eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Prevention of Irritant Contact Dermatitis Due to Hand Hygiene in Covid-19 Pandemic

Nopriyati[1], Damai Trilisnawati[1*], Yulia Farida Yahya[1], Mutia Devi[1], Theresia Lumban Toruan[1]

[1] Department of Dermatovenerology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
COVID-19
Hand hygiene
Hand sanitizers
Dermatitis irritant
Health personnel

*__Corresponding author:__
E-mail address: dr.damai@gmail.com
(Damai Trilisnawati)
All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/bsm.v4i4.160

ABSTRACT

Irritant contact dermatitis (ICD) is an inflammatory epidermal disorder associated with physical or immunological provocation that results in the impaired skin barrier. The prevalence of ICD is found to be 17-30% in healthcare workers compared to the general population. The first-line management strategies of ICD is based on prevention. Intensive hand cleansing is one of the causes of ICD. Hand hygiene is a broad term that refers to any action of hand cleansing. Hand hygiene practices include hand washing and hand rubbing with antiseptics. Hand hygiene is the most effective preventive measure in preventing infection control, especially in the era of coronavirus (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since December 2019. This disease is transmitted through inhalation or contact with infected droplets. Prevention and mitigation actions are vital in controlling the infection.

1. Introduction

Dermatitis is an epidermal inflammatory disorder associated with physical or immunological provocation.[1] Irritant contact dermatitis (ICD) results in skin barrier disorder that can affect the concentration of bacteria, fungi, and other microorganisms to stimulate immune response.[1] ICD is an occupational health problem often occurs in healthcare workers in many countries. The prevalence of ICD is 17-30% in healthcare workers compared to the general population. The prevalence of ICD in the population of workers is 7 of the 10,000 workers, the highest was found in wet workers, especially healthcare workers.[2] ICD is twice as frequent in women than men and occur in all age groups.[3] Changes in structure and function of stratum corneum in dermatitis are disruption of stratum corneum bilayer and increased permeability, penetration, and inflammation. The epidermis responds by increasing the formation of stratum corneum resulting in hyperproliferation, structural damage, disruption of water-binding properties, insufficient hydration, and lack of desquamation.[4] During the process; intensive handwashing can cause changes in skin texture resulting in hand dermatitis in the future referred to as ICD.[5] Water can eliminate free amino acids, a component of the

natural moisturizing factor plays a role in skin protection. The acidity level of skin also increases immediately after contact with water. Shifting the acidity to neutral pH can increase protease activity and may impact the function and integrity of the skin barrier.[6] Washing hands with soap can lead to a paradoxical increase in the number of bacteria on the skin because soap can cause irritation and dry skin.[3]

Hand hygiene is a general term referring to the act of hand cleansing. Hand hygiene practices can include hand washing or hand rubbing with antiseptics.[7] Various preparations can be used to clean hands, such as water, soap, alcohol, chlorhexidine, chloroxylenol, hexachlorophene, iodine and iodophor, quaternary ammonium compounds, triclosan, and other agents. Hand hygiene is the most effective preventive measure in controlling infection especially in the era of coronavirus (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since December 2019.[8] As of May 4, 2020, 3,435,894 people was found contracted coronavirus novels with 239,604 deaths worldwide.[9] In Indonesia, 11,587 cases were confirmed with 864 mortalities. Meanwhile, in South Sumatra, as many as 185 (1.6%) verified claims.[10] The disease is transmitted through inhalation or contact with infected droplets. Contact transmission occurs when the contaminated hand touches mucosa of mouth, nose, or eyes. Viruses can also move from one surface to another with contaminated hands, facilitating the transmission of indirect contact.[11] SARS-CoV-2 is an enveloped RNA virus with nucleic acids and nucleocapsid proteins in virions. A lipid bilayer coats the virion surface of the virus, this layer has structural protein SARS-CoV-2.12 Prevention, and mitigation measures are the key to infection control.[13]

Irritant contact dermatitis is more commonly reported with ionophores. Other antiseptic agents can also cause ICD. Alcohol-based hand rub is still recommended as a standard procedure for hand hygiene because the potential for irritation is lower than other products in terms of skin tolerance, besides alcohol is also more effective in reducing the number of bacteria.[7,14] According to Loffler and Kampf's study in 2008 in Germany, an experimental study involving 521 nurses proved that 80% of ethanol disinfection procedures were better tolerated than washing hands with detergent. Research by Chowdhry et al. in 2017 in India showed alcohol is one of the safest antiseptic preparations. Although repeated use of alcohol-based hand rub can cause dry skin and irritation, alcohol is less irritating than soap and water.[15] ICD's first-line management strategies are based on prevention, such as replacing irritating products with less annoying products. Because the first line is more fundamental than treatment, prevention is usually prioritized.[16]

In this literature review, normal skin physiology, ICD and hand hygiene will be discussed to acknowledge ICD prevention due to hand hygiene in the pandemic era of COVID-19.

2.Normal Skin Physiology

The primary function of the skin is to reduce water loss, protect against abrasion and microorganisms, and act as a barrier to permeability. The epidermis is a layered squamous epithelium found on the surface of the body. Thus, the cuticle has several protective functions forming "epidermal barrier", including molecular-based barrier functions. Among the various skin barrier functions, the stratum corneum (SC) is one of the critical factors regulating skin sensitization.[17]

The epidermis consists of four layers of cells, namely stratum basalis (SB), stratum spinosum (SS), stratum granulosum (SG), and the stratum corneum (SC) (Figure 1). Keratinocyte proliferation occurs in SB, differentiates and migrates towards SS. Keratinocytes express different keratin intermediate filament collections in each layer. Keratin is an elastic fibrous protein expressed during keratinocyte differentiation. In addition to SC, tight junction (TJ) also acts to bind epithelial cells to form a functional barrier. Among some dendritic (SD) cells, specific SDs in the epidermis are called Langerhan cells (LC) and

are thought to be involved in the induction of antigen-specific T helper-2 (Th2) responses. Langerhan cell acts as an epidermal immune barrier system. The three skin barrier elements (SC as water-liquid interface barrier, TJ as liquid-liquid interface barrier and LC as the immunological barrier) protect the body as first-line defence mechanism.[17]

