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SPECIAL ARTICLE

DISINFECTANT CHOICES IN VETERINARY PRACTICES, SHELTERS AND HOUSEHOLDS

ABCD guidelines on safe and effective disinfection for feline environments

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Overview: Regardless of whether a pathogen is viral, bacterial, parasitic, fungal or an emerging unknown, the mainstay of infectious disease control is hygiene, and the cornerstone of good hygiene is effective disinfection.

Challenges and current choices: Certain pathogens present a challenge to kill effectively: parvovirus, protozoal oocysts, mycobacteria, bacterial spores and prions resist most disinfectants but can be eliminated through heat, especially steam, which will kill protozoal oocysts. Heat is the safest and most effective disinfectant, but cannot be universally applied. Temperatures in washing machines and dishwashers should be at least 60°C to eliminate pathogenic spores and resistant viruses. Enveloped viruses are susceptible to most disinfectants; of the non-enveloped viruses, parvovirus is recognised as being the most difficult to eradicate. Sodium hypochlorite is recommended for many applications: cleaning of floors, laundry, food preparation surfaces and utensils. Skin scrubs and rubs containing alcohols are more effective than those containing chlorhexidine, and less subject to contamination.

Disinfectants to avoid: Deficiency of the enzyme UDP-glucuronosyl transferase renders the cat susceptible to the toxic effects of phenol-based disinfectants (including many essential oils), so these should be avoided in feline environments. Quaternary ammonium compounds (eg, benzalkonium chloride) are also probably best avoided.

The future: Veterinary disinfection approaches in the future may include use of ultraviolet radiation and, increasingly, silver.

Introduction

Infectious disease is a major challenge for the domestic cat (*Felis catus*). In nature, a solitary creature, the cat has been forced, by domestication, to live sometimes in unnaturally dense populations (eg, shelters or breeding households), which results in exposure to unnaturally high doses of pathogens at a time when stress may already be compromising the cat's immune system and ability to deal with it. Hygienic routines and disinfection are the method of choice for eliminating meticillin-resistant *Staphylococcus aureus* (MRSA) or virulent systemic feline calicivirus (VS-FCV) from premises, and are especially important in situations where there is an emerging, or unknown, contagion, and neither vaccination nor specific testing are available.

> The mainstay of infectious disease control is hygiene, and the cornerstone of good hygiene is effective disinfection.

There are three priorities when choosing disinfectants for use around the cat: the first, obviously, is efficacy. The second is safety for the cat: the idiosyncrasies of the feline metabolism render the cat especially sensitive to many things that are perfectly safe for other species, such as phenol-based disinfectants. The third, which is outwith the scope of this article but also very important, is safety for humans; especially in veterinary hospitals and shelters, where exposure is likely to be a daily occurrence and long term. Cleaning chemicals have been associated with airway irritation, asthma, contact dermatitis and even, with prolonged exposure, neoplasia. The strongest airway irritants in cleaning products are bleach (sodium hypochlorite), which releases chlorine gas, hydrochloric acid and alkaline agents (ammonia and sodium hydroxide), which are commonly combined.[1] Cleaning agents are divided into

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European Advisory Board on Cat Diseases
The European Advisory Board on Cat Diseases (ABCD) is a body of experts in immunology, vaccinology and clinical feline medicine that issues guidelines on prevention and management of feline infectious diseases in Europe, for the benefit of the health and welfare of cats. The guidelines are based on current scientific knowledge of the diseases and available vaccines concerned.

The latest version of the guidance provided in this article is available at www.abcdcatsvets.org and www.abcd-vets.org

sensitisers (amine compounds, quaternary ammonium compounds [QACs], scents containing terpenes, isothiazolinones, formaldehyde) and irritants (chlorine, ammonia, hydrochloric acid, monochloramine, sodium hydroxide, QACs).[1]

Different pathogens require different approaches for effective disinfection; thus recommendation of a single disinfectant for all purposes is not possible. In addition, there is no single solution for all applications: for example, steam cleaning, which is necessary to eliminate protozoal oocysts from a premises,[2] is not feasibly applied to the hands of a veterinary surgeon or the skin of a cat. Although hand hygiene (Figure 1) has been recognised as the most important tool in nosocomial infection control since Semmelweis observed its immense effect on the incidence of childbed fever in 1847 (cited in Kampf and Kramer[3]), obtaining compliance remains a challenge over 150 years on.[4,5] Apparently people are more willing to use a hand rub than to wash their hands in water.[3]

For each class of pathogen, certain members have been identified as the most difficult to kill; for example, of the viruses, parvovirus is the most resistant – thus, if a disinfectant kills parvovirus, it is likely to kill most other viruses as well. There are many publications reporting on the virucidal activity of disinfectants against feline calicivirus (FCV), as this pathogen is often used as a surrogate for human norovirus,[6] which is difficult to grow in cell culture. Details of any special disinfection requirements for a particular feline pathogen are given in the respective ABCD guidelines.

By contrast, some organisms will die outside the host without any intervention (eg, feline leukaemia virus, feline herpesvirus). Survival times outside the host are presented elsewhere.[7,8]

These disinfection guidelines are intended for the general veterinary practitioner. Special areas, such as the disinfection of blood for transfusion, bone marrow/organs for transplant, and specialised equipment, such as endoscopes, will not be covered. For a review of endoscope disinfection, see Greene et al.[9]

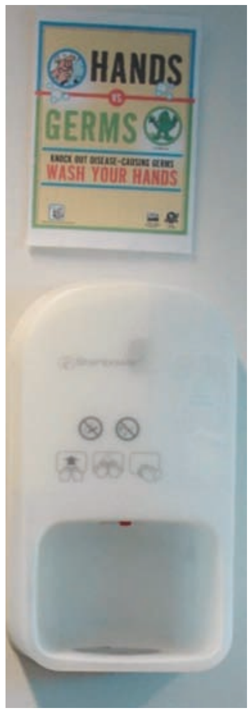


Figure 1 **Hand sanitisers are located by all of the doors of the University of Bern Veterinary Hospital, Switzerland.** *Courtesy of Dr Diane D Addie*

Definition and principles of disinfection

Disinfection is a potent means of reducing the number of pathogens on a surface: it minimises the risk of infection for animals and humans that come into contact with that surface. Disinfection does not result in sterility, which can be achieved by other methods, and only for very confined surfaces (eg, on instruments) or liquids (eg, infusion solutions).

Disinfection is always non-specific: it does not inactivate specific pathogens. A good disinfectant will kill most of the bacteria on a surface, including the pathogenic ones. Therefore, it is important that a disinfectant is capable of substantially reducing the bacterial burden on a surface; this is defined in most test protocols as a reduction in the number of infectious organisms by at least 4 $\log_{10}$.

Disinfection can be achieved by various methods: bacteria, viruses and other pathogens can be damaged and inactivated by physical treatment (which is basically heat and radiation) and also by chemical means. The latter is the most common approach to disinfection and can be applied to virtually all surfaces.

