

Review Article

Skin Decontamination 2021

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Abstract

Exposure to harmful chemicals, such as Chemical Warfare Agents (CWA), Toxic Industrial Chemicals (TICS) may cause serious skin and systemic organ damage, therefore rapid decontamination should reduce contact time and consequent health effects. Knowledge of chemicals and breakdown products is crucial to adapt and manage appropriate decontamination. Initiate First Decontamination rapidly by pragmatic and operational method e.g. disrobing to limit percutaneous penetration, cross contamination and reduce health systemic consequences. Secondary Decontamination, targeted towards the contaminant, is based on essential key actions: adsorption, neutralization, degradation. Those specific technologies, should be considered to design it and improve its efficiency. Low-level chemical detection may serve as an indicator to control residual contamination. Best practices could emerge to standardize the highlights of decontamination process, especially for skin decontamination notably by encouraging people to participate and cooperate to promote decontamination outcomes. Constraints, because of skin application, needs to manage the choice of appropriate decontaminants. Wounds and damaged skin will be treated in further studies.

Keywords: Skin decontamination; Prevention; Adsorption; Neutralization; Degradation; Decontamination process; Best practices

Introduction

Decontamination, aimed to eliminate the contaminant and its human consequences, should be as rapid for the most efficient process.

We propose approaches for operational and societal objectives depending on i) hazardous chemical nature, ii) its persistence and cross contamination risk, iii) event circumstances e.g. location and numbers involved.

Best practices in skin decontamination may emerge from such information including a decision support tool to reach the lowest level of chemical concentration as a « chemical no contaminant level ».

Time and concentration of decontamination solutions are necessary to reach efficient skin decontamination. Therefore products mustn't irritate skin to be operational.

Contamination

Definition : Contamination results from chemicals forms of, such

as vapor, steam, aerosol, dust, liquid or solid contaminant while gaseous products are considered as non contaminant because of their form. Gas mixed with water or other solvents, such as aerosols, become contaminants.

Contamination : The first or direct contamination, results from direct contact with the hazardous substance. Secondary decontamination, also called cross contamination, results of an uncontaminated person, surface, or piece of equipment contacts them.

Skin Contamination : Contaminants i.e. liquids and solids, spread on the Stratum Corneum (SC), diffuse through the layers; anatomical pathways may favor penetration and accumulation of chemicals, depending on their characteristics such as physico-chemical properties (log P, hydrophilicity, lipophilicity, Molecular Weight (MW), as outlined in tables (1-24) of the thesis [1]. The complex heterogeneous skin structure provides several penetration routes through Stratum Corneum (SC) barrier: the intercellular, intracellular and follicular pathways.

Penetration mechanisms deal with the control of intercellular penetration lipids route, and through skin appendages (follicular pathway) that appears to contribute more than previously thought [2] Tables 1,2.

Percutaneous penetration

Although the stratum corneum plays a critical role in the function of the permeability barrier, there are many structures and components which interact before entering the body [3]. The influence of water content on the cutaneous permeation of exogenous molecules are of primary importance in physiology and pharmacology [4]. Sebum, electrolytes, cutaneous flora form a relatively simple ecosystem which protects skin. Chemicals able to dissolve this milieu diffuse through the SC. Kinetic transfer is boosted, according to the rule of five, especially for molecules of small size, low melting temperature and appropriate partition coefficient [5].

Molecules passively diffuse through the SC, described as a brick and mortar model [6]. Penetration pathways are essentially inter and intracellular. Penetration between SC corneocytes is the path by which most compounds penetrate the intracellular way (proteins), while the lipid bilayer intercellular route favors lipophilic compounds. The intrafollicular pathway is considered as a non predominant route [7].

Systemic effects, which severity of toxidromes depends on chemical factors (dose, physicochemical characteristics) result from the passage across viable epidermis and dermis. Some of them, recognizable, may help to select a class of chemical substances.

Skin contaminants

According to persistence and lethality, skin contaminants chemicals are arranged by families : tables 1-24 [1]. Variables affecting agent diffusion such as contamination time (residence time surface), temperature, concentration, (surface density per unit of surface area) are essential parameters to estimate potential effects. Dermal penetration increases its duration of contact.

Some chemicals may cause, by dermal absorption, inhalation, cutaneous and ocular burns exacerbating systemic effects. Therefore medical and/or surgical treatment may be required to complement decontamination [8,9]. Toxidromes must be considered after chemical events, to provide treatment and therapeutics in case of systemic effects [10]. In emergency situations, chemicals are considered for short-term toxicity, secondary contamination and remain capacity should be considered for long-term contamination risk. Persistence of chemical agent, in the absence of active decontamination, presents a risk due to their remain capacity [11].

Priorities and opportunities

Skin decontamination after exposure to contaminants e.g. Chemical Warfare Agents (CWA), dangerous Toxics Industrial Chemicals (TICs) or fine particles is a priority to save lives from

terrorism, criminal attack, accidents or accidental work exposure. Since the usage of chemical weapons caused as many deaths during wars, but not only, defense department and authorities exhort scientists to explore data on opportunity and risks of remaining contaminants in case of inefficient or inappropriate decontamination process. Detection of low-level chemical contamination should be an indicator of decontamination efficiency and a way for further studies [12].

Prevention and protection

Time post-exposure remains a key factor to prevent health effects. Saving time leads to reduce contact time skin-chemical after exposure ; therefore individual and collective protection are essential. Collective protection is essentially based on 3 main principles : Time, Screen Distance.

Personal Protective Equipment (PPE) appropriate for the risk is absolutely required before initiating rescue efforts and working closely with contaminated casualties [13]. Security level is defined by the rules applicable in respective countries [14].

Decontamination

Definition: Decontamination usually consists in physical removal or neutralization of hazardous contaminants from personnel or material. New technologies suggest both removing and degrading agents. But washing with water, cleaning with or without surfactants, are clearly the most intuitive decontamination methods.

Decontamination is an essential phase to avoid cross contamination, stop chemical percutaneous penetration and save lives.

Decon success depends, in particular upon, properties of the agent, environmental conditions and skin surface. Both chemistry and engineering are required in decontamination design [15].