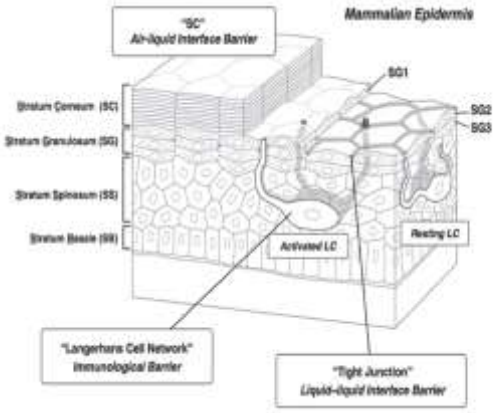

Figure 1. Mammalian epidermis structure and three skin barrier elements[17]

Stratum corneum is the results of dead cell products of SG1 layer and consists of 10-20 layers of dead cells. Stratum corneum consists of keratin intermediate filaments, water-soluble lipids, proteins (enzymes) and humectants. SC barrier described as a "bricks and mortar" model (Figure 2). Corneocytes with envelope cell proteins are described as "bricks", whereas lipid layers are described as "mortars". Lipid "mortar" plays a vital role in the function of the skin barrier, and the ceramide contained therein plays a role in the regulation of skin barrier. The "bricks and mortar" arrangement functions in the management of permeability, preventing dehydration, and antimicrobial activity.[18] In the final SG layer, SG1 cells undergo cell death program but are not a usual 'apoptosis', classified as 'cornification'. The critical process of cornification consists of three processes, namely formation of intracellular keratin tissue, the structure of cornified envelopes (CE) (cross-linking between lipids and proteins), and formation of fats between cells.[17]

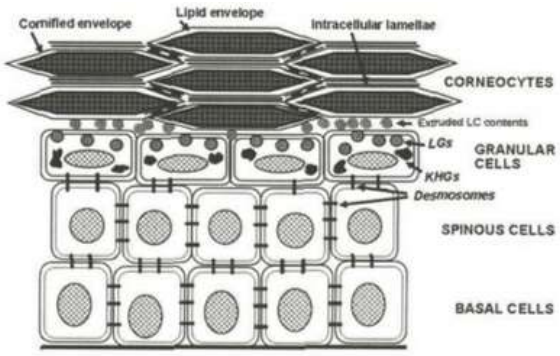

Figure 2. Brick and Mortar[19,20]

Keratohyaline granules (KHG) form gradually in the cytoplasm of SG3 cells before cornification occurs. Keratohyaline granules consist of electron-dense amorphous materials. Keratohyaline granules consist of keratin complexes (mainly from keratin 1 and 10) and keratin binding proteins, such as profilaggrin (F-granules) or loricrin (L-granules). Profilaggrin is a mammalian protein, insoluble, and highly phosphorylated. Profilaggrin consists of amino-terminal Ca^{2+}-binding proteins and associated filaggrin monomers. Filaggrin is SC's main keratin binding protein. During the SG1 to SC transition, KHG also gradually disappeared. Although the mechanism for removing KHG is still unknown, dephosphorylation of profilaggrin is considered as the first step in the dissociation of the keratin-profilaggrin complex in KHG. The phosphorylated profilaggrin is cleaved to produce filaggrin monomers during the SG1 to SC transition. The filaggrin monomers produced bind SC keratin filaments. Keratin filaments are arranged to form a membrane template in SC, shaped like a cube. This three-dimensional structure is considered necessary for SC hydration and gives rigidity to each SC layer.[17]

During the SG1 to SC transition, an increase in intracellular Ca^{2+} induces terminal differentiation. The main target of Ca^{2+} is transglutaminase (TGase). Transglutaminase is a cross-linked Ca^{2+} enzyme that is bound to isopeptide bonds. Increased TGase I activity and cytoplasmic cross-linking protein products TGase III epidermal differentiation complex (EDC) genes, involucrin, loricrin, envoplakin,

periplakin, and small proline-rich protein families (SPRR), etc. under the plasma membrane. Mammalian EDC genes, namely loricrin, involucrin, SPRR protein, and types of proteins merge with S100 (filaggrin). Filaggrin is a skin-specific protein and is involved in the formation of keratin tissue in SC functioning as a moisturizer or production of natural moisturizing factors (NMF).[17]

Another critical process of cornification in the formation of intercellular lipids due to secretion of lamellar bodies (LB). Lamellar bodies are organelles derived from the Golgi apparatus and contain phospholipids, glucosylceramide, sphingomyelin, and cholesterol. During the SG1 to SC transition, LB secretes its contents into extracellular space between SG1 and SC, including various types of proteases, protease inhibitors and lipids such as glycosylceramides. This component is essential in the formation of SC barrier.[17]

After cornification, SC dead layers will accumulate and change their properties through various chemical reactions. Different chemical reactions occur during migration (bottom-up) and SC maturation. From the profilaggrin processing step, SC can be divided into three hydration zones (lower, middle and top). The central SC zone is functioning as the primary SC permeability barrier.[17]

3.Hand Hygiene

Hand hygiene is a general term referring to the act of hand cleansing. Hand cleansing in the form of washing hands with plain soap and water or antimicrobials soap and antiseptic hand-rubbing to reduce or inhibit the growth of microorganisms without rinsing or drying.[5] Healthcare workers must comply with "My 5 Moments for Hand Hygiene" WHO, i.e. before touching the patient, before septic procedures or aseptic, after exposure or at risk of bodily fluids, after contacting the patient, and after affecting patient's environment. WHO recommends a six-step hand washing technique covering the entire surface of both hands skin.[5] The step to clean hands with alcohol-based hand rub is done for 20-30 seconds. While cleaning hands with soap and water can be done for 40-60 seconds with the same steps, then hands are thoroughly dried with disposable tissue.

