consent only is given, the healthcare professional should document this, and consent would not extend beyond direct provision of care.

When patients capture and transfer their own images – specific considerations
Patient images are usually sent to Dermatologists from GPs, via secure transfer (e.g., using e-RS or other approved platforms). During the COVID-pandemic, many new temporary pathways for transfer of patient images to dermatology departments have been established, including direct transfer of images from patients using generic e-mail services or mobile messaging. These images are often used to support telephone consultations, in a similar way to video-consultation but using 'still' images.

- If a clinician requests that the patient sends images, patients need to understand that there are the usual risks associated with sending any images via the internet. This constitutes a non-secure transfer and images are not subject to information governance and data protection until they have been received by the healthcare professional. Likewise, any images patients take and hold on their own phones may not be secure.

- Once the image has been received by a healthcare professional, any onward data transfer and storage should meet the NHS data protection and information governance requirements of the health care organisation.

- If a clinician requests that the patient sends images, the routine documented consent pro-cess should be undertaken verbally and documented with a message explaining consent (e.g., 'by sending these images you consent to them being held in your medical record') or by sending a written patient consent form for the patient to complete and return.

- Where images are suitable for teaching, consent forms can be sent to patients electronically and either completed electronically (e.g., with e-signature) or patients can return a photograph of the completed printed form.

- For temporary COVID-19 generic email addresses it is advisable to set up an autoreply which can relay important information to patients, highlighting that the mailbox is not monitored actively and that the photos are sent on the understanding that the process is not secure. Mailbox capacity can quickly fill up; we recommend liaising with your medical photography team to ensure photographs can be moved into a shared access point in your organisation where they can be accessed by other health care professionals as required.

- The BAD are aware that in the context of COVID-19 some dermatologists are deleting e-mailed patient images following the virtual consultation and managing patient images as a 'still' form of video-consultation (where no data is stored e.g., NHS Attend Anywhere). Images are deleted based on clinical judgement, with documentation of verbal consent, and patients are advised to retain the images. This option is being used where there are significant resource barriers for clinicians +/- medical photographers to archive large volumes of emailed images, (particularly of common conditions such as eczema or acne where images would not normally be taken within a face-to-face consultation) or when patients do not wish to have their images stored in their hospital record. It is recommended that images are retained when they have been used to make clinical judgements on patient care.

The guidance above is intended to support departments manage patients in whom image transfer has not involved their GP, particularly patients referred prior to COVID-19 lockdown.

As part of COVID-19 recovery it is recommended that departments develop or reinstate se-cure long-term pathways for new patients, involving either image capture in the GP surgery or secure image transfer between patient and GP (e.g., eConsult® and accuRx®) with written con-sent attached, followed by secure transfer to dermatology departments using A&G or e-RS referral pathways, where images are automatically stored in approved NHS systems.

Further information
BAD teledermatology (link)
BAD Clinical Services Unit (link)

From the website of the American Academy of Dermatology Association (link)

COVID-19: Guidance for dermatology patients for remote consultations

Running your practice safely during the ongoing COVID-19 pandemic
With the current COVID-19 pandemic, many dermatology practices are operating differently. These recommendations should help you keep your practice operating safely during the pandemic. Based on the CDC definition of COVID-19 risk exposure most dermatology practices fit into the low-risk category.

Step 1: Understanding your community's rate of COVID-19 prevalence
Communities with greater prevalence will require more stringent procedures, while those with a lower incidence of COVID-19 may function in a different manner.

1. The federal government has stated that a downward trajectory of documented cases over a 14-day period should occur before opening practices to elective visits and procedures. However, most states have "opened" to various degrees in spite of rising case numbers, allowing elective visits and procedures to proceed.

2. Consult with your local and state public health department for local requirements. The AMA has developed a helpful chart summarizing each state's directives on elective, non-urgent, or non- es-sential procedures. The situation is changing with some regularity as "hotspots" crop up around the country.

3. Have a plan in place for patients who appear with COVID-19 symptoms and may need to be test-ed. Consider finding testing locations in your area where you can recommend patients can go for testing or refer the patient to their primary care physician. Consult the CDC's guidance on Covid-19 testing.