Instituting decontamination by universal methods is the priority, but an appropriate decon should be set up immediately after contaminant identification to better target an acceptable level of health protection.

Decontaminants: Properties of the agent in decontamination, also called decontaminant are essential to preserve the skin and avoid percutaneous penetration.

This highlights that the versatile decontaminants, such as dry sorbents, must be used quickly before an appropriate specific or technical decontamination [16].

Skin decontaminants must not be corrosive, to prevent damage by decontaminant processes. Therefore decontamination of eyes [17] and wounds are treated specifically in the first aid of medical care.

Essential Decontaminant Properties: Decontaminant's characteristics, such as solubility, stability in a medium, reactivity, nature and lifespan of its breakdown products, must be considered. Temperature, concentration and pH may influence those parameters [1]. An optimum medium dissolves the agents and promotes the desired reaction [18].

Managing decontamination

Self-Care Decontamination: It is essential to prevent contamination by developing clean habits for citizens and rescuers, regarding awareness, and contamination avoidance.

Self-care includes i) casualties moving away from the contamination source ii) wiping contaminant off exposed skin and hair; and iii) disrobing to minimize chemicals penetration into skin and thereby limit contaminant dose [19].

Assisted- decontamination: This concept occurs from practical and operational observations. In emergency situations, we tend to help each other. This instinctive reflex needs to be consolidated and developed. Assisted-decontamination of chemical agents could serve as a forum for advanced teaching, learning and facilitate development in the emerging field of decontaminants. Therefore some simple and fast manipulations could be taught as collaborative techniques from the earliest age.

Disrobing, Cut out: Disrobing, also called cut out, is proposed in every case and widely recognized amongst scientists. In contrast there will be a delay between initial chemical exposure and decon set up for civilians compared to military response [20]. It's a challenge for authorities to reduce the time required to deploy decontamination processes after chemical exposure and limit potential citizens health impacts. Removing clothing is a simple and high effective action to remove external contaminants in the first minutes after the incident. Disrobing can remove 80-90% of contamination and specifically the external layer of clothes [21]. Disrobing needs an ethical approach which must be organized on the crime scene, in the hospitals for emergency part and widely advised to individuals returning at home after exposure.

First Decontamination

First decontamination process, also called emergency or early decontamination must be immediately set up, eventually before the identification of the hazardous substance. Essential to save victims and avoid cross contamination, first decontamination must be considered when contamination is suspected by the emergence of toxidromes e.g. clinical symptoms of vesicants, such as blistering, swelling, whereas cholinergic symptoms e.g. copious secretions, respiratory muscles paralysis are significant of nerve agent exposure. This essential process of early decontamination allows a rapid set up of medical countermeasures [22] therefore versatile decontaminants able to adsorb the largest part of hazardous chemicals may be used as the first line .

Secondary Decontamination

Secondary or technical decontamination may complete the first decontamination. In some cases, gross mass water decontamination could be required on the crime scene to rapidly aid all exposed people.

If first decontamination has been performed following gross mass water decontamination process based on the channel water of fire fighter trucks, a secondary decontamination may be set up in mobile units, providing mass showering facilities that allow more thorough decontamination with warm or lukewarm water and soap, and bleach if necessary [23]. Caution should be practiced when skin is washed as the Wash-In (W-I) effect may increase local cutaneous and systemic toxicity.

Experimental data on various chemicals are urgently needed. In any case, decontaminants applied onto the skin must be harmless and efficient.

Decontamination Control

Measuring efficiency of decontamination procedures towards chemicals agents, breakdown products or degraded chemicals need to be evaluated.

Some techniques, as skin wipes are useful to measure toxicant levels on the skin surface, predict dermal absorption and the potential systemic contamination level [24,25].

The efficiency of Fuller earth towards the 4-Cyanophenol, as chemical agent , was assessed ex-vivo [26]. Studies, based on application of non-toxic chemicals , also called simili, to measure the efficiency of water shower ladder pipe systems, underlined that : under certain conditions, showering in the presence of contaminated clothing resulted in the transfer of chemicals to the skin surface [27]. Quantitative comparison of different decontamination protocols were carried out by the topical application of a UV-fluorescent compound onto human volunteers. This highlights that performance of protocols is necessary to assess efficiency. Improve decontamination procedures is a priority to manage short and long- term chemical incident [28]. Low-level chemicals require technologies able to detect low concentrations, in the order, at least, of Part Per Million (ppm).

Design of Decontamination Process

Decontamination methods could be developed following various concepts.

Rank them in three categories i) physical removal, ii) washing, iii) neutralization ranging from the simplest to the most elaborate process, in reference to the mechanism of action described for the methods.

Highly specific and advanced techniques such as nanoparticles technologies, chelation, enzymatic actions and gel formulations may offer opportunities in complement of conventional techniques. Some of devices remove physically, neutralize and degrade contaminants (three in one).

Physical Removal

Physical removal consists in the mechanical action of removing chemical agent from skin. Thus performed by adsorptive powders, free or fixed on a substrate, but also by wipes brushes and some impregnated adsorptive tissues or plainly adsorbant. This process remains conventional and essentially dry.

Dry decontamination uses adsorptive properties of powders or fabrics to passively remove contaminants from the skin surface and especially effective for liquid contaminants.

Adsorbents Powders : Adsorptive powders are largely used in decontamination due to their specific surface area ($\text{m}^2 \cdot \text{g}^{-1}$) leading to highly adsorption chemicals. Bleaching powders, mostly combined with adsorbing materials, provide the basis for skin decontamination [29]. Nevertheless, powders are inappropriate for decontamination of mucous membranes (eyes) and wounds and may cause serious damage. Fuller earth (FE), carbonaceous, activated or not, resins polymers mixture (XE-555), activated alumina (A-200) are adsorbants with the capacity to encapsulate toxic agents [30].

Activated Alumina A-200/ Sorbent Decon System (SDS) : Activated alumina is a potentially efficient adsorbent material for some chemicals because of high adsorption capacity and removal efficiency at the implementation levels [31]. Sorbent Decon System is made of 65% aluminium oxide [32].