SARS-CoV-2 is a lipid bilayer enveloped virus, SARS-CoV-2 tends to be more sensitive to the disinfection process than most other viruses so that it can be eliminated by hand cleansing process.[28] Transmission of SARS-CoV-2 can be through respiratory or contact droplets. Contact transmission occurs when the contaminated hand touches mucosa of mouth, nose, or eyes. Viruses can also move from one surface to another with contaminated hands which facilitates the transmission of indirect contact. So hand hygiene is paramount to prevent the spread of SARS-CoV-2 virus.[29]

WHO and CDC recommend healthcare workers wash their hands with soap and water if hands look visibly dirty or if exposed to blood or other bodily fluids. However, cleaning hands using alcohol-based hand rub is the preferred method for hand antisepsis in all clinical conditions if hands do not look dirty.[3,7] If alcohol-based hand rub and soap are not available, healthcare workers can use dirt or soil. Dust may be able to inactivate pathogens by increasing acidity. However, the land may be contaminated with faeces, so it is necessary to consider the risks that can occur.[28] The following are hand hygiene preparations, such as water, soap, alcohol, chlorhexidine, chloroxylenol, hexachlorophene, iodine and iodophors, quaternary ammonium compounds, triclosan, and other agents:

a. Water

Water is an excellent solvent for a large number of substances and is often called the universal solution. Water is stable and has a high boiling point and has a very high surface tension which is a critical characteristic for cleaning dirty hands. Water alone cannot directly remove impurities such as fat, oil, and protein. So that water alone cannot wash dirty hands. Soap or detergent must be applied with water followed by running water. Skin pH can increase immediately after contact with water.

Shifting pH to neutral pH can increase protease activity and have an impact on the function and integrity of the skin barrier.[6,7] Although warm water can dissolve dirt and oil residue suspensions, washing hands quickly using antimicrobial soap is no more effective than washing hands for 30 seconds with water cold and without soap.[7]

b. Soap

Soap is a detergent-based product containing esterified fatty acids and sodium or potassium hydroxide. Soap is available in various forms, including bar soap, tissue, and liquid. Cleaning using soap is associated with detergent properties that can remove fat and dirt, dust, and different organic substances from the hands. Plain soaps have minimal antimicrobial activity. But washing your hands with plain soap can remove transient flora. Three mechanisms of soap cause deactivation of SARS-CoV, namely destroying viral membranes, simple elution mechanisms, and blocking viral cells into the nucleus through hydrophobic-hydrophobic interactions.[30] Washing hands with plain soap can cause paradoxically increased numbers of bacteria in the skin because soap can cause irritation and dry skin, so adding humectants to soap preparations can reduce irritation. Humectants help the stratum corneum absorb water by drawing water from the dermis into the epidermis. Glycerol can be added to soap preparations as a humectant. Other humectants such as hyaluronic acid, urea, and alpha hydroxy acid can be used as long as they are not toxic and do not cause allergies. Glycerol is preferred because of its proven safety.[7,31]

c. Alcohol

Most alcohol-based antiseptics contain ethanol, isopropanol or n-propanol, or a combination of both products. Antimicrobial activity of alcohol is due to the ability of alcohol to denature proteins. Alcohol solution containing 60-80% alcohol is the most effective alcohol, while alcohol with higher concentrations become less potent. Some enveloped (lipophilic) viruses are susceptible to alcohol when tested in vitro. Alcohol has several advantages, such as elimination of viruses, the short time needed to clean hands (20-30 seconds), product availability, better skin tolerability, and does not require secure infrastructure (clean water supply, sink, soap, or hand towels).[5] The efficacy of alcohol-based hand hygiene products is influenced by several factors, including the type of alcohol used, alcohol concentration, contact time, the volume of alcohol used, and whether the hands were wet when ethanol was used.[7] In a study conducted by Rabenau et al. in 2005 in Germany, 45% isopropanol, 30% n-propanol and 0.2% mecetronium ethyl sulphate could inactivate SARS-CoV, regardless of organic load.[32]

The use of alcohol for hand antisepsis tends to cause dry skin unless humectants are added to alcohol formulation. Dry skin due to alcohol can be reduced or removed by adding 1-3% glycerol. Alcohol-based hand rub is still recommended as a standard procedure for hand hygiene because the potential for irritation is lower than other products on skin tolerance, besides alcohol is also more effective in reducing bacteria.[7,14] Alcohol-based hand rub that contains humectants and can be well tolerated still may cause a burning sensation on damaged skin. Alcohol-based hand rub products containing strong perfume are poorly tolerated.[7]

d. Chlorhexidine

Chlorhexidine is almost insoluble in water, but digluconate can dissolve in water. Chlorhexidine has in vitro activity against enveloped viruses such as herpes simplex virus, human immunodeficiency virus (HIV), cytomegalovirus, influenza, and respiratory syncytial virus (RSV).[5,33] Based on a study conducted by Geller et al. in 2012 in France, chlorhexidine was shown to have an anti-coronavirus 229E activity that was time-dependent and concentrated in chlorhexidine and allowed a reduction of 3 log10, but only after a contact time of 60 minutes.[34] Chlorhexidine used as prescribed can be well tolerated. The incidence of ICD increases with increasing chlorhexidine concentration. Irritant contact dermatitis can occur at concentrations of 4% chlorhexidine. Allergic reactions to chlorhexidine

gluconate are infrequent .[7,26]

e. Chloroxylenol

Chloroxylenol known as para-chloro-meta-xylenol (PCMX) is a halogen-substituted phenolic compound often used as a preservative in cosmetics and other products and as an antiseptic. Chloroxylenol 0.12% can reduce 3 log10 viral titers for 30 seconds. The antiseptic activity of chloroxylenol is strongly influenced by the presence of organic matter but neutralized nonionic surfactants. Chloroxylenol is generally well-tolerated, and allergic reactions are relatively rare.[3,7]