Physical disinfection

Heat and steam

Heat is by far the most broad-spectrum method of disinfection. Moist heat is more effective than dry heat, especially under pressure. When used correctly, steam under pressure (ie, autoclaves) is also the most efficient means of achieving sterility.[9] Steam cleaners are widely available and can be used on soft furnishings (eg, carpet), as well as floors and work surfaces.

In veterinary hospitals, shelters and the home, heat can be used in dishwashers, washing machines and incinerators to inactivate infective agents. Introduction of a dishwasher was one of the measures that ended an outbreak of MRSA in a human neonatal hospital.[10] Household dishwashers modified to achieve a temperature of 71°C were even proposed as a substitute for autoclaving in smaller surgeries.[11] However, care must be taken that the dishwasher itself does not become a source of cross-contamination.[12] Sterilisation efficacy is dependent on the duration of exposure of the pathogen to heat, and on whether or not a chemical disinfectant is also used.

Human safety needs to be considered. Zoonotic infections may be indirectly transmitted to laundry workers; albeit from a human source (ie, not zoonotic in this particular example), there is a report of *Salmonella* being transmitted to laundry workers.[13] One heavily contaminated item can contaminate an entire laundry load, as viruses can be transferred from contaminated to uncontaminated laundry during washing.[14,15] It has been demonstrated that *Cryptosporidium* species oocysts can attach to fabrics during machine washing.[16] In a human hospital, a nosocomial outbreak of *Microsporum canis* infection was linked to laundry contamination.[17]

The temperature needed for decontamination depends on the duration of the wash cycle and the detergent type.[15] For mycotic contaminants, Ossowski and Duchmann[18] found that reliable decontamination was achieved by laundering at 60°C, regardless of the textiles and detergents used. Nims and Plavsic report that 60°C (or higher) is the optimal temperature for inactivating FCV.[19] Temperatures of 56°C and above will kill 99% of *Giardia* cysts.[20] Addition of sodium hypochlorite with detergent significantly reduced the numbers of viruses in laundry,[14] and the addition of activated oxygen bleach increased efficacy against a number of bacteria.[15] However, parvovirus can resist temperatures of 80°C for at least an hour.[21]

Microbial size is an important determinant in the fabric attachment–detachment process during the machine washing cycle, with larger microorganisms showing greater transference to, and retention on, fabric swatches than smaller ones. Transfer efficiencies are higher for cotton towelling than for other fabric types, both before and after the washing machine spin cycle, indicating that it is not only the properties of the microorganism that influence transfer efficiency but also the properties of the fabric.[16] Moriello recommends two washings and stresses the importance of not overloading washing machines to be rid of *M canis* spores.[22] It should also be borne in mind that the lint trap may harbour contaminants.[22]

Ultraviolet-C radiation

Ultraviolet light radiation in the C range (UV-C; typically 254 nm) and B range (UV-B; 280–320 nm) has been investigated for disinfecting water, food preparation surfaces[19] and hospital rooms. UV-C-emitting devices were shown to significantly reduce the bioburden of important pathogens (*Clostridium difficile* and vancomycin-resistant enterococci, though not *Acinetobacter*) in real-world settings such as hospital rooms.[23]

Parvoviruses and circoviruses appear to be more susceptible to UV-C inactivation than are the caliciviruses.[19]

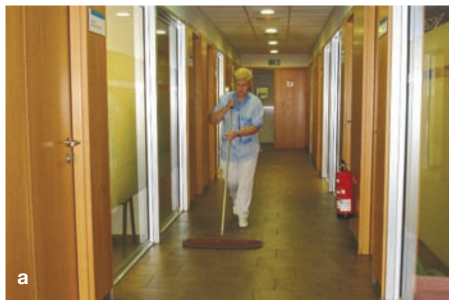


Figure 2 **(a) The cleaner at the University of Barcelona Veterinary Hospital, Spain, works all through the day (and not just before opening time, as in so many hospitals). This spotless hospital prioritises hygiene over appearance. (b) Rounded corners where floor meets wall in this veterinary hospital consulting room in Stromsholm, Sweden, facilitate floor cleaning.** *Images courtesy of Dr Diane D Addie*

Chemical disinfection

Both pure active substances and commercial disinfectants can be used for efficient disinfection, provided they are applied at an effective microbicidal concentration. Commercially available products usually contain a combination of various active substances. Side effects are minimised but, above all, they are efficacy tested and the microbicidal concentration is determined by an independent body.

In Europe, chemical disinfectants are considered as biocides and need to be licensed. The licensing procedure is complex and expensive (see box below), and will inevitably lead to a substantially reduced supply of available products in the future. It will, therefore, become even more important to choose the right disinfectant for a given purpose.

In veterinary practice, cleaning and disinfection of the surfaces (floors, walls, tables, etc) in various areas of the clinic has to be performed on a regular basis, up to several times a day (Figure 2). In both the veterinary clinic and shelter setting, special attention has to be given to the use of products with proven efficacy against a broad spectrum of microorganisms and viruses, which are safe for use with animals (and used in compliance with local regulations).

Efficacy testing and licensing of biocides

In Europe, chemical disinfectants are considered as biocides and are licensed under the EU Biocides Regulation (Regulation 528/2012).

All disinfectants affect the environment to a varying degree and will react with inert materials, such as the surface to be disinfected. The licensing procedure, therefore, includes tests for the ecotoxicological effect of the biocide, as well as the potential to harm animals and humans, and to be compatible with various materials.

The licensing procedure has been in place since September 2013, and the first licensed commercial chemical disinfectants will begin to be sold this year. Up until now, interim regulations have allowed use of the established disinfectants and voluntary efficacy testing; the latter performed according to established guidelines, such as those from the German Veterinary Medical Society (DVG) and the Association for Applied Hygiene (VAH), or other national or international test protocols.

Alcohol

Rubbing alcohol (USP)/surgical spirit (BP) is used primarily for topical application, especially following a chlorhexidine- or iodine-based scrub prior to surgery, or is applied immediately after a dog or cat bite (it stings, but is remarkably effective in preventing bacterial infection sequelae). It is prepared from a special denatured alcohol solution and contains approximately 70% v/v of pure, concentrated ethanol (ethyl alcohol) or isopropyl alcohol (isopropanol). Individual manufacturers can use their own 'formulation standards' in which the ethanol content usually ranges from 70–99% v/v. It is colourless. Instruments (eg, thermometers) may be disinfected by immersion in alcohol-based solutions: contamination of such solutions has rarely been reported.[24]

Alcohols have a non-specific mode of action, consisting mainly of disrupting the cell membrane or virus envelope, as well as denaturation and coagulation of proteins. Cells are lysed, and the cellular metabolism disrupted.[3] In terms of bactericidal activity, the following ranking has been generally established: n-propanol > isopropanol > ethanol. Bactericidal activity is higher at 30–40°C than at 20–30°C. In terms of virucidal activity, ethanol is superior to the propanols.[3] In one study, alcohols, and particularly ethanol, exhibited poor activity against all non-enveloped viruses.[25] In another, parvovirus resisted exposure to alcohol for 5 mins.[26] Taken orally, concentrated alcohols are lethal.