Step 2: Clean your practice
It is important to properly prepare your clinic space to ensure you, your staff, and patients continue to remain healthy and safe while practicing.

1. Clean and disinfect your entire practice according to World Health Organization (WHO) standards:

a. 70% ethyl alcohol to disinfect small areas between uses, such as reusable dedicated equipment (for example, thermometers); OR

b. Sodium hypochlorite at 0.5% (equivalent to 5000 ppm) for disinfecting surfaces; OR

c. Any disinfectant products that meet the EPA's criteria for use against SARS-CoV-2.

d. If your practice has been closed for more than seven days, you can perform your normal routine cleaning procedures as the virus that causes Covid-19 has not been shown to survive on surfaces longer than this time, according to the CDC.

2. Using the WHO recommended standards above, wipe exam tabletops, countertops, exam beds/tables, doorknobs, and exam light buttons/handles between each patient during the clinic day.

3. Using the WHO recommended standards, wipe all common high-touch areas at the end of the day, including but not limited to:

a) Exam room: exam tabletops, countertops, exam beds/tables, doorknobs, and exam light buttons/handles, chairs, and faucet handles.

b) Bathroom: all bathroom surfaces, urine-sample pass through areas/trays, and toilets.

c) Reception: all countertop surfaces and chairs.

d) Offices: all surfaces and chairs.

e) Lab, kitchen, and break room: all surfaces and countertops.

f) Empty all trash cans.

Step 3: Reorganize your practice to minimize patient contact and increase sterilization

1. Put up signs to notify patients of COVID-related precautions and add markings where necessary to maintain appropriate social distance (e.g., tape marking in front of reception for patients to maintain distance from staff and each other). Use the Academy's sign template.

2. Reduce the number of chairs in waiting rooms and appropriately space them apart.

3. Remove magazines and other reading materials from patient care areas.

4. If pens are required for patients to fill out forms, clean them between each patient (use one penholder for clean pens and another for used pens).

5. Place additional hand sanitizers and wipes in the waiting room for patients as well as in high-traffic areas for staff.

6. Have hand sanitizer and/or a place to wash hands with soap and water in each exam room.

7. Consider keeping all doors open on the patient path from the entrance through the office to the exit, to minimize the need to touch surfaces.

8. Determine if physical barriers would be helpful to protect staff from patients exposed to COVID-19. For example, is there a sneeze guard that could be installed to limit contact between front desk staff and patients?

9. Limit visitors to essential vendors and suppliers. Consider having virtual meetings whenever possible, such as with pharmaceutical reps.

10. For Mohs surgery, have the patient stay in their assigned room through all stages and repair. They should only leave the room for restroom breaks. Snacks can be brought to the patient in the room as needed.

11. COVID-19 transmission has not been documented through blood or tissue fluid. Therefore, for ablative laser procedures, no change is needed in current practice. Specifically, continue wearing the same type of personally protective equipment (PPE) as before the COVID-19 pandemic and using smoke evacuators to protect the operator and assistants from bloodborne and tissue pathogens and carcinogens in the laser plume. Similarly, for dermabrasion, masks and face shields are a reasonable measure to protect the operator and assistants from bloodborne pathogens.

12. Implement digital tools to assist your practice in maximizing social distancing where appropriate:

a) Connections must be compliant with HIPAA and use web browsers with encrypted communications, such as Chrome, Firefox, or Safari.

b) If you have an electronic health record (EHR), contact your vendor to determine if there are any applications you can install to reduce in-person contact. Such examples include patient portals, online bill pay, electronic orders for staff, electronic prescriptions, and electronic lab orders.

c) Visit the Academy's Health IT resource center for specific guidance on digital tools to adopt in your practice during this time.

d) Continue using teledermatology for appropriate patients. It is important to consider that relaxed regulations may revert to pre-national health emergency rules after the emergency is over.