f. Hexachlorophene

Hexachlorophene is bisphenol consisting of two phenolic groups and three chlorine groups. The antimicrobial activity of hexachlorophene serves to deactivate the essential enzymes in microorganisms. Hexachlorophene can inhibit 3C-like (3CL) protease, which is a crucial enzyme in SARS-CoV life cycle. The body can absorb 7,35 Repeated use of hexachlorophene 3% through the skin. Infants routinely bathed with hexachlorophene can experience neurotoxicity (vacuolar degeneration). The FDA stated hexachlorophene should not be used regularly to bathe infants and is classified as an unsafe and ineffective antiseptic handwashing preparation. Hexachlorophene has been banned throughout the world due to high skin absorption rate and toxic effects.[7]

g. Iodine and iodophors

Iodine is an effective antiseptic since the 1800s. Iodine often causes irritation and skin discolouration. Ionophores are used to replace iodine as the active ingredient. Iodine molecules rapidly penetrate cell walls of microorganisms and deactivate cells forming complexes with amino acids and unsaturated fatty acids resulting in impaired protein synthesis and cell membrane disruption. Combining iodine with various polymers increases iodine solubility to reduce skin irritation. The polymers most often incorporated into iodophors are polyvinyl pyrrolidone (povidone) and ethoxylated nonionic detergents (poloxamer).[7] Povidone-iodine has better virucidal activity than chlorhexidine. The use of povidone-iodine against the MERS-CoV virus, in vitro, proved that 1% concentration for 30 seconds effectively reduced viral activity >99.99%.[36] A high amount of free iodine causes skin irritation. Ionophores cause less skin irritation and fewer allergic reactions than iodine, but iodophors cause ICD higher than other antiseptics commonly used for hand hygiene.[7]

h. Quaternary ammonium compounds

Quaternary ammonium compounds consist of nitrogen atoms associated with four alkyl groups. Alkyl benzalkonium chloride is most widely used as antiseptic. Other compounds used as antiseptics include benzethonium chloride, cetrimide, and cetyl peridium chloride. Quaternary ammonium compounds have relatively weak activity against mycobacteria and fungi and have better activity against lipophilic viruses. In general, quaternary ammonium compounds are relatively well tolerated

i. Triclosan

Triclosan is a nonionic substance developed in the 1960s. In a study conducted by Dellano et al. in 2009 in New Jersey, triclosan 0.05% was proven to reduce murine hepatitis virus (MHV) which is SARS-CoV surrogate without viral recovery for 30 seconds.[37] triclosan has persistent activity on the skin that is influenced by pH, the presence of surfactants or humectants, and ionic properties. Most formulas containing triclosan less than 2% are well tolerated and rarely cause allergic reactions.[7]

j. Other agents

The efficacy of washing hands with hypochlorite solution for 30 seconds is no more effective than washing hands with distilled water. Hand washing using hypochlorite 4% solution for 5 minutes is 30 times more effective than washing hands with isopropanol 60% for 1 minute. Hypochlorite solutions tend to be very irritating to the skin when used repeatedly and have a strong odour; these agents are rarely used to clean hands nowadays. Several other agents are being evaluated by the FDA to use as antiseptics in health facilities.

However, the efficacy of these agents has not been adequately assessed. Products that use traditional antiseptic concentrations (for example, low iodophor concentrations) or agents contained new compounds with antiseptic properties tend to be used by healthcare workers. For example, the addition of silver-containing polymer to ethanol carrier (Surfacine) can produce preparations that have persistent antimicrobial activity. New compounds with in vitro activity must be tested in vivo to determine the agent's ability to reduce skin flora.[7]

4.Etiopathogenesis

Elements of hand hygiene, including friction, water, drying, surfactants, and disinfectants, have significant effects on the epidermal barrier. Water alone can eliminate free amino acids, a component of natural moisturizing factors that play a role in maintaining hydration for plasticization and desquamation of SC. The acidity level of the skin increases immediately after contact with water. The acidity level needed by enzymes is effective in form and integrity of SC, such as lipid metabolism, bilayer structure, ceramide synthesis and desquamation, and protection of skin surface from bacterial colonization. Exposure to surfactant soap/cleansers and water has a significant effect on structure and function of the skin, including impaired composition and structure of SC lipid bilayers, epidermal inflammation, and increased permeability (Figure 3). Epidermis hyperproliferation, structural damage, reduced water-binding properties, inadequate hydration, and dry desquamation. SC turnover increases after chronic surfactant exposure. Skin neurosensory irritation (SNI) such as discomfort, stinging, burning, itching, and tingling. The causative factors are SC disorders, increased immune response, accelerated nerve response and increased levels of epidermal nerve growth factor.[6]

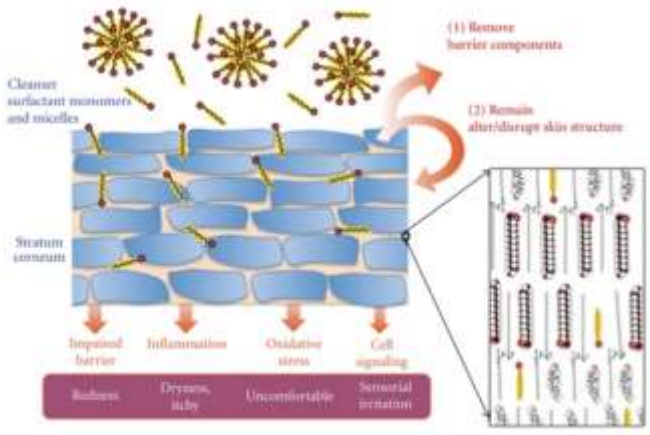

Figure 3. Disruption of skin barrier due to exposure to cleansing products[30]

