

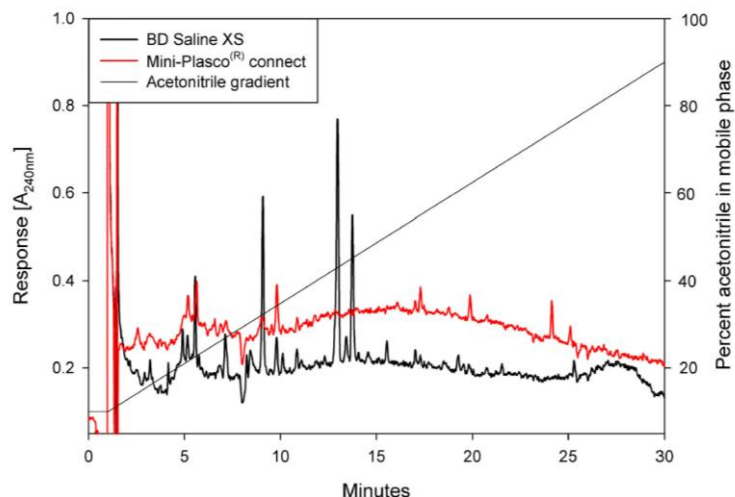
Leaching effects caused by high temperature steam sterilisation of prefilled plastic syringes.

Introduction

Many chemical additives that give plastic products their desirable performance properties also have environmental and human health effects. People are exposed to these chemicals by using products manufactured and stored in plastic packages. Chemical compounds migrate from the plastic packaging into the products stored in the containers. The phenomenon of substance leaching from plastic containers into food products and solutions is well known and has been extensively studied. Since the first reports of leaching from plastic containers, several compounds have been banned for use as plasticizers in plastic packaging containers. Among the factors affecting leaching are: the chemical structure of the compound being leached, the nature of the packaged product, the processing and storage temperature of the finished products. The leaching effect is significantly more pronounced when plastic containers are heated. Everyone is familiar with the warnings about exposing food and solutions in plastic containers to high temperatures, most notably at home in our microwave ovens. We are warned that high temperatures cause leaching and extraction of undesirable compounds from the plastic containers into the food in the container. In the world of healthcare products, solutions are stored in plastic containers and are exposed to high temperatures in order to sterilise the solutions. Examples of this situation are intravenous solution bags. In the past, these bags contained a plasticizer known as DEHP. High temperature steam sterilisation causes this compound to leach into the solution. Since this compound is suspected to be carcinogenic, it has been banned from use by government regulators. Prefilled syringes are another example of a healthcare product that contains a solution and depending upon the manufacturer of the product, could be processed by high temperature steam sterilisation.

What are the effects of exposing prefilled plastic syringes to high temperature steam during the steam sterilisation process?

High temperature steam sterilisation exposes syringes to temperatures of 121°C for prolonged periods of time in order to sterilise the solution in the syringe. The solution reaches or surpasses the boiling point and as a result, undesirable chemical compounds are extracted from the plastic syringe and rubber piston into the solution. There are other unwanted effects as well, such as swelling of the rubber piston, effectively locking or sticking the piston onto the syringe barrel (piston lock effect). One class of leachable compounds known to have undesirable effects are referred to as Volatile Organic Compounds (VOC's).



Results of analysis of saline from BD Saline XS syringe. The identification and concentrations of the VOC's are as follows: 2-methyl-2-propanol (8,500 ppb), 2-methyl-2-butanol (700 ppb), ethyl-butyl ether (400 ppb).

Laboratory test results have revealed that dissolved VOC's such as ethers in the saline solution of some brands of saline flush syringes can be up to 400% higher than syringes that are sterilised using lower temperature sterilisation methods. Ether compounds are known to cause unpleasant taste and odours as well as nausea and vomiting in some patients (inhaled anesthetics are ethers that have this same undesirable effect). This information seems to be supported by two publications that report undesirable secondary effects including nausea and vomiting in as many as 75% of all patients who have their catheters flushed with some brands of prefilled saline syringes.