Step 4: Maintain appropriate PPE for staff

1. Check OSHA's PPE standards (29 CFR 1910 Subpart I) and ensure there is enough appropriate PPE for all your staff. The Academy offers a way for members to purchase PPE through the AAD Member Buying Program. Review CDC guidance and some state guidelines on how to optimize the supply of face masks.

2. Masks and eye protection should be worn by all staff interacting with patients and patients should come into the office wearing a mask.

3. Whenever a staff member needs to remove or adjust their PPE, they should first wash their hands with soap and water for 20 seconds or rub them with an alcohol rub. They should then again wash their hands with soap and water for 20 seconds or rub them with an alcohol rub after they have touched and/or adjusted their PPE.

4. Consider the necessity of conserving PPE during the pandemic. The same mask may be worn for several days and either sterilized or put aside for 5-7 days and reused.

Step 5: Set your patient schedule including telemedicine visits

The treating dermatologist should make the decision of which visits should be transitioned to telemedicine and which need to be done in person. Here are some guidelines to help you schedule patients:

1. Consider priority scheduling of patients that were the most urgent during the time the practice was closed or limited to essential services only but could not be seen in person.

2. Continue offering telemedicine (if waivers are still in effect) during downtime in your practice. Use this workflow (PDF download) to help you implement telemedicine in your practice while seeing patients.

3. Minimize in-person follow-up visits by using absorbable or buried sutures for surgical procedures. Consider doing teledermatology follow-up visits whenever practical.

4. If you don't offer online appointments, consider enrolling in an online platform so patients can schedule appointments in an easier manner and staff aren't overwhelmed with phone calls from the pent-up demand.

5. Let patients know of the steps your practice is taking to keep them safe at the office in your communications with them.

6. Consider making your cancellation policy more flexible as patients may fear visiting practices during this time.

Step 6: Organize your staff

Follow CDC updates and check with your state and local public health departments on regulations concerning group gatherings. Try to limit the number of staff per room in your practice and consider the following guidance:

1. Educate staff on social distancing in break rooms or lunch areas so they sit at least six feet apart. Staff should wear PPE for office staff meetings or sit at least 6 feet apart.

2. Instruct staff not to share workstations or computers. If equipment must be shared, staff should be trained on properly cleaning between each use.

3. Practice social distancing with patients. Train staff to greet patients with a nod, smile, and/or wave. Do not shake hands or hug.

4. Tell staff not to come into the practice if they exhibit any flu-like illness, loss of taste or smell, other known COVID-19 symptoms, or if they have been in close contact with a COVID-19 infected individual. Staff should follow the CDC's Return to Work Criteria.

5. Screen staff each day prior to seeing patients for the presence of flu-like symptoms (cough, fever, sore throat, runny nose, nausea, diarrhea, or shortness of breath), loss of taste or smell, or close contact with individuals who may be infected with COVID-19. Consider non-contact temperature screening (the CDC defines 100.0+degree F as fever). If the screen is positive, consistent with possible COVID-19 infection, or there was close contact with an infected individual, the staff member

should be sent home and instructed to follow the CDC's Return to Work Criteria.

6. Summary of the CDC's Return to Work Criteria.

a) Except for rare situations, in symptomatic staff, a test-based strategy is not recommended to determine when staff should return to work.

b) The CDC defines health care worker close contact as being within about 6 feet of an infected person for a total of 15 minutes or more while not wearing recommended PPE. If staff wear PPE throughout the workday and socially distance at other times, they would not be considered at high risk of exposing their co-workers/patients or of being exposed to COVID-19 by them.

c) Staff with mild to moderate symptoms should not go to work and should self-isolate for 10 days from symptom onset and at least 24 hours fever-free without fever-reducing medication with other symptoms improved. Staff who were suspected of having COVID-19 and had it ruled out based on a clinical decision that COVID-19 is not suspected and testing is not indicated should be able to return to work (without other suspected or confirmed diagnoses).

d) If a physician evaluating a symptomatic staff member for COVID-19 decides that antigen testing is indicated and the test is negative, that would indicate that the staff member likely did not have active COVID-19 infection at the time the sample was collected. A second antigen test may be performed at the discretion of the evaluating physician, particularly when a higher level of clinical suspicion for COVID-19 infection exists. Staff who were suspected of having COVID-19 and had it ruled out with at least one negative test should be able to return to work (without other suspected or confirmed diagnoses).