5.Healthcare workers and hand hygiene

Compliance with hand hygiene causes product exposure to be higher. Hand hygiene opportunities range between <20 to >60 times per hour, and compliance rates are from 58% to 37%, respectively. Health workers in cold/dry climates tend to experience fissures in hands, peeling, and erythema worse than healthcare workers in warmer regions. The frequency of hand hygiene and age of health workers is also related to the severity of ICD. The type and composition of the product can also affect the integrity of the skin. Skin dryness is increased in liquid soap users compared to alcohol users. The use of alcohol-based hand rub with emollients results in better skin conditions compared to antiseptics containing CHG and washing water. Burning sensation from alcohol-based hand rub on irritated skin is ascribed to increased SC penetration and direct interaction with nerve endings of the skin.[6]

Effect of genetic factors on response to hand hygiene

a. Atopy

Damage to the stratum corneum, increased permeability, decreased ceramide, decreased natural moisturizing factors and mutations in the filaggrin gene characterize atopic dermatitis. Atopic skin shows subclinical inflammation, such as reduced

hydration, increased TEWL and increased SK turnover. Atopic without active skin disease show more intense response to SLS than non-atopic and more significant sensory irritation, which causes stinging and itching.[6]

b. Gene polymorphism

Decreased function of filaggrin gene polymorphism is found in 50% of patients with AD and hand dermatitis. Polymorphisms of R501X and 2282del4 filaggrin genes are associated with ICD among workers, including nurses, and maybe an independent factor in hand dermatitis. Variations in the IL1a gene, IL1a-889T polymorphism, are associated with lower IL1a levels in SC and more moderate skin irritation among wet workers. G to A (AA or GA) allele transition has a lower irritation threshold than GG type. An allele is more often found in patients with a history of allergies. The severity of wet worker skin irritation is related to the presence of AA.[6]

c. Gene expression with irritant exposure

After repeated exposure to SLS and nonanoic acid, 23 gene transcripts were found, which caused an irritant reaction. The initial response to SLS is characterized by an increase in matrix metalloproteinase 3 (MMP3) and decreased insulin growth-factor binding-protein 3 (IGFBP3) and non-coding maternally imprinted gene (H19).[6]

Sensory irritation

Skin neurosensory irritation (SNI) is a direct response to environmental or topical agents, including burning, stinging and itching. SC damage, rapid sensory nerve response and increased epidermal neural mediators, for example, nerve growth factor (NGF) are involved in the development of dermatoses including ICD The epidermal sensory nerve is near keratinocytes and affects the proliferation and thickness of the epidermis. Keratinocytes have sensory receptors, transient receptor potentials TRPV1, TRPV3 and TRPV4, which control water. TRPV4 improves repair of the epidermal barrier. Sensory nerves release neurotransmitters, including substance p (SP), alcitone gene-related peptide (CGRP), acetylcholine and neuropeptide Y (NPY). Inflammatory mediators can activate receptors on keratinocytes and myelinated sensory nerve fibres in response to external stimuli. SP and CGRP initiate inflammation, including erythema, oedema permeability and vasodilation and attract cytokines from keratinocytes to continue the inflammatory response. TNFa can induce the production of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF) and SP. NGF can activate macrophages that produce TNFa. TNFa and NGF are expressed by keratinocytes and are involved in the coordination of inflammation.[6]

6.Clinical Manifestation

Epidermal damage is a significant finding in ICD. ICD is characterized by redness, fissure, oozing, and pain (Figure 4). The area that often experiences ICD is eyelids, neck, antecubital fossa, wrist volar, and intertriginous. In cases of hand dermatitis, it is more evident between the finger, finger lines and intertriginous fold (Figure 5), irritants are concentrated and exacerbated by an increase in soap pH. [1]

(4)

The clinical symptoms of dermatitis depend on toxin involved, acute or chronic onset, localization, and several other factors. Severe irritant contact dermatitis is characterized by rapid onset (within a few hours), fast course, and quick resolution. Symptoms of acute ICD are characterized by macular or erythema papules, blisters, pustules, crusts and erosions. The lesions are well-demarcated, do not spread, and are accompanied by subjective symptoms such as burning and itching. Chronicity occurs in the skin, which is continuously exposed to the toxin. Chronic ICD is characterized by localized or diffuse lesions, initially with relatively firm borders but, becoming increasingly unclear, accompanied by scaly patches or patches and dry skin. The skin thickens due to infiltration of inflammatory cells, and skin folds become accentuation (lichenification). Hyperkeratosis, rhagades increasingly dominate the

clinical picture, and lichenification (Figures 6 and 7).[22,23]

Pustular and acneiform reactions can occur in ICD due to metals, halogens, oils, cosmetics, or other materials (Figure 8). Dermatitis due to metal show varied morphology. Some people show scaly and dry lesions; others show types of nummular and itchy lesions spreading to the arms. In factory workers, skin lesions are usually hyperkeratosis of fingertips. In hairdressers, injuries may be broken fingers, erythema, lichenification, fissures, vesicles and erosion (Figure 9). [24] Macerated reactions are usually in ICD patients using occlusive gloves (Figure 10).[1]

7.Differential diagnosis

Irritant contact dermatitis mimics other inflammatory dermatoses. The differential diagnosis of ICD is atopic dermatitis (AD), seborrheic dermatitis (SD), nummular dermatitis, and lupus erythematosus (LE). Both subacute and chronic lesions are marked with scaly skin, excoriations and lichenification. The distribution of AD lesions is based on the patient's age and disease progression. Seborrheic dermatitis is chronic and recurrent, often occurring in adolescents or young adults when sebaceous gland activity is increased. Lesions can be erythema, scaly and oily skin. Nummular dermatitis lesions are marked with coin-shaped plaques consist of papules and vesicles with well-bordered, measuring 1 to >3 cm, and usually have crust covering the surface of injury. LE lesions are distinguished by acute, subacute, and chronic. In subacute LE shows macules or papules that turn into hyperkeratotic papules or well-known annular plaques. In chronic LE, the lesion is most often in the form of macules, papules, or small purplish-red plaques with hyperkeratotic surfaces.[25]