Experience of unpleasant sensations in the mouth after injection of saline from prefilled syringes

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Abstract

Background: Nurses at The Norwegian Radium Hospital have reported that some patients notice an unpleasant smell or taste in accordance with flushing of intravenous lines with commercially available prefilled syringes. We have conducted a study in healthy volunteers to investigate the occurrence, consistency and intensity of this phenomenon.

Taste and/or Odour Disturbances in Pediatric Patients Undergoing IV Flush with Normal Saline Administered by Prefilled Syringe

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ABSTRACT

Background: At the Children's Hospital of Eastern Ontario, more than 6000 inpatients per year undergo IV saline flushes by prefilled syringe to assess and maintain patency of IV tubing. In studies involving adults, it has been reported that volatile substances may leach from syringe materials into the saline, leading to taste and/or odour disturbances.

Objective: To determine the incidence of taste and/or odour disturbances in pediatric patients after flushing of IV tubing with 0.9% sodium chloride (normal saline [NS]) from prefilled syringes.

Methods: Inpatients aged 5–18 years who had undergone routine flushing of central or peripheral IV tubing with commercially available prefilled NS syringes were interviewed. Children aged 5–10 years used a visual hedonic scale to rate taste and odour sensations, and those aged 11–18 years used a numeric rating scale.

Results: During the study period (April to July 2011), a total of 104 pediatric inpatients (21 aged 5–10 years and 83 aged 11–18 years) underwent NS flushing of central (10 patients [10%]) or peripheral (94 patients [90%]) tubing. For 100 of these patients, BD Posiflush NaCl 0.9% 10-mL sterile prefilled syringes were used, and for 4 patients BD Saline XS NaCl 0.9% 10-mL sterile prefilled syringes were used. Taste and/or odour disturbances were reported by 76 (73%) of the patients. Twelve patients described more than one taste or odour sensation. Taste and odour disturbances were detected by children in both age groups.

Conclusions: Flushing of IV tubing with prefilled NS syringes resulted in taste and/or odour disturbances in a pediatric population.

Key words: taste and odour disturbances, administration of IV saline flush, prefilled syringes

RÉSUMÉ

Contexte : Au Centre hospitalier pour enfants de l'est de l'Ontario, on procède chez plus de 6 000 patients hospitalisés par année au rinçage de leur tubulure i.v. au moyen de seringues préremplies d'une solution de chlorure de sodium à 0,9 % (solution physiologique salée [SP]) afin d'évaluer et de maintenir la perméabilité des tubulures. Lors d'études chez des patients adultes, on a signalé que des substances volatiles pourraient s'échapper du matériel composant la seringue et passer dans la SP, entraînant des altérations du goût ou de l'odorat.

Objectif : Déterminer l'incidence des épisodes d'altération du goût ou de l'odorat chez des enfants hospitalisés dont la tubulure i.v. a été rincée à l'aide d'une seringue préremplie de SP.

Méthodes : Des patients hospitalisés âgés de 5 à 18 ans chez qui on a procédé au rinçage habituel de leur tubulure i.v. périphérique ou centrale à l'aide de seringues commerciales préremplies de SP ont été interrogés. Les enfants âgés de 5 à 10 ans ont utilisé une échelle visuelle hédonique pour évaluer les sensations gustatives et olfactives et ceux âgés de 11 à 18 ans ont utilisé une échelle d'évaluation numérique.

Résultats : Au cours de la période de l'étude (avril à juillet 2011), on a procédé chez 104 enfants hospitalisés (21 âgés de 5 à 10 ans et 83 âgés de 11 à 18 ans) au moyen des seringues de SP au rinçage de leur tubulure centrale (10 patients [10 %]) ou périphérique (94 patients [90 %]). On a utilisé chez 100 de ces patients une seringue préremplie stérile BD Posiflush de 10 mL et chez quatre patients, une seringue préremplie stérile BD Saline XS de 10 mL. Des altérations du goût ou de l'odorat ont été signalées par 76 (73 %) patients. Douze patients ont décrit plus d'une sensation gustative ou olfactive. Des altérations du goût ou de l'odorat ont été notées dans les deux groupes d'âge.