e) Staff with severe or critical illness should not go to work and should isolate for 20 days from symptom onset and at least 24 hours fever-free without fever-reducing medication with other symptoms improved.

f) A staff member that has been exposed to a COVID-19 infected individual, should either not go to work and self-quarantine for 10 days or have a COVID-19 test done at 5-7 days after exposure and not go to work and self-quarantine until the result is known. If negative, they can return to work 7 days after exposure. If positive they should not go to work and self- quarantine for 10 days from the date of the test. If symptoms develop, follow the symptomatic healthcare worker algorithm above. If the staff member previously had COVID-19 within the past three months and remains without symptoms they do not need to quarantine and should not have a COVID-19 test done.

g) Asymptomatic staff without known exposure who decided to get a COVID-19 test and the test came back as positive should not go to work and should self-quarantine for 14 days. If symptoms develop, follow the symptomatic health care worker algorithm above.

h) Check with your local and state health department for any additional requirements for management of staff that are suspected of having COVID-19.

7. The CDC has created guidance regarding how to handle health care personnel who may have been exposed to COVID-19.

The AAD has also assembled information about the status of risks to personnel in healthcare facilities (PDF download) and will be updating it frequently. OSHA has also provided guidance on how to keep practices safe during a pandemic (PDF download).

8. If findings suggest the possibility of COVID-19 infection, consider referring staff to their primary care physician or local urgent care center for evaluation.

9. Follow HIPAA protocols if staff are diagnosed with COVID-19. You may inform patients and staff they have encountered someone who has tested positive for COVID-19; however, you cannot identify the staff without their consent.

10. Be flexible and accommodating with staff whenever possible. Childcare and schooling options may be limited during this time.

11. Make sure you communicate all new procedures with staff in advance of any changes/updates to your office procedures.

12. Check with your state's requirements on employee travel. Some state and local governments require people who have recently travelled to certain high COVID-19 prevalence areas to quarantine for 14 days.

13. Understand the employment-related legal considerations during the pandemic by reviewing the following Dermatology World articles:

a) Employment-related legal considerations during the COVID-19 public health crisis
b) Employment-related legal considerations during COVID-19, Part II
c) COVID-19 impact on employed dermatologists: Part 1
d) COVID-19 impact on employed dermatologists: Part 2

Step 7: Patient screening

1. Prior to arrival for an appointment or on the day before the appointment, check with the patient if they have developed any symptoms of a respiratory infection (e.g., cough, sore throat, fever, runny nose, or shortness of breath), diarrhea, nausea, or loss of taste or smell. Additionally, ask the patient if they have had any recent close contacts with others either diagnosed with or exposed to COVID-19. Consider using a screening tool. If COVID-19 is suspected, refer the patient to their primary care physician for evaluation and re-schedule their appointment to a later date. If a primary care physician is unavailable, refer the patient to an urgent care center. It may be prudent to receive written clearance from the treating physician as to when the patient can be seen in your practice and is clear of COVID-19 symptoms. Contact your malpractice carrier to consult on COVID-19 related care including expectations on patient pre-screening.

2. Instruct the patient to come to your practice alone unless they need a caregiver (or parent for children) with them at the visit. If unable to arrive alone, suggest the individual accompanying the patient wait in the car or outside the office for the duration of the appointment. Also, advise the patient that face masks are now highly recommended by the CDC for all persons, except for young children under age 2, anyone who has trouble breathing, or unable to remove the mask without assistance when they go out in public. Due to additional screening activities, allow extra time upon arrival.

3. Once the patient arrives, consider having them wait in their car or outside the office until called or texted on their cellphone. Ask about the presence of flu-like symptoms (cough, fever, sore throat, or shortness of breath), loss of taste or smell, and/or contact with potentially infected persons. Consider non-contact temperature screening (the CDC defines 100.0+ degrees F as fever).