8. Diagnosis

Anamnesis and clinical picture are very important in establishing the diagnosis. The history includes questions on the development of dermatitis and allergen exposure and evaluation of causality. ICD can be triggered by irritants such as frequent or prolonged contact with water, solvents, as well as cleansing agents or dust, causing irritation reactions. The onset of ICD is usually gradual, and the initial location is the area exposed to irritants. If irritant exposure is removed, it will improve clinical symptoms.[22,26] In addition to anamnesis and physical examination, supporting examinations also need to be carried out such as patch tests and laboratory tests.[1,22]

a. Patch test

Patch tests are needed to rule out a diagnosis of ICD. Irritant contact dermatitis due to work almost always requires patch testing specifically tailored to the job. It often involves dilution of product from occupational exposure alone for appropriate concentration and patch test materials.

b. Laboratory tests

Transepidermal water loss (TEWL) is a parameter of the skin's ability to maintain fluid homeostasis in the body. In addition to the stratum corneum, the keratinocyte also contributes to the skin barrier and provides pathogenic defences.[9] Transepidermal water loss is a parameter of barrier function. An increase in TEWL indicates an increase in permeability to antigens. TEWL is not routinely tested in clinical practice but is used in ICD study.[1,22]

9.Management

Healthcare workers have a high risk of irritant contact dermatitis. Repeated hand hygiene can cause chronic irritation that does not undergo resolution. Also, genetic factors, including atopic disease, filaggrin mutations and polymorphisms in 308 in the TNFa gene promoter influence the severity of ICD and response to treatment. Strategies to improve the health condition of healthcare workers include: a) identification of risk factors, b) proactive lotion treatment, c) use of alcohol-based hand rubs whenever possible, d) providing handwashing products with low irritation surfactants, and e) education about hand hygiene practices and the

impact on infections related to health facilities.[6]

Dermatitis must be treated quickly, and irritants must be avoided several weeks after clinical recovery.[1] The first-line management strategy is based on prevention. If this strategy cannot be applied, protective interventions such as protective gloves, topical therapy, and systemic therapy are recommended.[16]

Non-pharmacological

a. Hot water is not recommended for handwashing.[27]
b. After washing hands, rinse hands with gentle movements without causing physical irritation to the skin.[27]
c. Application of moisturizing products after washing hand

Application of moisturizing product after cleaning hands is an essential step in keeping the skin hydrated and preventing further abnormal skin reactions. Hydration products must be applied several times per day, especially immediately after washing hands. In order to reduce the risk of contact sensitization, it is recommended to use fragrance-free and hypoallergenic products.[7,21]

d. Do not wash hands before and after using alcohol-based hand rubs

Washing hands before using alcohol are not recommended because it removes the natural sebum layer that protects skin, thereby increasing skin irritation and dryness, as well as reducing bactericidal efficacy. Washing hands with soap and water after using alcohol is also not recommended because it removes the superficial sebum layer and emollients included in alcohol-based hand rub products thereby increasing the risk of dermatitis.[7,14,21]

e. Choosing less irritating products

Healthcare workers often clean their hands, so it is essential for health facilities to provide safe hand hygiene products for the skin. Although many hospitals offer soap in the hope of minimizing dermatitis, the use of water and soap is associated with dry skin and greater more significant than antiseptic products. One strategy to reduce irritation to soap is to use a hand based handrub containing humectants. Alcohol is better tolerated and is associated with better skin conditions than plain soap.[7] Loffler KampfKamf conducted an experimental study involving 521 nurses in Germany in 2008 concerning the potential for alcohol-related irritation. In the questionnaire given to study subjects, >50% believed that disinfection of hands with alcohol-based antiseptics was far more dangerous than washing hands with water and detergent. To examine this opinion, Loffler and Kampf conducted a patch test, and TEWL measurements were taken as parameters of damage to the barrier function and the corneometer for skin hydration parameters. After 48 hours of patch testing with 1-propanol, 2-propanol, and ethanol (60% to 90%), no barrier function was seen. A slight decrease in corneometer indicates loss of skin hydration. They subsequently researched to detect materials that cause more muscular irritation to skin. Over one week, repeated disinfection with ethanol 80% every day in one hand, while the other hand repeated washing tests with sodium lauryl sulfate (SLS) 0.5% detergent. The results show both procedures, alcohol disinfection and washing with soap, can cause skin barrier damage. Washing with soap causes more damage to the skin barrier. The disinfection procedure with ethanol 80% is better tolerated than washing with detergent.[27]

f. Use protective gloves

Protective gloves are used when contacting irritants, allergens, or infectious materials. Occlusive gloves are used for wet work but only for a short time. Patients who have a history of ICD are advised to use cotton gloves to coat occlusive gloves if the duration of use of gloves is >10 minutes.[1,16]

Pharmacological

a. Topical therapy

Hand hygiene guidelines recommend the use of lotions or creams to reduce skin irritation. ICD study on healthcare workers in supporting the effectiveness of specific lotions and creams is shown in Table 1.[6]

b. Systemic therapy

Systemic therapy may be needed in conditions where a topical treatment is not sufficient. Short-term systemic corticosteroids (3 days to 2 weeks) can be given, especially for broad, acute, severe, and refractory ICD. Long-term oral cyclosporine can help patients with resistant hand dermatitis. Other immunomodulators such as azathioprine, mycophenolate mofetil, or methotrexate can also be considered for contact dermatitis.[22]