Conclusions : Le rinçage de la tubulure i.v. au moyen de seringues préremplies de SP a entraîné des altérations du goût ou de l'odorat dans cette population d'enfants hospitalisés.

These ether compounds as well as other VOC's are thought to be leached and/or extracted from the syringe barrel and gasket during the high temperature steam sterilisation process used by most prefilled syringe manufacturers to sterilize their prefilled syringes. VOC's can vary significantly from one brand to another. For example one brand of saline flush syringe was found to contain VOC's at levels 400% higher than brands that are sterilised using a low temperature process such as gamma irradiation.

Product : **Sodium Chloride 0.9 % (Saline)**
 Lot # 11197
 Code/Ref : 3705C (salin medxl)
 Description: Liquide incolore, pas de particule étrangère. : Conforms.

#	TEST	METHOD	SPECIFICATION	RESULT
1	Limit of 2-methyl-2- propanol	M-RES-01	To report	936 ppb
2	Limit of 2-methyl-2-butanol	M-RES-01	To report	Not detected
3	Limit of ethyl-buthyl-ether	M-RES-01	To report	37 ppb

Product : **Sodium Chloride 0.9 % (Saline)**
 Lot # 3185189
 Code/Ref : 306572 (salin BD)
 Description: Liquide incolore, pas de particule étrangère. : Conforms.

#	TEST	METHOD	SPECIFICATION	RESULT
1	Limit of 2-methyl-2- propanol	M-RES-01	To report	1000 ppb
2	Limit of 2-methyl-2-butanol	M-RES-01	To report	Not detected
3	Limit of ethyl-buthyl-ether	M-RES-01	To report	164 ppb

Results of VOC analysis of saline from 2 different brands of saline syringes. Ether concentration in the BD brand saline solution is more than 4 times higher.

Although VOC's have been discovered in one particular brand of saline flush syringe, It is suspected that most if not all syringes that are high temperature steam sterilised result in leaching and extracting of VOC's at higher levels than those that are sterilised using lower temperature sterilisation methods. Manufacturers who sterilise their syringes by the steam sterilisation process claim there are no side effects other than transient odours and taste that lasts only a very short period of time.

In case of extreme plunger resistance, it is recommended that excessive force is not exerted.


Some patients may experience a transitory taste or odour during flushing. This minor effect ceases shortly after the procedure is completed.

8. After use, dispose of in accordance with recognised procedure in your institution. (Fig. 6)

DO NOT RE-USE.

■ See package insert for additional information.

Recommendation: A slower administration rate is recommended to minimize a possible unpleasant taste some patients may experience.



Terminally Sterilized
Latex Free, Preservative Free
Lot: 3116677

However the long term effects of repeated exposure to high levels of VOC's are unknown. The effects of exposure to these compounds in patients having long term vascular access devices that are flushed with saline on a regular basis and over long periods of time (Hemodialysis, Oncology and TPN patients for example) are unknown. The other concern is the effect of VOC's on pediatric patients. A recent publication from a pediatric hospital has reported very high adverse incident rates. Reports include the sensation of bad taste and smell, reports of stale, metallic, plastic and sweet tastes as well as reports of nausea and vomiting in compromised patients. The long term exposure effects in these patients are unpronounced known.

Conclusion

All plastic container and closure systems will leach chemical compounds to some extent. But some types of plastics might leach more and some types of sterilisation methods are particularly more effective at leaching higher amounts of compounds into the solution. Steam sterilisation appears to produce higher levels of VOC's. The results being adverse effects to patients during use. Leaching is a phenomenom that affects all syringes that are processed by higher temperature steam sterilisation.

When selecting which Brand to use in your institution, select a brand that has been sterilized using a low temperature sterilisation process such as gamma irradiation. Low temperature gamma irradiation sterilisation process release fewer leachables. Perform a taste test to compare various brands and select the brand that most resembles the taste of a saline solution and not a solution that has a taste like plastic or metal.