Park et al[27] evaluated seven hand sanitisers containing various active ingredients, such as ethanol, triclosan and chlorhexidine, and compared their virucidal efficacy against FCV and a norovirus faecal extract. Based on the results of a quantitative suspension test, only one ethanol-based product (72% ethanol, pH 2.9) and one triclosan-based product (0.1% triclosan, pH 3.0) reduced the infectivity of FCV (by ⩾3.4 log units). FCV is susceptible to low pH.

The priorities when choosing disinfectants for use around the cat are efficacy, safety for the cat and safety for humans.

Properties of an ideal disinfectant

- Broad antimicrobial activity
- Rapid bactericidal action
- Reasonable persistence in treated potable water
- Ease of use
- Solubility in water
- Relative stability
- Relative non-toxicity at used concentrations
- No poisonous residues
- No colour
- No staining
- Low cost
- Ready availability

From Rutala and Weber[28]

Chlorine releasers

Sodium hypochlorite

Sodium hypochlorite (bleach) has been used as a disinfectant for more than 100 years. It has many of the properties of an ideal disinfectant (see box),[28] and is relatively safe around cats, which is why sodium hypochlorite-based disinfectants are widely used, both in the veterinary surgery and in the home. Rapid inactivation on contact with matter means that items must be first cleaned before they can be effectively disinfected using sodium hypochlorite.

The efficacy of sodium hypochlorite in cleaning and disinfection processes depends on the concentration of available chlorine and the pH of the solution. Hypochlorous acid (HOCl) is a weak acid and dissociates to the hypochlorite ion (OCl^-) and proton (H^+), depending on the solution pH. It is generally believed that HOCl is the active compound in the germicidal action, whereas the concentration of OCl^- is a key factor determining the cleaning efficiency. This implies that the optimal pH for the germicidal activity of sodium hypochlorite differs from that for its cleaning activity.[29] Activity is reduced in the presence of heavy metal ions, biofilms, organic material, low temperature, low pH or UV radiation.[28]

Hypochlorites are lethal to most microbes, although viruses and vegetative bacteria are more susceptible than endospore-forming bacteria, fungi and protozoa. Clinical uses in healthcare facilities include hyperchlorination of potable water to prevent *Legionella* species colonisation, chlorination of water distribution systems used in haemodialysis centres, cleaning of environmental surfaces, disinfection of laundry, local use to decontaminate blood spills, disinfection of equipment, decontamination of medical waste prior to disposal and dental therapy. Despite the increasing availability of other disinfectants, disinfectants based on hypochlorites continue to find wide use in hospitals.[28]

Household bleach (0.0314%, 0.0933% and 0.670% sodium hypochlorite, pH 8.36–10.14) produced a >5 log reduction in *Listeria monocytogenes*, *Escherichia coli* O157:H7 and *Salmonella typhimurium* pathogens after 1 min at 25°C.[30]

Oxidising agents

Hydrogen peroxide

Hydrogen peroxide is often flushed directly into contaminated or infected wounds where its effervescent action and increased oxygenation retard anaerobic bacteria. It should not be used on closed wounds because of the risk of embolism.[9] It is also used as a disinfectant for nebuliser and anaesthetic equipment.[9] Hydrogen peroxide is not very stable and dissociates into H_2O and O_2.

After 1 min at 25°C, 3% hydrogen peroxide (pH 2.75) achieved a >5 log reduction in both *S typhimurium* and *E coli* O157:H7 burdens.

Compared with 1 min at 25°C, greater reductions in *L monocytogenes* ($P < 0.05$) were obtained after 10 mins of hydrogen peroxide treatment at an initial temperature of 55°C.[30]

Potassium peroxymonosulfate

Potassium peroxymonosulfate is an oxidising disinfectant that is usually combined with a surfactant and inorganic buffer in commercially available preparations.[9] It is highly bactericidal and virucidal, even against parvovirus (when exposed for 10 mins).[9] However, there is concern that it can corrode surfaces.

Potassium peroxymonosulfate has been shown to significantly reduce FCV titres.[19,31]

Peracetic acid

Peracetic acid (peroxyacetic acid or PAA) is an organic compound with the formula CH_3CO_3H; it is generated in situ by some laundry detergents. It is a weaker acid than acetic acid, and is always sold in solution with acetic acid and hydrogen peroxide to maintain the stability of the peracid. It is corrosive due to the acetic acid; however, additives in some commercial products reduce this side effect.

Faecal indicator bacteria (*Enterococcus faecium*), virus indicator (male-specific [F^+] coliphages [coliphages]), and protozoa disinfection surrogate (*Bacillus subtilis* spores [spores]) were tested by Park et al.[32] Scanning electron microscopy revealed that peracetic acid targets the external layers of spores. Concentrations of 5 ppm (contact time: 5 mins), 50 ppm (10 mins) and 3000 ppm (5 mins) were needed to achieve a 3 log reduction of *E faecium*, coliphages and spores, respectively.

Peracetic acid concentrations as low as 0.0025% were effective in decreasing *Salmonella* species artificially applied to chicken carcases, while concentrations of 0.02% were effective in decreasing *Campylobacter* species numbers, extending the shelf-life of the carcases to 15 days.[33]

Pruss et al[34] studied the antimicrobial efficacy of a peracetic acid–ethanol sterilisation (PES) procedure in allogenic avital bone transplants against three enveloped viruses (human immunodeficiency virus type 2, Aujeszky's disease virus, bovine virus diarrhoea virus) and three non-enveloped viruses (hepatitis A virus, poliovirus, porcine parvovirus). PES led to a reduction in virus titres of more than 4 log_{10}. Only hepatitis A virus showed a reduction below 4 log_{10} (2.87) with residual infectivity. For *Staphylococcus aureus*, *E faecium*, *Pseudomonas aeruginosa*, *B subtilis* (including spores), *Clostridium sporogenes*, *Mycobacterium terrae*, *Candida albicans* and *Aspergillus niger,* a titre reduction below the detection level (5 log_{10}) was achieved after an incubation time of 2 h.

Disinfection is a potent means of reducing the number of pathogens on a surface. It does not result in sterility and is always non-specific.

Aldehydes

Chlorhexidine

Chlorhexidine gluconate is widely used as a patient/surgeon skin scrub, and for hand hygiene (both wet washing and rubs). Its antimicrobial activity occurs more slowly than that of alcohols. Both chlorhexidine and povidone–iodine cause an immediate reduction in bacteria; however, the reduction when using chlorhexidine is more dramatic. Unlike chlorhexidine, povidone–iodine shows a lack of cumulative and residual activity.[35]

Resistance to chlorhexidine has been described.[36,37] Also, multiple nosocomial outbreaks have been linked to contaminated chlorhexidine.[24] Most reports have been traced to the use of contaminated water to prepare diluted preparations and/or the practice of reusing bottles to dispense chlorhexidine without adequate disinfection. Although most outbreaks have occurred with solutions containing less than 2% chlorhexidine, an outbreak has been reported with solutions of 2–4% chlorhexidine.[24]

Chlorhexidine was shown to be ineffective against FCV.[27]

Jarral et al conclude their review of 593 papers thus: '[T]here is no evidence suggesting the use of chlorhexidine during hand scrub reduces surgical site infections, which perhaps explains why guidelines from the World Health Organization, the Centers for Disease Control and Prevention and the Association for Perioperative Practice do not recommend one specific antimicrobial over another for hand scrub.'[35]

Iodine/iodophors

Iodine has broad-spectrum activity against gram-positive and gram-negative bacteria, fungi, protozoa and, to some extent, viruses.[9,24] Destruction of bacterial spores requires moist contact for more than 15 mins.[9] Iodine is widely used as a preoperative scrub on patients' skin. It has a synergistic effect when combined with alcohol and, since it is only slightly soluble in water, it tends to be dissolved in alcohol.