Fuller's Earth (FE)

Fuller's earth powder, an alumina silicate, chemically inert abundant in nature and known for its adsorptive properties [33] provides decontamination opportunities for chemical, biological, radiological and nuclear agents. Since Prehistory there are indications for clays mixed with water to cure wounds, soothe irritation as a method of skin cleansing [34]. This might have been due to their mimicking animals e.g. pachyderm; many of which instinctively use minerals for the above purposes. FE, recommended for skin decontamination, is provided as powder in container and prefilled gloves and may be applied applied onto skin after short chemicals exposure [35]. Clays mineral, consisting of hydrous layers silicates, can be studied in function of their structure, composition, introducing classification support tool [36]. More than twenty years later, Fuller earth powder is, among other options, considered as the reference [37] in skin decontamination for mass casualties, as described in official French and European documents, and recognized as an excellent for overall casualty

decontaminant i.e. adsorbent for CWA [38]. FE has been assessed, ex vivo, for its adsorption capacity and decontamination efficiency, comparing four different formulations in skin decontamination [26].

American kit M291 - Carbonaceous Resins XE-555

A solid sorbent, M291, skin decon kit consists of 6 foil-packaged nonwoven fiber pads filled with XE-555, 2.8 g of XE-555 carbonaceous resins with a total water content of 25 wt %. This non-toxic sorbent of high adsorption capacity was formulated for use where rapid decontamination is essential [39-41] XE-555, Ambergard® is a non irritating skin decontaminant proposed by the American Army for soldiers in battlefied situations [26,27] and depends on competition between ion-exchange resin and adsorption within the carboneous resin, XE-555 efficiency results may differ. Resins, made of a styrene/divinyl benzene copolymer, are composed of a high surface area carbonized macroporous styrene/divinylbenzene resin (the sorptive resin), a strong acid (sulfonic acid groups) cation-exchange resin, and a strong base (tetraalkylammonium hydroxide groups) anion-exchange resin. The sorptive resin rapidly absorb liquid agents, and the reactive resins promote hydrolysis of physisorbed agents [18]. Acidic and basic groups in Ambergard® XE-555 Resin promote the destruction of trapped chemical agents. The M291 SDK weighs 45 grams and measures 112 x 112 x 36 mm suggested for an area coverage of 1300 cm^2 at challenge level of 2.5 $\text{g} \cdot \text{m}^{-2}$ of agent per individual Decon Packet and used to decontaminate skin following exposure or contamination to liquid chemical agents [42]. M291 SDK is regulated by the Food & Drug Administration (FDA) as a medical device.

Activated Charcoal : Molecules such as drugs or poisons adsorbed onto the huge surface 800-1,200 $\text{m}^2 \cdot \text{g}^{-1}$ or more with superactivated charcoals 2,800-3,500 $\text{m}^2 \cdot \text{g}^{-1}$ [43] are held there by van der Waals forces (physisorption). For some substances this adsorption may provide a tightly bound chemisorption [44].

Adsorbents Gloves

Adsorbent Glove Fibertect® : This adsorption filter material provides high adsorption capacity (2.5 times its weight in liquid contaminant) and low breakthrough [24]. FiberTect®, a three layer, inert, flexible, drapable, nonwoven composite substrate is proposed for absorbing and adsorbing CWA, Toxic Industrial Chemicals (TICs), and pesticides. The three layers of material include a top and bottom fabric and a center of fibrous activated carbon that is needle punched into a composite fabric. Top and bottom layers (polyester and unbleached Raw Cotton), provide structural coherence, improving mechanical strength and abrasion resistance, while the center layer acts as the active decontaminant. The inner adsorbent layer, made of activated carbon (ACN-K), whose precursor material is phenolic carbon, is a nonwoven fabric

structure [45,46]. FiberTect® does not present a health or safety hazard to personnel ; FiberTect®, a patented technology (US7, 516,525) indefinite shelf life, is self-contained and packaged for easy use, storage, and transport.

Fuller's Earth Glove : An emergency glove for decontamination, based on FE adsorptive properties which was expected in case of liquid contamination on skin or equipment was developed by French army, in 1971. The patent, individual decontamination apparatus, developed as the kit for military, containing an absorbent mitten capable of absorbing toxic agents, was granted in 1991 [47].

This type of powdered FE's glove could present some disadvantages e.g. i) cloud of powder with the risk of contamination transfer, ii) glove form, iii) adsorptive powder without destruction of the adsorbed toxic [In the current state of science we've got in the data].

Brushing / Wiping

Tools as, brushes, sponges and wipes may be used in skin decontamination with adapted processes to limit spreading and skin damage. Wipers require minimal training and provide immediate decon capability and are effective in removing physically contaminants, therefore, they may systematically be used.

Wiping, Fibertect®, industrial wipes, M291 kit, FE prefilled gloves are essential tools in decontamination.

Wipes

Impregnated Wipers : CeBeR™ Multi-Purpose Wipe (CeBeR MPW) developed by Steris for the American army, may be used to avoid cross contamination [48]. Those wipes, containing isopropyl alcohol and emollient, are recognized to facilitate physical removal (10 years shelf life) and intended for first responder and government use. It is a self-contained, low cost chemical decontamination wipe, simple to use and carry which has been proven efficiency for removal of chemical contamination from surfaces.

Nonwoven Composite Pad

The nonwoven composite pad, formed of three-layered non-woven composite pad was developed at Hobbs Bonded Fibers (Waco, TX), using a manufacturing-scale needle-punching line, viscose fibers, polyester fibers, and the nonwoven activated carbon fabric [32]. The viscose fibers, in the top, were single-needle-punched (top to bottom) to provide liquid absorption capability. The middle porous activated carbon nonwoven fabric serves as the adsorbent. The bottom polyester fabric, prepared by single needlepunching, like the top fabric, enhances the overall structural integrity and strength of the composite. These pads are

robust and sufficiently flexible to conform to difficult shapes and spaces, absorb large quantities of liquids, adsorb toxic vapors, and are compatible with a wide range of toxic or hazardous chemicals including bleach. Nowadays, composite nonwoven materials, attractive and versatile materials, are developed for a variety of applications, including hygiene, medicine. This technologies should provide an opportunity in decontamination of wounded or injured skin [49].