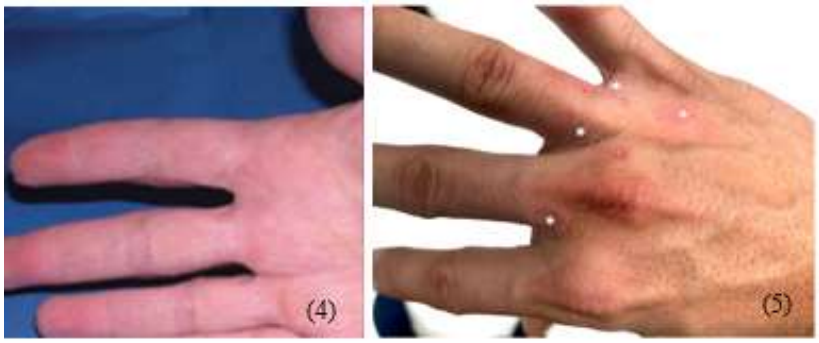

Figure 4. Irritant dermatitis on healthcare workers[1]. **Figure 5.** Clinical characteristics of ICD in patients who wash hands frequently in 1 month without applying moisturizer. Sign * indicate xerosis, scaly erythema patches on dorsum, tip and between fingers resulting in lichenification[21]

Figure 6. Initial ICD lesions in interdigital with mild erythema and superficial scaly. **Figure 7.** Erythema is more clearly visible, infiltration, rhagades, erosions, and crusts[3]

Figure 8. Scales between fingers with erythema, lichenification, fissure, vesicles and erosion in hairdressers[24]

Figure 9. Maceration due to use of occlusive gloves[1]

Table 1. **Effects of treatment on healthcare workers[6]**

Type	Usage, Duration	Composition	Result
Barrier cream	ad libitum, four weeks	Aluminium chlorohydrate in water, paraffin liquidum, behenyl alcohol, glycerine, octyl palmitate, Buxus Chinensis, ceteth-10, stearate-20, dimethicone	Improvement, dryness reduced by week 1
Barrier cream vehicle	ad libitum,four4 weeks	Water, paraffinum liquidum, behenyl alcohol, glycerine, octyl palmitate, Buxus Chinensis, ceteth-10, steareth-20, dimethicone) and the vehicle control (no aluminium chloral hydrate)	Improvement, dryness reduced by week 1
Lotion (Lubriderm)	4x daily, four weeks	Mineral oil, petrolatum, lanolin, sorbitol, stearic acid, etc., in water	The lotion had more significant improvement than cream, both improved skin after one week
Cream (Hand Sense)	4x daily, four weeks	Glycerine, isopropyl myristate, triethanolamine, stearic acid, dimethicone, etc., in water	The lotion had more significant improvement than cream, both improved skin after one week
Petrolatum-based cream (Locobase)	ad libitum, two-week crossover	Paraffin (mineral oil), petrolatum vs no treatment	Normalized skin

			texture and increased skin hydration with treatment; dryness increased and hydration decreased
Cream(Baktolan)	4x daily, two weeks	Water, liquid paraffin, petrolatum, liquid paraffin, wax, etc.	Decreased dryness and increased hydration treatment
Cream	3x daily, 2 weeks	Not specified	Decreased erythema, TEWL & increased hydrations. no treatment
Skin lipid cream (Locobase Repair)	2x daily, eight weeks	Ceramide 3, oleic and palmitic fatty acids, cholesterol with glycerine, petrolatum, etc.	Significant improvement in hand eczema
Cream	2x daily, 8 weeks	Traditional petrolatum-based cream	Considerable increase in hand eczema
Cream (Remedy)	10x daily, two weeks	Dimethicone, aloe vera, ascorbic acid, ascorbyl palmitate, canola oil, cetyl alcohol, cholecalciferol, citric acid, citrus oils, Diazolidinyl urea, glycerine, glyceryl stearate SE, glycine, hydroxytyrosol, l-proline, l-taurine, methylparaben, methylsulfonylmethane, n-acetyl-l-cysteine, niacinamide, olive oil	Redness decrease vs usual and control; Excess erythema decrease vs general and command; Dryness decrease vs untreated control
Cream (CleanCare™ Amino + Derm at work, typical lotions at home)	10x daily, two weeks	Water, glycerine, isopropyl palmitate, stearic acid, butylene glycol, lysine HCL, Arginine HCL, aspartic acid, glutamine, proline, glycine, alanine, glyceryl stearate, stearyl alcohol, polysorbate 60, cetyl alcohol; usual lotions: water, glycerine, and petrolatum or mineral oil	Dryness decrease vs untreated control

10.Complication

Complications caused by ICD can be in the form of ACD and immune responses to less potent allergens:

a. Allergic contact dermatitis

Allergic contact dermatitis depends on ICD in either the context of previously inflamed skin or the irritant nature inherent in the sensitizer. Toll-like receptors in mouse models trigger innate responses that initiate an adaptive immune response and can initiate an inflammatory response to skin microorganisms.[1]

b. Increased immune response to allergens is less potent

Less potent antigens such as propylene glycol tend to cause ACD in patients with barrier disorders. In general, patients whose innate immune responses are activated (for example, in wet workers) are more susceptible to allergens with less potent allergens.[1]

11.Conclusion

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease (COVID-19) pandemic occurring since December 2019. Proper hand hygiene is the most important, simple, and inexpensive way to reduce the prevalence of infection. Intensive hand washing can cause various changes in skin texture and even hand dermatitis. The first-line of ICD's management strategy is based on prevention. Prevention is prioritized over other interventions. The approach that can be done to prevent ICD is by using alcohol-based hand rub containing humectants and applying moisturizing products after cleaning hands to keep skin hydrated. If prevention strategies cannot be affected, protection interventions using protective gloves, topical therapy, and systemic therapy are recommended.