Iodophors are less irritating to skin than iodine compounds,[24] and are non-staining.

Iodine surgical scrub was effective in killing MRSA[38] and parvovirus.[21]

Quaternary ammonium compounds/ benzalkonium chloride

The QACs are chemicals that alter the surface tension of an organism and are classed as cationic detergents. They are used for disinfection but are inactivated by organic material, soap and hard water. They are fungicidal, bactericidal and virucidal against some enveloped viruses at medium concentrations, but there is no evidence that they are effective against parvovirus.[9] Benzalkonium chloride was unable to eradicate a mature *Salmonella* biofilm (though reduced an immature one).[39] Scorza and Lappin[40] claimed that the compound Roccal (Winthrop Laboratories, New York) was effective at inactivating *Giardia* cysts.

Bacterial adaptation to QACs is documented. Worryingly, exposure to gradually increasing concentrations of this type of disinfectant results in reduced susceptibility not only to the QACs themselves but also to antibiotics, as well as cross-resistance to phenicol compounds (florfenicol and chloramphenicol) in 90% of *E coli* strains.[41] Extensive use of QACs at subinhibitory concentrations may lead to the emergence of antibiotic-resistant bacteria and may represent a public health risk.[41]

Household products

Sodium bicarbonate

The advantages of sodium bicarbonate over the available chemical disinfectants for food contact surfaces are its safety, ready availability and low cost. Sodium bicarbonate at concentrations of 5% and above was found to be the most effective, with 4 $\log_{10}$ (99.99%) reduction in FCV titres on food contact surfaces with a contact time of 1 min. Virucidal efficacy was enhanced when sodium bicarbonate was used in combination with aldehydes or hydrogen peroxide.[42] However, sodium bicarbonate was shown to be ineffective against *L monocytogenes*, *E coli* O157:H7 and *S typhimurium*, even after 10 mins at 55°C.[30] Therefore, since bacterial reduction is important in the disinfection of food contact surfaces, it is preferable to use a cat-safe disinfectant (eg, sodium hypochlorite) and thoroughly wash it off (preferably with very hot [>60°C] water).

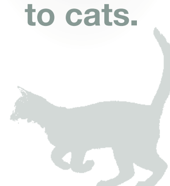
Acetic acid (household vinegar)

Cheap and readily available, household vinegar (2.5% and 5% acetic acid) can be used for cleaning as well as for cooking. After 1 min at room temperature (25°C) undiluted vinegar (pH 2.58) reduced *S typhimurium* numbers by over 5 log units; and at a starting temperature of 55°C, exposed for 10 mins, it significantly reduced *L monocytogenes* numbers.[30] However, acetic acid fumes make it fairly unpleasant to work with and it is unlikely that it would be chosen in practice over a commercially available disinfectant.

Citric acid (lemon juice)

A 5% solution of citric acid reduced *L monocytogenes* numbers after 10 mins at an initial temperature of 55°C.[30] However, little is known about the general disinfectant properties of citric acid.

The antimicrobial activity of essential oils is due to small terpenoids and phenol compounds, which are toxic to cats.



Essential oils

Essential oils have been shown to have some effect against *M canis* in vitro and in vivo.[43] A mixture composed of 5% *Origanum vulgare*, 5% *Rosmarinus officinalis* and 2% *Thymus serpillum*, in sweet almond oil, was administered to seven infected, symptomatic cats: four of the seven cats recovered.[43] Vázquez-Sánchez et al[44] evaluated the potential of 19 essential oils in removing the foodborne pathogen *S aureus* from food-processing facilities: thyme oil was the most effective. Thosar et al[45] evaluated five essential oils against four common human oral pathogens (*S aureus*, *Enterococcus faecalis*, *E coli* and *C albicans)*; eugenol oil (oil of cloves), peppermint oil and tea tree oil exhibited significant inhibitory effects.[45]

However, the antimicrobial activity of essential oils is due to a number of small terpenoids and phenol compounds;[45] since these are toxic to cats, essential oils should only ever be used under supervision of a qualified veterinary surgeon. Essential oil toxicity has been reported (see Table 1, page 601).[46–48]

Silver compounds

Silver has been used for centuries for making cutlery and dishes, based on an innate understanding of its antimicrobial action. The antibacterial, antifungal and antiviral activities of silver have generated a lot of interest in recent years. A wide variety of applications of silver has recently emerged for consumer products, ranging from disinfecting medical devices, textiles, cosmetics and home appliances to water treatment. The antimicrobial action of silver or silver compounds is proportional to the bioactive silver ion (Ag^+) released and its availability to interact with bacterial or fungal cell membranes. Silver metal and inorganic silver compounds ionise in the presence of water, body fluids or tissue exudates. The silver ion is biologically active and readily interacts with proteins, amino acid residues, free anions and receptors on mammalian and eukaryotic cell membranes. Bacterial (and probably fungal) sensitivity to silver is genetically determined and relates to the level of intracellular silver uptake and its ability to interact with and irreversibly denature key enzyme systems.[54]

Recent advances in nanotechnology have enabled the production of pure silver as nanoparticles, which are more efficient than silver ions. This has paved the way for new strategies for using pure silver against a wide array of pathogens – particularly multiresistant pathogens, which are hard to treat with available antibiotics.[55] It is believed that the silver nanoparticles are able to interact with disulphide bonds of the glycoprotein/protein contents of microorganisms such as viruses,

Toxicity of disinfectants to cats

Due to the cat's fastidious eating habits, there are fewer feline toxicity incidents than there are canine.[48,58–61] Nevertheless, cats spend an estimated 5–25% of their waking time in grooming; hence disinfectants used in the cat's environment (home, shelter, veterinary surgery, etc) must be safe in case inadvertent ingestion via grooming occurs. Additional routes of toxicity include transdermal absorption;[50,62] or inhalation of irritant or toxic fumes. The cat may present with caustic burns to the paws or other areas that are in direct contact with disinfectant, and/or ulceration of the tip of the tongue and oesophagus through attempting to groom the toxin off.[9,63,64]

Possible poisoning by household products was the second most common reason (after ingestion of drugs) for telephone calls to the Kansas State University between 2009 and 2012: 15.5% of 1616 calls were related to potential poisoning of dogs and cats by household products; and, of those, 17 calls related to cats and household cleaners.[58] However, it is worth emphasising that in most reports on domestic animal poisoning, disinfectants do *not* play a major role – the major culprits being human medications, ethylene glycol, lead, lily plants and topical pesticides.[59,61,64–71]

Deficiency of the enzyme UDP-glucuronosyl transferase renders cats extremely sensitive to the adverse effects of phenol-based products (see below). Actual case reports of disinfectant toxicity in the literature are few and far between, with most published papers on toxicity in the cat having been deliberately perpetrated in the name of science. Disinfectant toxicity in cats is summarised in Table 1.