Wipe Spray Wipe™

The decon process is broken down in to three steps, commonly referred to as Wipe, as the initial physical removal, spray, by application of detergent as decon solution (hypochlorite calcium, bleach solution and/or dichloroisocyanurate), and wipe for the final removal and drying [50]. Information is derived from the Decontamination process guide and quick reference card set 2016 Jeffrey J Berrigan®. The WSP, Wipe Spray Wipe™ decontamination process is utilized with the permission of Strategic Response Solutions LLC.

Managing Wipes Selection

Many common items that are considered absorbent demonstrate some degree of affinity for both water and oil-based substances ; their results may be presented in absorbency (grams of water or oil absorbed per grams of test product) [20].

Domestic wipes does not represent the best choice to adsorb hazardous chemicals, and are limited with bleach solutions. Wipes, as decontaminants, require high technology for hazardous chemicals.

Neutralization and Degradation Technics

Neutralization is treated here because of combination of support, adsorption and degradation. Combined action of adsorption, neutralization and degradation successfully destruct chemicals and represent a major issue in skin decontamination. High technology program target decontaminants able to treat the whole problem of contamination with a solution three in one.

Elsewhere, a major drawback has been identified with the possible inhalation of such adsorptive powders depending essentially of their particle size [51]. Therefore skin decontaminants, which lack dangerous effects to mucous membranes and wounds, are being developed such as specific technology based on metal oxide nanoparticles (Nps) cerium oxide (CeO₂) Nps, enzymes or specific chemical e.g. oximes for nerve agents. New generations of decontaminants, metal oxides Nps, CeO₂ NPs in water degrade organo phosphorous compounds e.g. nerve agents , pesticides [52,53]. Metal oxide nanoparticles [54] providing high surface area allows adsorption and simultaneous destruction of toxic chemicals , e.g. 1g provide a surface area exceeding 200 m².

Metal Oxide Nanoparticles

Cerium oxide, CeO_2 is known for its biomedical application as a reactive sorbent for degradation of organophosphates such as parathion and chlorpyrifos in solvent media (heptane, acetonitrile) under ambient conditions. Formulation of NPs (thickening aqueous dispersions of CeO_2 were tested for skin decontamination with encouraging results [53].

MgO , Al_2O_3 , and CaO , nanosized particles, are promising potential reactive sorbent materials owing to their high surface area, strong adsorbability, and potential reactivity toward chemical warfare agents. Those Nps remove the agent rapidly from the contaminated surfaces, degrade them in situ and hence render them nontoxic [55]. If degradation may present clear benefits, we must be careful with their use on skin [56]. Nanosized particles of MgO , Al_2O_3 , and CaO , which at least one dimension reach 100 nanometers, or less are developed in skin decontamination [57] but the regulation of Nps has to be considered in respect the rules for health [58].

Magnesium Oxide Nanoparticles: Single metallic oxide, MgO , nanocrystals highly reactive adsorb, neutralize and degrade chemical agents. MgO nanoparticles with sizes ranging from 10 to 30 nm, have been incorporated in a polyvalent device DEC'POL®.

Whereas nanosized particles of MgO are not recommended for a cutaneous application, Nps are incorporated in the structure of a « superabsorbant material » DEC'POL® device and proposed for skin decontamination, by transfert, neutralization and degradation due to its active material [59].

Cerium Oxide Water Formulation: Cerium oxide, CeO_2 , is known for its biomedical application as a reactive sorbent for the degradation of nerve agents [60], organophosphates such as parathion and chlorpyrifos in solvent media (heptane, acetonitrile) under ambient conditions. Formulation of NPs thickening aqueous dispersions of CeO_2 were tested for skin decontamination with encouraging results [52,53].

Dermal Decon Gel: Dermal Decon (DD) gel is a formulation created after high knowledges in chemical partition binding to stratum corneum proteins, lipids and hydration effects [25]. DD gel, rapidly drying gel -peel off film is prepared with ingredients, such as carboxy methyl cellulose for its water capacity adsorption, Lutrol® for binding chemicals properties, Kollidon SR®, binding and absorbent for polar and non-polar compounds, and Fuller's earth as adsorbing agent. Decontamination efficiency has been compared to several decontaminants [61]. The main advantages are that massage is unnecessary, Additional cleanup is unnecessary compared to the Reactive Skin Decontamination Lotion (RSDL). DD gel has been compared on hairy and non-hairy skin after 30-min dermal exposure to paraoxon (pesticide organophosphorous). DD gel is proposed for absorbance, binding, extraction, and detoxification in skin decontamination, Acute toxicity is not

studied, but its components are used in pharmaceutical or cosmeceutical industries, or as decon absorbance with no or low toxicity [62].

Suspensions and Emulsions

Suspensions : Successful decontamination of FE suspension, enabling a dramatic reduction of skin contamination after a brief exposure scenario, appears to be rapid, reliable and should be formulated in a new device ready to use for self decontamination [26].

Pickering Emulsions : Pickering emulsions, i.e. solid-stabilized emulsions, containing silica (S-PE) or Fuller's earth (FE-PE), where solid is silicea (S) or Fuller earth (FE) selected for their high specific surface area [63].

Washing

Water : Water decon is largely used in mass decontamination and optionally added detergents or bleach solutions. Wash and rinse may be set up quickly, and rinse a large part of involved persons, hairs, body and skin. The main advantage of this raw material (water) is the speed with which it can be initiated by the first responders using fire apparatus that is generally readily available. First responders are organized to prepare channel of water as Ladder Pipe System (LPS), with the major drawback of the unheated water [20,27]. Water is used in mobile Units of Decontamination (UMD), and may be heated with adapted systems, the major drawback is that installation on the crime scene needs time (around 30 minutes), even for trained fire fighters. Temperature and time shower are standardized to an optimal decon method [20,64]. It is relevant to consider the issues after decontamination by water. Mechanical washing may more or less remove hydrophilic viscous products; however viscous hydrophobic substances are more difficult to remove. Water helps the physical removal of chemicals and hydrolysis some i.e. sulfur mustard [18]. Water can exacerbate skin lesions caused by sulfur mustard. Viscous and oily substances, difficult to remove mechanically, may be wiped on the surface of the skin before decontamination. Water may enhance dermal absorption of certain chemicals, a phenomenon known as the wash-in effect (W-I) [65]. In some regions of France, the formal process of wet (showering) decontamination is often preceded by dry decontamination of casualties using Fuller's earth (glove, powder). This can more rapidly achieve the initial decontamination and may assist in reducing gross contamination prior to showering [66].