If findings suggest possibility of COVID-19 infection, refer the patient to their primary care physician or local urgent care center for evaluation and re-schedule their appointment to a later date. Screen any accompanying individuals who visit the practice as well.

4. Consider creating as much of a paperless check-in process as you can. Ask the patient to complete all their required pre-visit paperwork online through your patient portal, or securely email forms in advance.

5. Practice social distancing when you greet patients and staff with a nod, smile, and/or wave. Do not shake hands or hug.

6. Determine if any procedures being done that day will require additional PPE such as ablative laser procedures or dermabrasion. Most dermatologic procedures are NOT believed to generate aerosols or droplets.

7. Some states may restrict procedures requiring PPE, so you may need to assess with your state public health agency as to which procedures are permitted during the pandemic. For example, cryotherapy is considered a procedure but does not deplete PPE.

8. Some hospitals and ambulatory surgery centers require COVID-19 testing (antigen) of patients undergoing procedures in those facilities. If you operate in such an environment, follow the requirements. Patients undergoing such preoperative testing must quarantine between the time they get the test and admission to the facility.

9. Despite screening patients, all patients should be treated as potentially being infectious with COVID-19. Patients known or suspected to have COVID-19 that need treatment for a dermatologic condition related to or exacerbated by COVID-19 should be seen by telemedicine whenever appropriate. If an in-person visit is required, all safety precautions in the office should be followed carefully. In addition, the patient should interact with only one dedicated staff member plus the physician. They should stay in one exam room throughout the encounter, with the door closed. After the encounter, thoroughly disinfect all surfaces.

Step 8: Keep communicating with patients

1. Inform patients of the steps your practice is taking to prevent COVID-19 infections through social media, your practice website, and other marketing channels. See the Academy's sample scripts (PDF download).

2. Try different patient schedules to maximize social distancing. Consider extending office hours to keep patient visits from overlapping with each other.

3. Consider gathering patient preferences for communication channels (e.g., text, email) so they can stay informed of your practice's changes through the pandemic.

4. Be prepared to take any necessary steps if there is a resurgence of cases in your community or clinic once you have reopened. Keep communication channels with patients open so you can inform them of any changes.

For full information, please read the original relevant pages in the AAD website.

Contact Dermatitis / Patch Testing

1st to 3rd September 2021
European Society for Contact Dermatitis
Amsterdam, Netherlands
www.escd2021.com

8th to 10th June 2022
European Society for Contact Dermatitis
Amsterdam, Netherlands
www.escd2022.com

Dermatology - International

20th to 21st April 2021
AAD Virtual Meeting Experience (VMX)
Virtual Meeting
www.aad.org/member/meetings-education/aad-vmx

6th to 8th May 2021
16th EADV Symposium
Virtual Meeting
https://eadv.org/calendar/show/598

7th to 8th May 2021
21st European Dermatology Congress
Amsterdam, Netherlands
https://www.clocate.com/conference/european-dermatology-congress/66472/

12th to 14th May 2021
ESPD Annual Meeting
Virtual Meeting
www.espd.info

21st to 22nd June 2021
22nd World dermatology Congress
Tokyo, Japan
https://www.clocate.com/conference/world-dermatology-congress/65366/

15th to 18th September 2021
Ibero-Latin American Congress of Dermatology 2021 (CILAD)
Madrid, Spain
www.cilad2021.org

22nd to 25th September 2021
14th World Congress of Paediatric Dermatology
Edinburgh, Scotland
www.wcpd2021.com

22nd to 25th September 2021
European Society for Dermatological Research
Virtual Meeting
www.esdrmeeting.org

29th September to 2ND October 2021
EADV Congress
Vienna, Austria
https://eadv.org/calendar/show/60

3rd to 6th November 2021
18th World Congress of Cancers of the Skin
Buenos Aires, Argentina
www.cilad.org/wccs/

10th to 13th November 2021
International Congress of Dermatology
Virtual Meeting
www.icd2021.com.au

The COVID-19 pandemic has caused the postponement or cancellation or change of format for all congresses that were originally scheduled for the latter part of 2020 and well into 2021. Check the society and congress websites frequently for updated information.