Susceptibility to phenols

The domestic cat (*F catus*) shows remarkable sensitivity to the adverse effects of phenolic compounds, including acetaminophen and aspirin, as well as structurally related toxicants found in the diet and environment.[72] This idiosyncrasy results from pseudogenisation of the gene encoding UDP-glucuronosyltransferase (UGT) 1A6, the major species-conserved phenol detoxification enzyme.[72] Glucuronidation is quantitatively the most important of the six routes by which xenobiotics (toxins) are conjugated, and therefore eliminated, from the body.[51] Cats have a carnivorous diet and, as a result of lack of exposure to plant-based toxins (phytoalexins), have presumably lost the need to metabolise these toxins via glucuronidation, which is common in most herbivores and omnivores.[72]

bacteria and fungi.[55] Silver nanoparticles are attractive because they are non-toxic at low concentrations and have broad-spectrum antibacterial action against at least 12 species of bacteria including multiresistant MRSA, multidrug-resistant *P aeruginosa*, ampicillin-resistant *E coli* O157:H7 and erythromycin-resistant *Streptococcus pyogenes*.[55]

There is a growing trend for developing food-packaging materials with antimicrobial properties. Martínez-Abad et al[56] incorporated silver ions into polylactic acid (PLA) films. The films demonstrated strong antimicrobial efficacy against *Salmonella enterica* and FCV in vitro, with increasing effects at higher silver concentrations. In vivo, antimicrobial activity was very much dependent on the food type and temperature: in lettuce samples incubated at 4°C for 6 days, 4 log colony forming units of *Salmonella* were inactivated using the films and no infectious FCV was reported. On paprika samples, no antiviral effect was seen on FCV infectivity and films showed less antibacterial activity on *Salmonella*.

Advances in biotechnology have enabled incorporation of ionisable silver into fabrics for clinical use to reduce the risk of nosocomial infections and for personal hygiene.[54] Although veterinary use of silver has not yet taken off, in 2012, Woods et al[57] reported the use of a combination of nanocrystalline silver dressing and subatmospheric pressure therapy to treat a resistant wound infection, following tumour removal and radiation therapy, in a difficult-to-manage surgical site in a cat.

Antiparasitic disinfection in cat husbandry relies on thorough cleaning and, whenever possible, steam cleaning to minimise the number of infectious parasites.

Chemical disinfectants against parasites

In Europe there is no uniform protocol for efficacy testing of chemical disinfectants against parasitic infections. The only guideline available is from the German Veterinary Medical Society (DVG), with the test organisms being oocysts of the coccidia species *Eimeria tenella* and eggs of the nematode *Ascaris suum*. The specific context for this testing is the disinfection of large animal housing. The disinfectants that pass this test are exclusively products based on cresols and phenols – substances that are considered highly toxic for cats. Products based on other active substances, such as aldehydes and peracetic acid, have not been tested against these agents or have been shown not to be efficacious (U Truyen, personal communication).

Antiparasitic disinfection in cat husbandry has, therefore, to rely on thorough cleaning and, whenever possible, steam cleaning to minimise the number of infectious parasites.

Summary

Table 2 presents a summary of the disinfectants discussed in these guidelines. The unique metabolism of cats requires that extra caution is taken when using disinfectants around them.

Table 1 Reported toxicity in cats associated with disinfectant use

Substance	Clinical signs	Treatment	Reference
Benzalkonium chloride	Chemical burns when put undiluted onto skin, conjunctiva or mucosae. Cats also developed oral and oesophageal ulceration after licking treated skin		Greene et al[9]
Hexachlorophene*	Hindlimb paralysis in 3–5 days. Cardiovascular collapse, corneal ulcers, trembling, lethargy and weakness. Status spongiosis, astrocytosis, and microgliosis of the cerebral and cerebellar white matter and corticospinal tracts	Slow IV administration of 30% urea (2 g/kg in 10% invert sugar)	Hanig et al[49] Thompson et al[50]
Phenol	Dark green urine Carcinogen		Garg[51] Shukla[52]
Pine oil containing disinfectant (eg, Pine-Sol; Clorox)	Unresponsive pupils and extreme ataxia were observed prior to death. Pathological changes consisted of severe acute centrilobular hepatic necrosis and renal cortical necrosis		Rousseaux et al[53]
Essential oils in flea treatment (peppermint oil, cinnamon oil, lemongrass oil, clove oil, thyme oil)	In a study of 39 cats and 9 dogs with a history of exposure to natural flea preventives, the onset of adverse effects (agitation, anorexia, erythema, fasciculation, hiding, hyperactivity, hypersalivation, hypothermia, lethargy, panting, retching, seizures, tachycardia, tremors, vocalisation, vomiting, weakness) occurred within 24 h in 39 of 44 exposed animals which developed signs. The duration of signs in 24 animals ranged from 30 mins to 149 h. The products were used as per label in 77% of animals (n = 37). Death (1 cat; n = 1/28; 4%) or euthanasia (1 cat and 1 dog; n = 2/28; 7%) was reported in three animals	Of 28 animals with known outcome, 50% (n = 14) recovered with bathing alone while others received intravenous fluids, muscle relaxants, and anticonvulsive medications	Genovese et al[46]
Tea tree oil	Clinical signs (increased salivation/drooling, signs of CNS depression or lethargy, paresis, ataxia, tremors, hypothermia, coma, dehydration, elevated AST and ALT) developed within 2–12 h and lasted up to 72 h. A significant association with severity of illness was found for age and weight, with a higher prevalence of major illness in younger and smaller cats	Wash off oil, activated charcoal per os, dexamethasone	Bischoff and Guale[47] Khan et al[48]

*Now banned worldwide because of its high rate of dermal absorption and subsequent toxic effects
CNS = central nervous system; AST = aspartate aminotransferase; ALT = alanine transaminase

Table 2 Summary of disinfectants and their potential for use in the feline environment (continued on page 602)

Disinfectant	Concentration/dilution	Uses	Comments
Heat and steam	Recommended temperature–pressure–exposure time to produce sterilisation with an autoclave is 121°C at 15 psi for 15 mins or 126°C at 20 psi for 10 mins. Prions require a heat of 130°C for 30–60 mins to inactivate.[9] For washing machines/dishwashers, a 30 min cycle at 60°C is required	Instruments, floors, work surfaces, dishes, bedding	The most effective, safe and broad spectrum of disinfection methods. Moist heat (steam) is the most effective for eliminating protozoal oocysts such as *Toxoplasma* and *Isospora*. In outbreaks of enteric infections, cardboard litter trays, which can be incinerated, can be used
Sodium hypochlorite (bleach)	5–6% bleach diluted at 1:32 or less, depending on use*	Water decontamination, cleaning surfaces, food utensils, litter trays, floors, laundry, instruments and foot baths*	The best all-round chemical disinfectant. Inactivated by organic debris. One of the few chemicals that will inactivate parvovirus and kill clostridial spores. Loses activity if stored for a long time.[9] Caution: can release toxic chlorine gas
Alcohol		Hand rubs are more likely to be used than hand washes[3] and reduce bacterial and viral titres more effectively	Contamination of alcohol-based solutions has rarely been reported.[24] Ineffective against parvovirus[26]
Ethanol	70–90% concentration for 1 min – the higher the concentration, the more effective. At least 90% concentration required for MRSA control[38]	Used along with isopropanol in rubbing alcohol/surgical spirit and in hand sanitisers	More effective against FCV than isopropanol,[73] but poor activity against all non-enveloped viruses.[25] No sporicidal activity