- | | |
|---|---|
| <ul style="list-style-type: none"> • <u>Low temperature sterilization</u>
(Gamma Irradiation) • <u>Terminal sterilization</u> • <u>Sterile field compatible</u> • <u>No transitory taste or odor during flushing</u> • <u>No lock effect. Easy glide piston.</u> | <ul style="list-style-type: none"> • <u>High temperature sterilization</u>
(Autoclave steam sterilisation) • <u>Terminal sterilization</u> • <u>Sterile field compatible</u> • <u>Transitory taste or odor and nausea during flushing</u> • <u>Piston Lock effect.</u> |
|---|---|



Frequently asked questions (FAQ's)

What is High temperature sterilisation?

High temperature sterilisation, also referred to as steam sterilisation is the process of exposing equipment and other objects (including prefilled syringes) to extremely high temperatures in the range of 121°C for at least 15 minutes in a device referred to as an autoclave, in order to inactivate organisms such as bacteria, viruses, fungi and spores. High temperature sterilisation is a very effective method to sterilize products.
(https://en.wikipedia.org/wiki/Steam_sterilizer)

How can you identify a product that has been high temperature steam sterilized?

You can identify steam sterilized product by the following information contained in a square box on the label: STERILE: (with a thermometer graphic next to the word STERILE)

ISO15223 and EN980 are the industry standards that define how to identify a product that is steam sterilized (<http://www.cetest.nl/medical-symbols-font.htm>)



What happens to plastics when they are exposed to very high temperatures?

Except in very rare cases, most if not all plastics will undergo changes when exposed to high temperatures.

The most extreme effects caused by steam sterilisation occur in “Heat Labile” plastics and include melting, degradation and destruction of the plastic. A lesser known, but well understood effect of exposure of plastics to high temperatures is a phenomenon called leaching. Leaching is the effect of extracting chemical compounds from a container and closure into the solution. The effect can occur at any temperature but high temperatures will have a very pronounced effect.

<https://en.wikipedia.org/wiki/Leaching>

[https://en.wikipedia.org/wiki/Extraction_\(chemistry\)](https://en.wikipedia.org/wiki/Extraction_(chemistry))

<http://www.fda.gov/downloads/Drugs/Guidances/ucm070551.pdf>

What happens when prefilled plastic syringes are sterilized by high temperature steam?

The extreme temperature of the solution in the syringe, will extract chemical compounds from the plastic syringe container and the rubber piston into the solution contained in the syringe.

How can I tell if there are extracted chemical compounds in the prefilled syringes that I am using at my institution?

Your tongue and nose (taste and smell) are sophisticated and sensitive detection instruments. When it comes to prefilled saline syringes, the test is very simple. Take the “taste test”. Remove the cap from a prefilled saline syringe that you are currently using in your facility and squirt some of the solution into your mouth. Ideally, compare the solution to other brands, specifically to a brand that has been sterilised by a low temperature sterilisation process. Draw your own conclusions based on your taste and smell sensations.

<https://en.wikipedia.org/wiki/Taste>

<https://en.wikipedia.org/wiki/Olfaction>

<http://www.brainfacts.org/sensing-thinking-behaving/senses-and-perception/articles/2012/taste-and-smell/>

What type of chemical substances can be leached into the solution?

Volatile Organic Compounds as well as other compounds such as plasticizers, antioxidants, lubricants, silicones, plastics, rubber compounds, plastic monomers etc...

https://en.wikipedia.org/wiki/Volatile_organic_compound

What is the effect on patients when the solutions in the syringe contains VOC's and the solution is administered to a patient?

The immediate effects are well documented and published in scientific studies. They appear to vary on a patient by patient basis and can be as innocuous as the perception of a specific taste or smell or as serious as nausea and vomiting. The serious effects appear to be more commonly reported in compromised patients undergoing chemotherapy. Not all the effects, especially the effects of long term exposure in very sick patients or in small patients are fully known

Is there a sterilization process that creates less Volatile Organic Compounds in the solution?

Yes. Products that are sterilized at lower temperatures will produce less VOC's and less leachables in the solution by the simple fact that the solutions are not exposed to higher temperatures during sterilisation.

How can you identify a product that has been low temperature gamma irradiated?

You can identify gamma irradiated product by the following information contained in a square box on the label: STERILE: (with the letter "R" next to the word STERILE)