Detergents: Detergents and soaps, decrease surface tension, increasing solubility and viscosity of the agents [67,68]. Surfactants which effect permeability characteristics of several biological membranes including skin, may solubilize stratum corneum lipids. Despite surfactants are considered as chemicals penetration enhancers, especially by transdermal route [69,70], they are used

in skin decontamination [71]. The European project, ORCHIDS (Optimisation Research of CHEMical Incident Decontamination Systems) protocol, consists of a 1.5-minute shower with a mild detergent, Argos™, supplemented by physical removal [72]. This soap is composed of anionic substances, alkylbenzene sulfonate sodium alkyléthersulfate sodium, non ionic, diethanolamide de coprah, and adjuvants [51]. The role of surfactants, largely developed in decontamination processes, must be evaluated before skin utilisation [65,68,73]. According to their nature, anionic, cationic, nonionic, zwitterionic, their potential enhancements effects could be assessed [74]. A surfactant is a chemical that mixes readily with both oil-like and water-like chemicals. This include soaps, detergents, emulsifiers and wetting agents (Table II).

Specific Technologies

Neutralization: Neutralization is a process of chemically reacting an agent to form other less- toxic chemicals.

There are four main types of chemical reactions involved in neutralization, i) substitution, ii) oxidation, iii) chelation and iv) enzymatic and biodegradation. Neutralization was initiated by Lewis, in 1959 who recommended initial copious water skin decontamination followed by neutralization of acid skin splashes with a solution of weighed sodium bicarbonate ($\frac{1}{2}$ ounce ; 14.2g.), or 1% of sodium citrate for alkaline skin splashes, followed by more copious amounts of water [75].

Neutralization by Substitution: Neutralization by substitution is essentially performed by water hydrolysis or nucleophilic active decontamination developed in the Reactive Skin Decontamination Lotion (RSDL) [76].

Hydrolysis: Substitution by hydrolysis depends on pH which may be increased by pH modification depending on the agent and the media. Hydrolysis takes place at any pH, some hydrolysis products are still dangerous but less toxics e.g G agents hydrolysis lead to methylphosphonic acid and Hydrogen Fluorid (HF) [77]. Sulfur mustard hydrolyzes slowly to form thiodiglycol (TDG) [78,79]. Products of hydrolysis must be considered in the decontamination process.

Nucleophilic Substitution: Rapid nucleophilic decon is efficient for decontamination but non appropriate for skin [80]. But, Reactive Skin Decontamination Lotion (RSDL), is based on a mechanism chemically similar to hydrolysis, but at milder pH. Active ingredient, a nucleophilic compound (2,3 butanedione monoxime), also called, Diacetyl Monoxime (DAM) is dissolved in a glycol solvent which dissolves most agents and allow them to be rinsed off with water. Decontamination must be initiated within 5 to 10 minutes to be high efficient [81]. RSDL destroys CWA without corrosive effects, and counteract the inflammator process, especially against sulfur mustard [35]. RSDL, a skin decontaminant FDA approved (2002), [82]. This viscous yellow lotion impregnated in a

polymer sponge (pH 10.5) is water soluble, therefore easy to eliminate after decon, and presented in individual packets ready to use (5 year shelf life). The sponge is applied in a overlapping circular motion to skin, requiring at least 2 minutes contact to achieve neutralization of agents (nerve agents, pesticides). For safety DAM, active ingredient of RSDL may be percutaneous absorbed (MW 101.10 ; log P (octanol-water) 1.740) [83]. The acute toxic effects of DAM, observed after injection to rats and rabbits appears due to the compound itself [84]. RSDL is not approved for eyes, or in wounds [82]. Safety precautions are recommended for RSDL: short time application (< 6 hours), rinsing after decontamination and respect the incompatibility with solid bleaching.

Neutralization by Oxidation: Oxidation is a reaction of an agent with an oxidizing chemical, able to break many types of bonds. The most common oxidizers used in decon processes are bleaches (hypochlorites) such as after World War II, bleaching powders, permanganate (KMnO₄) and peroxides (hydrogen peroxides and peroxy acids). By World War II, superchlorinated bleaches, were the most common general purpose decontaminants [18,29]. Oxidizers composed of hypochlorites, proposed for skin decontamination are bleach 2-6 wt % NaClO in water, dutch powder, Ca (O Cl)₂ + MgO, activated solution of hypochlorite (ASH), 0.5% Ca(OCl)₂ + 0.5% sodium dihydrogen phosphate buffer + 0.05% detergent in water and self-limiting activated solution of hypochlorite (SLASH) .5% Ca(OCl)₂ + 1% sodium citrate + 0.2% citrate acid + 0.05% detergent in water. However, there are disadvantages to using bleach as a decontaminant: and the necessary extemporaneous preparation due to the active chlorine content of the bleach gradually decreases with the storage and its corrosivity for skin surface.

Sodium dichloroisocyanurate (NaDCC) considered as an alternative to hypochlorites, generating pH neutral bleach when added to water [18]. Fichlor (sodium N-N dichloroisocyanurate) detoxifies VX effectively by simple oxidation, but the pH influences nerve agents degradation kinetics. Tablets of Na DCC offer the advantage of the stability (3 years storage) and an easily mixture with surfactants.