Table 2 Summary of disinfectants and their potential for use in the feline environment (continued from page 601)

Disinfectant	Concentration/dilution	Uses	Comments
Isopropanol	40–60% concentration for 1 min	Used along with ethanol in rubbing alcohol/ surgical spirit and in hand sanitisers	Less effective than ethanol against FCV[73]
Hydrogen peroxide		Initial flush for wounds for its effervescent action and oxygenation, which retards anaerobes	Do not use in closed wounds (risk of air embolism)
Sodium bicarbonate	5% for 1 min is effective against FCV[42]	Can be used on hands, and food surfaces and containers	Cheap and safe, but not effective against some bacteria,[30] so **not recommended**
Acetic acid (household vinegar)	Undiluted vinegar (pH 2.58) (2.5% and 5% acetic acid) for 1 min at room temperature will reduce *Salmonella typhimurium,* and at a starting temperature of 55°C for 10 mins will reduce *Listeria monocytogenes*[30]	Food surfaces and containers	No information about activity against viruses/parasites. Unlikely to be used in practice due to odour
Citric acid	5% citric acid solution for 10 mins	Food surfaces and containers	Reduces *L monocytogenes* after 10 mins at an initial temperature of 55°C.[30] Efficacy against other pathogens unknown
Chlorhexidine	0.5% in water, saline, lactated Ringer's solution or alcohol[9]	Preoperative skin scrub and hand wash. Gives up to 2 days' antiseptic protection of skin after a single application[9]	Does not inactivate FCV[27] or dermatophytes (though works with miconazole). Should never be used in the ear (ototoxic)[74] or eye[9] Skin irritant at ⩾4% concentration[3]
Iodine/iodophors	1–10% solution applied topically	Preoperative patient/surgeon skin scrub. 1:50 dilution of povidone-iodine for ocular preoperative surface disinfection. Hand rub	Can be skin irritant. Iodine surgical scrub has proven effective in killing MRSA.[38] Synergistic effect when used with alcohol
Potassium peroxymonosulfate		Cleaning surfaces and instruments. Foot baths	Bactericidal and virucidal, even against parvovirus (10 mins exposure).[9] Good activity in presence of organic material. Can even be used on carpets. However, can corrode surfaces. Proven efficacy against FCV[19,31]
Quaternary ammonium compounds (eg, benzalkonium chloride)	0.001–1%	Used as soap and antiseptic. Have unusual ability to kill *Giardia* cysts at 4°C and room temperature	Algicidal, fungicidal, bactericidal and virucidal against some enveloped viruses. Do not reliably inactivate FCV, herpesvirus and parvovirus. Harbour opportunistic bacteria (eg, *Serratia* species).[9,24] Inactivated by organic materials, soap and hard water. Concern about widespread use leading to antibiotic resistance,[41] so **not recommended,** except possibly where there is *Giardia* infection
Phenol-based; eg, hexachlorophene, essential oil of tea tree or clove (eugenol)			**Not recommended** around cats: toxic and caustic
Ultraviolet-C radiation	Fluence ⩾30 mJ/cm^2	For reducing bacterial contamination in whole rooms	FCV is more resistant than parvovirus to UV-C.[19] Effective against enterococci and *C difficile* but not *Acinetobacter.*[23] Decreased efficacy in presence of organic material[19]
Silver compounds		Impregnated wound dressings	Safe antimicrobial but at present in cats has only been used in wound dressings

This table lists disinfectants used in veterinary practices, catteries, shelters and around the home, showing the most notoriously difficult to eradicate pathogens as sentinels for efficacy
*For a detailed examination of the uses of bleach, see table 93-1 in Greene et al.[9] FCV = feline calicivirus

KEY POINTS

- Disinfectants should be chosen on the basis of efficacy, safety for cats and safety for human users.
- Cats are susceptible to phenol-based disinfectants, including certain essential oils.
- Heat, especially moist heat, is the safest and most effective disinfectant. Temperatures in washing machines and dishwashers should be at least 60°C to eliminate pathogenic spores and resistant viruses.
- Alcohols, and particularly ethanol, are excellent against bacteria but have poor activity against non-enveloped viruses.
- Bleach is effective and relatively safe, but its activity is reduced by the presence of heavy metal ions, biofilms, organic material, low temperature, low pH or UV radiation.
- Enveloped viruses are susceptible to most disinfectants; of the non-enveloped viruses, parvovirus is universally recognised as being the most difficult to eradicate.
- Skin scrubs and rubs containing alcohols are more effective than those containing chlorhexidine, and less subject to contamination.
- Quaternary ammonium compounds (eg, benzalkonium chloride) are not recommended.
- The future of veterinary disinfection may include ultraviolet radiation and more use of silver.

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References

1 Quirce S and Barranco P. **Cleaning agents and asthma.** *J Investig Allergol Clin Immunol* 2010; 20: 542–550.

2 Ernst JV, Lindsay DS and Current WL. **Control of *Isospora suis*-induced coccidiosis on a swine farm.** *Am J Vet Res* 1985; 46: 643–645.

3 Kampf G and Kramer A. **Epidemiologic background of hand hygiene and evaluation of the most important agents for scrubs and rubs.** *Clin Microbiol Rev* 2004; 17: 863–893.

4 Fuller C, Besser S, Savage J, et al. **Application of a theoretical framework for behavior change to hospital workers' real-time explanations for noncompliance with hand hygiene guidelines.** *Am J Infect Control* 2014; 42: 106–110.

5 Umit UM, Sina M, Ferhat Y, et al. **Surgeon behavior and knowledge on hand scrub and skin antisepsis in the operating room.** *J Surg Educ* 2014; 71: 241–245.

6 Steinmann J. **Surrogate viruses for testing virucidal efficacy of chemical disinfectants.** *J Hosp Infect* 2004; 56 Suppl 2: S49–54.

7 Addie DD. **Control of viral diseases in catteries.** In: Bonagura JD and Twedt DC (eds). Kirk's current veterinary therapy XIV. Philadelphia: Saunders Elsevier, 2008, pp 1299–1305.

8 Möstl K, Egberink H, Addie D, et al. **Prevention of infectious diseases in cat shelters: ABCD guidelines.** *J Feline Med Surg* 2013; 15: 546–554.

9 Greene CE, Weese JS and Calpin JP. **Environmental factors in infectious disease.** In: Greene C (ed). Infectious diseases of the dog and cat. 4th ed. St Louis, MO: Saunders Elsevier, 2012, pp 1078–1100.