References

1. Nedorost ST. Irritant dermatitis. In: Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, Mcmichael AJ, et al., editors. Fitzpatrick's Dermatology. 9th ed. McGraw-Hill Education; 2019. p. 414–28.
2. Callahan A, Baron E, Fekedulegn D. Winter season, frequent hand washing, and irritant patch test reactions to detergents are associated with hand dermatitis in health care workers. Dermatitis. 2013;24(4):170–6.
3. Kampf G, Loffler H. Hand dermatitis: hand hygiene consequences among healthcare workers. Ind Health. 2007;45:645–52.
4. Visscher M, Canning J, Said D, Wickett R. Effect of hand hygiene regimens on skin condition in health care workers. Am J Infect Control. 2006;34(10):111–23.
5. WHO. WHO Guidelines on hand hygiene in health care: a summary. Switzerland; 2009. p. 1–64.
6. Visscher MO, Wickett RR. Hand hygiene compliance and irritant dermatitis: a juxtaposition of healthcare issues. Int J Cosmet Sci. 2012;1–13.
7. WHO. WHO guidelines on hand hygiene in health care (advanced draft). Switzerland; 2007. 1–216 p.
8. Lotfinejad N, Peters A, Pittet D. Hand hygiene and the novel coronavirus pandemic: the role of healthcare workers. J Hosp Infect. 2020;1–5.
9. WHO. Coronavirus disease (COVID-19). Situation Report – 105 [Internet]. 2020 [cited 2020 May 4]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200504-covid-19-sitrep-105.pdf?sfvrsn=4cdda8af_2.
10. BNPB Indonesia. Gugus tugas percepatan penanganan COVID-19 [Internet]. 2020 [cited 2020 May 4]. Available from:

https://covid19.go.id.

11. Rothana HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal Autoimmun. 2020;1–4.
12. Liu C, Yang Y, Gao Y, Shen C, Ju B, Liu C, et al. Viral architecture of SARS-CoV-2 with post-fusion spike revealed by Cryo-EM. BioRxiv. 2020.
13. Guo Y-R, Cao2 Q-D, Hong Z-S, Tan Y-Y, Chen S-D, Jin H-J, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. Military Med Res. 2020;7(11):1–10.
14. Batalla A, García-Doval I, Torre C de la. Products for hand hygiene and antisepsis: use by health professionals and relationship with hand eczema. Actas Dermosifiliogr. 2012;103(3):192–7.
15. Chowdhry S, Lokhande A, D's ouza P. KAP study about the use of hand disinfectant with alcohol-based hand rubs (ABHRs) among health care staff of ESI model hospital, Basaidarapur, New Delhi, India. EC Pulmonol Respi Med. 2017;4:183–93.
16. Bauer A, Rönsch H, Elsner P, Dittmar D, Bennett C, Marie-Louise, et al. Interventions for preventing occupational irritant hand dermatitis (Review). Cochrane Database Syst Rev. 2018;(4):1–89.
17. Matsui T, Amagai M. Dissecting the formation, structure and barrier function of the stratum corneum. Int Immunol. 2015;27(6):269–80.
18. Wickett RR, Visscher MO. Structure and function of the epidermal barrier. AJIC J. 2006;34(10):99–110.
19. Lynde C. Moisturizers for the treatment of inflammatory skin conditions. J. Drug. Derm. 2008; (7): 1038-43.
20. Madison KC. Barrier Function of The Skin: "la raison d'etree" of The Epidermis. J. Invest Dermatol. 2003; 121: 231-241.
21. Beiu C, Mihai M, Popa L, Cima L, Popescu MN. Frequent hand washing for COVID-19 prevention can cause hand dermatitis: management tips. Cureus. 2020;12(4):1–7.
22. Brasch J, Becker DT, Aberer W, Bircher A, Kränke B, Jung K Ten, et al. Guideline contact dermatitis. Allergo J Int. 2014;23:126–38.
23. Nosbaum A, Vocanspn M, Rozieres A, Hennino A, Nicolas J-F. Allergic and irritant contact dermatitis. Eur J Dermatol. 2009;19(4):1–8.
24. Frosch PJ, John SM. Clinical aspects of irritant contact dermatitis. In: Contact Dermatitis. 5th ed. 2011. p. 305–45.
25. Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, et al. Fitzpatrick's Dermatology. 9th ed. McGraw-Hill Education; 2019. p.363–438.
26. Andersen E. Soap Opera—Myths Versus Facts Regarding Hand Hygiene. AAOHN J. 2007;55(7):261–2.
27. Loffler H, Kampf G. Hand disinfection: How irritant are alcohols?. J Hos Infect. 2008;70:44–8.
28. WHO. Water, sanitation, hygiene and waste management for the COVID-19 virus. 2020.
29. WHO. Interim recommendations on obligatory hand hygiene against transmission of COVID-19. 2020.
30. Chaudhary NK, Chaudhary N, Dahal M, Guragain B. Fighting the SARS CoV-2 (COVID-19) pandemic with soap. Preprints. 2020.
31. Purnamawati S, Indrastuti N, Danarti R, Saefudin T. The Role of Moisturizers in Addressing Various Kinds of Dermatitis: A Review. Clin Med Res. 2017;15(3–4):75–87.
32. Rabenaua HF, Kampfb G, Cinatla J, Doerra HW. Efficacy of various disinfectants against SARS coronavirus. J Hos Infect. 2005;61:107–11.

33. Kampf G, Kramer A. Epidemiologic Background of Hand Hygiene and Evaluation of the Most Important Agents for Scrubs and Rubs. Clin Microbiol Rev. 2004;17(4):863–93.
34. Geller C, Varbanov M, Duval RE. Human Coronaviruses: Insights into Environmental Resistance and Its Influence on the Development of New Antiseptic Strategies. Viruses. 2012;4(11):3044–68.
35. Hsu JT-A, Kuo C-J, Hsieh H-P, Wang Y-C, Huang K-K. Evaluation of metal-conjugated compounds as inhibitors of 3CL protease of SARS-CoV. FEBS Lett. 2004;574(1–3):116–20.
36. Kirk-Bayley J, Sunkaraneni S, Challacombe S. The use of Povidone Iodine nasal spray and mouthwash during the current COVID-19 pandemic may reduce cross infection and protect healthcare workers. SSRN. 2020.
37. Dellanno C, Vega Q, Boesenberg D. The antiviral action of common household disinfectants and antiseptics againstmurine hepatitis virus, a potential surrogate for SARS coronavirus. Am J Infect Control. 2009;37(8).