Hypochlorite solutions are efficacious when used to topically decontaminate intact skin. However, few studies examined the efficacy of decontamination of chemically contaminated wounds. Observations were performed after HD contamination. The lesions induced following decontamination are presumed due to the mechanical flushing of HD onto the peri-lesional skin, or by chemical damage induced by the solution, or HD-solution interaction. Comparing the decontamination efficacy of sodium hypochlorite (0.5% and 2.5% solutions), calcium hypochlorite (0.5% and 2.5% solutions), is essential to manage skin decon with bleaching oxidizers [85]. In skin decontamination by oxidizers, it is recommended to prepare the bleach solution 0.5% from certified

lots of 5% household bleach diluted 1 to 10 [76]. Nevertheless, bleaching is not universal in skin decon, hypochlorite, diluted 10-fold from household bleach solution (0.5% concentration), is ineffective for agents such as VX, which require a significantly higher amount of hypochlorite for effective decontamination, but at this concentration hypochlorite, effective for VX, is skin damaging [40].

The formula of diluting Eq.1 $C_1 \cdot V_1 = C_2 \cdot V_2$, applied for dilution of sodium hypochlorite. C_1 is the initial concentration of the bleach solution, V_1 the initial volume. C_2 is the desired concentration appropriate, in this case, for skin decontamination 0.5 %, therefore V_2 is calculated as a total volume of the bleach solution extemporaneous prepared.

$$C_1 = 5\% \quad V_1 = 1 \text{ L}$$

$$C_2 = 0.5\% \quad V_2 = 10 \text{ L}$$

Eq. 1

$$V_2 = \frac{C_1 \cdot V_1}{C_2}$$

Decontamination by oxidation is restricted in skin decontamination, and the results of testing reinforce the difficulty associated with developing a universal decontamination technology for cleanup of CWA in a civilian setting [86].

Chelation

Diphoterine[®] : Diphoterine[®] and Hexafluorine[®], developed by Laboratoire Prevor, are referenced as medical device class IIa for technical skin and eyes decontamination [15].

Diphoterine[®] consists of a custom-made molecule which effectively attracts and renders harmless among others both hydrogen ions (H^+) and hydroxide ions (OH^-), is a water-soluble powder. The rinsing and diluting effects of an equal volume of water (in the commercial preparations) are most likely retained. It is a polyvalent (actively binds multiple substances), amphoteric, hypertonic, chelating molecule with active binding sites for acids, bases, oxidizing agents, reducing agent, vesicant, lachrymators, irritants, solvents, etc. Its effective in preventing or decreasing the severity of burns, to rapidly decrease pain, and has resulted in fewer requirements for medical or surgical burn care, other initial decontamination and less work time [8,87].

Hexafluorine[®]: Hexafluorine[®], colorless sterile aqueous solution of pH 7.2-7.7, slightly hypertonic, is an amphoteric, hypertonic, polyvalent compound for decontaminating hydrofluoric acid (HF) eye and skin splashes within the first 2 minutes to be efficient in reducing burns and consequences [88].

Enzymatic Decontamination and Biodegradation

Enzymatic decontamination, specific of the chemical were developed from 1946, and more after the selection of organophosphorus anhydrase (OPA) was selected in 1987 as a generic name for all enzymes capable of catalytically hydrolyzing organophosphorous compounds [18]. Two promising candidates in the enzymatic decon, Organophosphorus Acid Anhydrolase (OPAA) from a strain of *Alteromonas* obtained from Grantsville Warm Spring, Utah and Organophosphorus Hydrolase (OPH) from *Pseudomonas diminuta* or *Flaviobacterium*. High specificity, and restrictions of pH and temperature of those enzymes limits the use in mass decontamination, but they are potentially sufficiently benign to be used directly on the skin of personnel and casualties. Research demonstrates the considerable potential of bacteria to sequence cloned gene [89]. Biodegradation of sulfur mustard is underway to decrease potential toxicity.

Prospectives

Decontaminating skin by capture and destruction of the contaminants is under research. Compared to liquid decontaminants, less is known concerning the interaction of agents with solid decontaminants, in order to enhance knowledge on the interaction solid agent, high technology developed by scanning or transmission electron microscopy, diffraction high resolution and infrared spectroscopy will be helpful. Synchrotron beamlines are available for a quick and efficient characterization and should offer opportunities to visualize bindings inter molecules and kinetic of those interactions.

Conclusion

In the case of decontamination for humans involved in a chemical exposure, physical removal compared to neutralization is by far easier to set up. Initiated with the disrobing, and personnel protection, equipment, goal is to remove bulk contamination and remove user from suit in a timely efficient manner. Dry decon, based on powders, adsorptive gloves wipe systems, should be first considered for chemicals, to ensure efficient decon, manage the emergency response and ensure immediate first aid and medical countermeasures.

Wet decon, by washing with detergent or not, rinse is a universal method with some constraints in the organization when mass exposure is involved.

Conversely neutralization can be considered only after identification of the chemical, Some constraints limit the neutralization as first decon such as its time consumption, volume dependence, and may be hazardous.

	PHYSICAL REMOVAL				Washing		NEUTRALIZATION		TECHNICAL SPECIFIC
	AD-SORPTION / SORBENTS POWDER	ADSORPTION/ DEVICES WIPING	ADSORPTION/SUSPENSIONS	NPs METAL OXIDE Adsorption + Neutralization + Degradation	WASHING	DE-TERGENTS	SUBSTITUTION / NUCLEOPHILIC	OXIDATION	CHELATION (a) / ENZYMATIC (b)
DISROBING / CUT OUT	a) Fuller's earth (FE) b) Activated Alumina A-200 c) Aluminum Oxide (Guild A200) 65% Al ₂ O ₃ d) XE-555 carbo-naceous resins , Amber-gard®	a) Composite nonwoven pad b) Adsorbent glove FIBER-TECT® c) Fuller earth glove d) DEC'POL[1]® e) American kit M291 (XE-555)	1 FE Suspension [2]	a) MgO Nps DEC'PO ^L ®	Water at any pH hydrolysis Water at defined pH to increase hydrolysis	detergents anionic (SLS) ³ - cationic / mild soap	RSDL [4] (2,3 butanedione monoxime)	KMnO ₄ Ca(OCl) ₂ Household bleaching NaO-Cl(0.5%)	a) DiphoterineO HexafluorineO b) organophosphorus anhydrase (OPA) Organophosphorus Acid Anhydrolase (OPAA) Organophosphorus Hydro-lase (OPH)
¹ Ouvry Laboratoire Technology ² Comparison of four different fuller's earth formulations in skin decontamination A Roul et al. (J Applied Toxicology.2017) ³ SLS sodium lauryl sulfate anionic detergent ⁴ Reactive Skin Decontamination Lotion (RSDL)									

Table 1: Skin decontamination summary technical tools.