10 Ağca H, Topaç T, Ozmerdiven GE, et al. **Investigation of methicillin resistant *Staphylococcus aureus* in neonatal intensive care unit.** *Int J Clin Exp Med* 2014; 7: 2209–2213.

11 Ebner W, Eitel A, Scherrer M, et al. **Can household dishwashers be used to disinfect medical equipment?** *J Hosp Infect* 2000; 45: 155–159.

12 Ståhl Wernersson E, Johansson E and Håkanson H. **Cross-contamination in dishwashers.** *J Hosp Infect* 2004; 56: 312–317.

13 Standaert SM, Hutcheson RH and Schaffner W. **Nosocomial transmission of Salmonella gastroenteritis to laundry workers in a nursing home.** *Infect Control Epidemiol* 1994; 15: 22–26.

14 Gerba CP and Kennedy D. **Enteric virus survival during household laundering and impact of disinfection with sodium hypochlorite.** *Appl Environ Microbiol* 2007; 73: 4425–4428.

15 Honisch M, Stamminger R and Bockmühl DP. **Impact of wash cycle time, temperature and detergent formulation on the hygiene effectiveness of domestic laundering.** *J Appl Microbiol* 2014; 117: 1787–1797.

16 O'Toole J, Sinclair M and Leder K. **Transfer rates of enteric microorganisms in recycled water during machine clothes washing.** *Appl Environ Microbiol* 2009; 75: 1256–1263.

17 Shah P C, Krajden S, Kane J, et al. **Tinea corporis**

caused by *Microsporum canis*: report of a nosocomial outbreak. *Eur Epidemiol* 1988; 4: 33–38.
18 Ossowski B and Duchmann U. **Effect of domestic laundry processes on mycotic contamination of textiles.** *Hautarzt* 1997; 48: 397–401.
19 Nims R and Plavsic M. **Inactivation of caliciviruses.** *Pharmaceuticals (Basel)* 2013; 6: 358–392.
20 Mtapuri-Zinyowera S, Midzi N, Muchaneta-Kubara CE, et al. **Impact of solar radiation in disinfecting drinking water contaminated with *Giardia duodenalis* and *Entamoeba histolytica/dispar* at a point-of-use water treatment.** *J Appl Microbiol* 2009; 106: 847–852.
21 Mahnel H. **Studies on inactivation of viruses in drinking and surface water. A contribution to the decontamination of water by field methods** [author's translation]. *Zentralbl Bakteriol Orig B* 1977; 1165: 527–538.
22 Moriello KA. **Decontamination of laundry exposed to *Microsporum canis* hairs and spores.** *J Feline Med Surg*. Epub ahead of print 26 May 2015. DOI: 10.1177/1098612X15587575.
23 Anderson DJ, Gergen MF, Smathers E, et al. **Decontamination of targeted pathogens from patient rooms using an automated ultraviolet-C-emitting device.** *Infect Control Hosp Epidemiol* 2013; 34: 466–471.
24 Weber DJ, Rutala WA and Sickbert-Bennett EE. **Outbreaks associated with contaminated antiseptics and disinfectants.** *Antimicrob Agents Chemother* 2007; 51: 4217–4224.
25 Eterpi M, McDonnell G and Thomas V. **Disinfection efficacy against parvoviruses compared with reference viruses.** *J Hosp Infect* 2009; 73: 64–70.
26 Rabenau HF, Steinmann J, Rapp I, et al. **Evaluation of a virucidal quantitative carrier test for surface disinfectants.** *PLoS One* 2014; 9: e86128.
27 Park GW, Barclay L, Macinga D, et al. **Comparative efficacy of seven hand sanitizers against murine norovirus, feline calicivirus, and GII.4 norovirus.** *J Food Prot* 2010; 73: 2232–2238.
28 Rutala WA and Weber DJ. **Uses of inorganic hypochlorite (bleach) in health-care facilities.** *Clin Microbiol Rev* 1997; 10: 597–610.
29 Fukuzaki S. **Mechanisms of actions of sodium hypochlorite in cleaning and disinfection processes.** *Biocontrol Sci* 2006; 11: 147–157.
30 Yang H, Kendall PA, Medeiros L, et al. **Inactivation of *Listeria monocytogenes*, *Escherichia coli* O157:H7, and *Salmonella typhimurium* with compounds available in households.** *J Food Prot* 2009; 72: 1201–1208.
31 Su X and D'Souza DH. **Inactivation of human norovirus surrogates by benzalkonium chloride, potassium peroxymonosulfate, tannic acid, and gallic acid.** *Foodborne Pathog Dis* 2012; 9: 829–834.
32 Park E, Lee C, Bisesi M, et al. **Efficiency of peracetic acid in inactivating bacteria, viruses, and spores in water determined with ATP bioluminescence, quantitative PCR, and culture-based methods.** *J Water Health* 2014; 12: 13–23.
33 Bauermeister LJ, Bowers JW, Townsend JC, et al. **The microbial and quality properties of poultry carcasses treated with peracetic acid as an antimicrobial treatment.** *Poult Sci* 2008; 87: 2390–2398.
34 Pruss A, Göbel UB, Pauli G, et al. **Peracetic acid-ethanol treatment of allogeneic avital bone tissue transplants – a reliable sterilization method.** *Ann Transplant* 2003; 8: 34–42.
35 Jarral OA, McCormack DJ, Ibrahim S, et al. **Should surgeons scrub with chlorhexidine or iodine prior to surgery?** *Interact Cardiovasc Thorac Surg* 2011; 12: 1017–1021.
36 Braoudaki M and Hilton AC. **Adaptive resistance to biocides in *Salmonella enterica* and *Escherichia coli* O157 and cross-resistance to antimicrobial agents.** *J Clin Microbiol* 2004; 42: 73–78.
37 Condell O, Iversen C, Cooney S, et al. **Efficacy of biocides used in the modern food industry to control Salmonella – links between biocide tolerance and resistance to clinically relevant antimicrobial compounds.** *Appl Environ Microbiol* 2012; 78: 3087–3097.
38 Perona PJ, Johnson AJ, Perona JP, et al. **Effectiveness of various hospital-based solutions against community-acquired methicillin-resistant *Staphylococcus aureus*.** *J Long Term Eff Med Implants* 2013; 23: 23–29.
39 Corcoran M, Morris D, De Lappe N, et al. **Commonly used disinfectants fail to eradicate *Salmonella enterica* biofilms from food contact surface materials.** *Appl Environ Microbiol* 2014; 80: 1507–1514.
40 Scorza V and Lappin M. **Enteric protozoal infections.** In: Greene C (ed). Infectious diseases of the dog and cat. 4th ed. St Louis, MO: Saunders Elsevier, 2012, pp 785–801.
41 Soumet C, Fourreau E, Legrandois P, et al. **Resistance to phenicol compounds following adaptation to quaternary ammonium compounds in *Escherichia coli*.** *Vet Microbiol* 2012; 158: 147–152.
42 Malik YS and Goyal SM. **Virucidal efficacy of sodium bicarbonate on a food contact surface against feline calicivirus, a norovirus surrogate.** *Int J Food Microbiol* 2006; 109: 160–163.
43 Mugnaini L, Nardoni S, Pinto L, et al. **In vitro and in vivo antifungal activity of some essential oils against feline isolates of *Microsporum canis*.** *J Mycol Med* 2012; 22: 179–184.
44 Vázquez-Sánchez D, Cabo ML and Rodríguez-Herrera JJ. **Antimicrobial activity of essential oils against *Staphylococcus aureus* biofilms.** *Food Sci Technol Int*. Epub ahead of print 3 October 2014; pii: 1082013214553996.
45 Thosar N, Basak S, Bahadure RN, et al. **Antimicrobial efficacy of five essential oils against oral pathogens: an in vitro study.** *Eur J Dent* 2013; 7 Suppl 1: S71–77.

46 Genovese AG, McLean MK and Khan SA. **Adverse reactions from essential oil-containing natural flea products exempted from Environmental Protection Agency regulations in dogs and cats.** *Vet Emerg Crit Care (San Antonio)* 2012; 22: 470–475.

47 Bischoff K and Guale F. **Australian tea tree (*Melaleuca alternifolia*) oil poisoning in three purebred cats.** *J Vet Diagn Invest* 1998; 10: 208–210.

48 Khan SA, McLean MK and Slater MR. **Concentrated tea tree oil toxicosis in dogs and cats: 443 cases (2002–2012).** *J Am Vet Med Assoc* 2014; 244: 95–99.

49 Hanig JP, Krop S, Morrison, et al. **Observations on hexachlorophene-induced paralysis in the cat and its antagonism by hypertonic urea.** *Proc Soc Exp Biol Med* 1976; 152: 165–169.

50 Thompson JP, Senior DF, Pinson DM, et al. **Neurotoxicosis associated with the use of hexachlorophene in a cat.** *J Am Vet Med Assoc* 1987; 190: 1311–1312.

51 Garg SK. **General toxicology.** In: Garg SK (ed). Veterinary toxicology. New Delhi: CBS Publishers, 2007, pp 1–36.

52 Shukla Y. **Chemicals, drugs and plants-induced carcinogenicity and genotoxicity.** In: Garg SK (ed). Veterinary toxicology. New Delhi: CBS Publishers, 2007, pp 269–280.

53 Rousseaux CG, Smith RA and Nicholson S. **Acute Pinesol toxicity in a domestic cat.** *Vet Hum Toxicol* 1986; 28: 316–317.

54 Lansdown AB. **Silver in health care: antimicrobial effects and safety in use.** *Curr Probl Dermatol* 2006; 33: 17–34.

55 Lara HH, Garza-Treviño EN, Ixtepan-Turrent L, et al. **Silver nanoparticles are broad-spectrum bactericidal and virucidal compounds.** *J Nanobiotechnology* 2011; 9: 30.

56 Martínez-Abad A, Ocio MJ, Lagarón JM, et al. **Evaluation of silver-infused polylactide films for inactivation of Salmonella and feline calicivirus in vitro and on fresh-cut vegetables.** *Int J Food Microbiol* 2013; 162: 89–94.

57 Woods S, de Castro Marques AI, Renwick MG, et al. **Nanocrystalline silver dressing and subatmospheric pressure therapy following neoadjuvant radiation therapy and surgical excision of a feline injection site sarcoma.** *J Feline Med Surg* 2012; 14: 214–218.

58 Mahdi A and Van der Merwe D. **Dog and cat exposures to hazardous substances reported to the Kansas State Veterinary Diagnostic Laboratory: 2009–2012.** *J Med Toxicol* 2013; 9: 207–211.

59 Caloni F, Cortinovis C, Rivolta M, et al. **Animal poisoning in Italy: 10 years of epidemiological data from the Poison Control Centre of Milan.** *Vet Rec* 2012; 170: 415.

60 Forrester MB and Stanley SK. **Patterns of animal poisonings reported to the Texas Poison Center Network: 1998–2002.** *Vet Hum Toxicol* 2004; 46: 96–99.

61 McLean MK and Hansen SR. **An overview of trends in animal poisoning cases in the United States: 2002–2010.** *Vet Clin North Am Small Anim Pract* 2012; 42: 219–228.

62 Dorman DC, Buck WB, Trammel HL, et al. **Fenvalerate/N,N-diethyl-m-toluamide (Deet) toxicosis in two cats.** *J Am Vet Med Assoc* 1990; 196: 100–102.

63 Abou-Donia MB, Trofatter LP, Graham DG, et al. **Electromyographic, neuropathologic, and functional correlates in the cat as the result of tri-o-cresyl phosphate delayed neurotoxicity.** *Toxicol Appl Pharmacol* 1986; 83: 126–141.

64 Malik R, Ward MP, Seavers A, et al. **Permethrin spot-on intoxication of cats. Literature review and survey of veterinary practitioners in Australia.** *J Feline Med Surg* 2010; 12: 5–14.

65 Antoniou V, Zantopoulos N and Tsoukali H. **Fatal animal poisonings in northern Greece: 1990–1995.** *Vet Hum Toxicol* 1997; 39: 35–36.

66 Curti R, Kupper J, Kupferschmidt H, et al. **A retrospective study of animal poisoning reports to the Swiss Toxicological Information Centre (1997–2006).** *Schweiz Arch Tierheilkd* 2009; 151: 265–273.

67 Guitart R, Manosa S, Guerrero X, et al. **Animal poisonings: the 10-year experience of a veterinary analytical toxicology laboratory.** *Vet Hum Toxicol* 1999; 41: 331–335.

68 Hall K. **Toxin exposures and treatments: a survey of practicing veterinarians.** In: Bonagura JD and Twedt DC (eds). Kirk's current veterinary therapy XIV. Philadelphia: Elsevier Saunders, 2008, pp 95–99.

69 Hofstee AW. **Acute poisoning in animals in The Netherlands in the period 1985–1988.** *Tijdschr Diergeneeskd* 1989; 114: 1154–1158.

70 Hovda L R. **Toxin exposures in small animals.** In: Bonagura JD and Twedt DC (eds). Kirk's current veterinary therapy XIV. Philadelphia: Elsevier Saunders, 2008, pp 92–94.

71 Xavier FG, Kogika MM and de Sousa Spinosa H. **Common causes of poisoning in dogs and cats in a Brazilian veterinary teaching hospital from 1998 to 2000.** *Vet Hum Toxicol* 2002; 44: 115–116.

72 Shrestha B, Reed JM, Starks PT, et al. **Evolution of a major drug metabolizing enzyme defect in the domestic cat and other felidae: phylogenetic timing and the role of hypercarnivory.** *PLoS One* 2011; 6: e18046.

73 Kampf G, Grotheer D and Steinmann J. **Efficacy of three ethanol-based hand rubs against feline calicivirus, a surrogate virus for norovirus.** *J Hosp Infect* 2005; 60: 144–149.

74 Lai P, Coulson C, Pothier DD, et al. **Chlorhexidine ototoxicity in ear surgery, part 1: review of the literature.** *J Otolaryngol Head Neck Surg* 2011; 40: 437–440.