OPERATIONAL ¹ TOOL - CHOOSE THE DECON SYSTEM – 1-2-3							
1 - DISROBING – CUT OUT							
2 DRY PROCESS			2 HUMID PROCESS	2 SPECIFIC PROCESS	3 WET PROCESS		
ADSORBENTS POWDERS	ADSORBENTS WIPES AND MITTENS	ADSORBENTS AND DEGRADATION	NEUTRALIZATION / SUBSTITUTION NUCLEOPHILIC	CHELATION	WATER	DETERGENTS	NEUTRALIZATION / OXIDATION
Fuller's earth boxes powder (150 g)	Fuller's earth – Prefilled powdered glove ²	MgO Nps ³ DEC'POL® Decontaminable area 9m ⁴	RSDL ⁴ (2,3 butanedione monoxime) Medical device shelf life of five years ⁵ 21mL - 42mL packet	a)Diphoterine® Medical device Classe IIa Hexafluorine®	Water – pH a) Copious water (LPS ⁷) b) removal or hydrolysis Mobil Unit of Decontamination	Argos ⁸ (0.5%) ORCHIDS ⁹ Process	Bleach solution (0.5%)
Activated Charcol, Powdered (PAC)	Adsorbent glove FIBERTECT® Indefinite shelf life	American kit M291 Ambergard® XE-555. M291 SDK Medical device (FDA)					Dichloroisocyanurate (DCCNa) tablets C ₃ Cl ₂ N ₂ NaO ₂
Aluminum Oxide (Guild A200)	DEC'POL® mitt ¹⁰						

- Adsorbents and binding
- Adsorption – binding and degradation
- Neutralization substitution – oxidation
- Washing water and detergents
- Chelation

¹Every process needs to be performed wearing appropriate Personal Protection (Equipment PPE) and does'nt delay to set up medical countermeasures

²NBC-Sys, France

³NPs Nanoparticles

⁴Reactive Skin Decontamination Lotion (RSDL)

⁵Just open, wipe the skin after exposure, and rinse when time permits; 21 and 42 mL packets) .1mL of solution contains 173 mg of Dekon 139 and 35-43 mg of DAM in an MPEG and water solvent.

⁶Laboratoire PREVOR, France

⁷LPS Ladder Pipe System

⁸ARGOS® Detergent

⁹ORCHIDS : Optimisation Research of Chemical Incident Decontamination Systems

¹⁰To be used in case of chemical or biological contamination on equipment, weapons or skin (OUVRY, France)

Table 2: Skin decontamination summary technical operational tools.

Best practices in decontamination

How the project of best practices takes place

Skin decontamination has been widely studied, suggesting consideration both decontaminants and application processes whose main objective is to reduce contact time with the chemical after exposure and therefore health consequences. These numerous systems covers practically all degrees of efficiency that one wants to achieve. However, fundamental criteria may be lead in order to complet decon methods.

- Most above-mentionned methods may be not applicable in the context of chemical incident involving mass exposure because of expense. Therefore, basic decontaminants available on the world market, and easy to execute are usually used or put forward in the first line (Table I).
- Define the expected level for skin decontamination utilizing rigourous methods and safe applications onto skin including two main factors : i) various population i.e. children, elderly, disabled, ...and ii) number involved.

A best practices guide, expected to assist the best option in skin decontamination, considering first, the targetted population e.g. soldiers in war position exposed to CWA, civilian exposed unintentionally to TICs, contaminated individuals in disorderly arrival in hospitals, could emerge.

This guide may treat initial crucial actions to prevent contamination of first responders and cross contamination, offer a decision tool to deal with key issues with minimal delay according to decontaminants benefits and drawbacks.

Preventing the extent of contamination is essential to achieve improvement in clean habits, awareness, and avoidance of contamination, for respondeurs and populations. We suggest criteria in the chronological actions performed before decontamination.

Prevention and Personal Protective Equipement

In order to enable them to initiate rescue efforts and work closely with contaminated casualties, responders have to be equipped with appropriate Personal Protective Equipment (PPE). Adsorption filter material with high adsorption capacity and low break through behavior is patented Patent, US 7, 160,369 B2, since 2007 (2.5 times its weight in liquid contaminant) with an infinite shelf life. The adsorption layer has a first activated carbon layer with granular or spherical activated carbon particles [45]. Relative new classes of crystalline solids with tunable properties such as porosity and pore size, Metal Organic Frameworks (MOFs) may have great potential in future applications [90] and destruction of chemical warfare agents [91] .

Self-Care Decontamination

Self-care includes casualties moving away from the

contamination source; wiping contaminant off exposed skin and hair; and disrobing in order to stop contaminate penetration into the skin and thereby limit percutaneous penetration [19].

Disrobing, Cut Out

Disrobing is widely recommended. In contrast there will be a delay between initial chemical exposure and decon set up for civilians compared to military response [20]. It's a challenge to reduce the time required to deploy decontamination processes after chemical exposure and limit potential health impacts. Therefore, removing clothing, is consired as a simple and high effective action to remove external contaminants in the first minutes after the incident. Disrobing can remove 80-90% of contamination [21] Nonetheless it needs an ethical approach beforehand organized both on the crime scene , and in the hospitals [92].

Decontaminants

Which decontaminants and application process are interchangeable depending on their mechanism of action : adsorption added or not of adsorbed toxics degradation. Components in most cases are powders that might settle in gloves or included in pads. Skin decontaminants must not be corrosive, so that skin surfaces are not damaged by decontaminants. Therefore decontamination of eyes and wounds are treated separately. Depending on the magnitude of the change(s) in components and composition, mechanism of action and/or method of application, tests should prove the intended skin decontamination. Criteria tools and level of decontamination could be expected to improve and standardize systematically before approval both decontaminants and decon process (application and removing) ; thus completed by informations for each one on the necessary contact time to adsorb i) liquid at the surface ii) more or less in the first layers of SC depending on kinetics of adsorbents, iii) define the appropriate rate of decontamination efficiency and iv) methods to detect low-level residual contaminant.

Contraints in decontamination

Analysis and evaluation of decontamination methods require evaluation in safety and in decontamination efficiency. Even if, in vivo human skin, is considered as the best model, ethical, financial and safety considerations require testing with animal models which the most commun are pigs, monkeys , rats rabbits [93].

Propositions are limited to decontaminants attested or in progress, when applied on skin, to treat militarian and civilian mass casualties exposed to CWA or very dangerous TICS (Tables I, II). Nevertheless, powders, inappropriate for decontamination of mucous membranes and wounds, may cause serious damage [29]. New products intended for a topical application to the skin must be proven safe and effective before marketing. Some are approved as medical device, boosting user confidence. Therefore, establishment

of principles and test procedures to ensure safe manufacture and use of nanomaterials in the marketplace is urgently required and achievable. Quality means features and characteristics of a product, in this case to be applied to skin. Define a degree of confidence for the test outcome, demonstrate interchangeability for their products during the developmental process or after approval [94].

Improving decontamination management

Improving management decontamination of any chemical incident require first, securities in the choice of decontaminants, because of skin contact. The label of medical device should increase their attractivity and boost the confidence of users. Then, reduce contact time, introduce a scale to measure contamination residual level should increase the readability of decontamination efficiency. Perform in the design of decontamination methods, to not delay emergency medical care and therapeutics administration, is a crucial challenge to save and safe mass people [12].

Medical Devices

Medical devices, recognized in European Union (UE) and USA, and now, worldwide extended tend to guarantee great confidence in the decon materials. Qualification means that the FDA has evaluated the tool and concurs with available supporting evidence that the tool produces scientifically-plausible measurements and works as intended within the specified context of use which depends on e.g. the tool or product area in which the tool is proposed for qualification. European council 93/42/EEC of 14 June 1993 [95] concerning medical devices defines essential requirement e.g. time of use, and propose a classification based on the destination of the devices [96].

Why Skin Decon is a Societal Challenge

Societal challenge for skin decontamination concerns, in emergency, people after exposure to acute chemicals ; lifelong skin exposure and risk of chronic toxicity in relation to the exposome [97]. The comprehensive clinical research guide in skin decontamination, offering an extensive bibliography, would help governments and specialists to manage solutions that will decrease mortality and morbidity [98].

Skin : a Potential Target

Knowledge of the anatomical heterogeneity complexities of skin demands adapted system more or less sophisticated that further breaks down the diffusion and partitioning steps to limit systemic effects. Therefore immediate action to reduce the concentration of any substance onto and within the skin will subsequently reduce the amount available and the risk of entry into the systemic circulation. Correlation between the penetration level of chemicals and the SC essentially depends on the barrier function which constitutes a crucial physical obstacle protecting underlying tissues from aggressive environmental influences.

Consequences of percutaneous penetration are correlated both to inherent activity of chemicals and individual factors such as age, racial differences and more specifically anatomic site [99,100]. Therefore it is conceivable to partially explain the higher penetration in sites where sebaceous glands are more numerous and the thickness of the stratum corneum (SC). However, disorganization in intercellular lipids, lamellar sheets may imply subsequent disordering of the intercellular SC and also be a second reservoir of contamination [101]. Epidermal cells play a role in protection, such as Langerhans cells involved in the cutaneous immune system through the activation of cytokines, melanocytes provide photoprotection and neutralize free radicals, Merkel cells scattered in the basal layer play an important role in the sensory function.

Formation of a reservoir in the stratum corneum partly explains difficulties in decontamination methods and prediction of chemical penetration through it. The properties of the agent in skin decon are essential to preserve the skin and avoid percutaneous penetration and migration of toxic agents.

Psychosocial Potential Consequences

Presence of unusual product on skin provokes immediate reaction to clean it up or remove it. Chemicals disasters are associated with a variety of psychological, psychosocial and physiological distress. Psychological dimension is an essential phase at least as significant as the physical removal [92].

Disasters involving chemicals may cause more devastating long-term effects compared to natural disaster [102]. Psychophysiologic responses and biochemical correlate of disaster stress therefore the challenge is to prevent chronic effect. Depending on chemicals nature, sticky, viscous, heating, freezing, irritating, those must be physically removed. The barrier function of skin limits permeability and penetration. A survey requesting informations on people contamination impact could help to measure the individual stress factor, as an indicator.

Even if the challenge, after chemical exposure, is to prevent immediate effects and preserve skin people involved and the health consequences, social and long term effects are, at least, of equal importance to prevent chronicization after exposure [103]. Emotional charge linked to the event, both for casualties and rescuers, must be evaluated to assist, prevent the chronicization and help for the resilience. Depending of chemicals, toxidromes which irreversibility may cause long-term consequences are concerned in this part.

Highlights for decontamination methods

In case of decontamination for humans involved in a chemical exposure, physical removal compared to neutralization is by far easier to execute. Initiated with disrobing, and the personnel

protection ; goal is to remove bulk contamination and user from clothing, in a timely efficient manner according to ethical considerations.

Dry decon, based on powders, adsorptive gloves, wipe systems, has to be first considered to ensure efficient decon, manage the emergency response, immediat first aid and medical countermeasures. Wet decon, by washing with detergent or not, rinse is a universal method with some constraints in the organization for target population depending on the location. We have tools and methods appropriate to the target population, pediatric, elderly, diseased people, disabled persons and ethnic attentions.

Some constraints limit the neutralization such as it's time consumption, volume dependant, and may be hazardous.

Conclusion

Best practices for decontamination should be strongly encouraged to share and develop standard of good practices. Decontamination profiles should be organized in order to obtain a desirable or appropriate level quality to protect public human health considering the toxicity of contaminants chemicals. A guide of best practices will be helpful to compare and assess methods quality, until the required low-level toxicity is being achieved, considering current data of the science. Professional deontology, ethical considerations, human rights should guide the developement of appropriate and operational responses in decontamination, till obtain the necessary public confidence in the legitimacy of implemented measures.

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