Epidemics and e-cigarette epidemic

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Abstract

The electronic cigarettes use is growing rapidly. There is great controversy about their safety and their potential role in reducing the risk of smoking and eventually in quitting. But they constitute a reminder that bacteria and viruses are destroyed by propylene glycol vapor, as well as virus development is inhibited by the elevation of the temperature of the inhaled air. These effects, once demonstrated by very serious studies, are somewhat forgotten. The emergence of the electronic cigarette may open new perspectives for research in the prevention of bacterial and viral epidemics

Key-words:
Electronic cigarette – Propylene glycol – Viral Epidemics – Virus - Bacteria.

Résumé

L'usage des cigarettes électroniques se répand très rapidement. Le débat est vif concernant leur inocuité et leur rôle potentiel pour réduire le risqué à fumer voire à abandoner le tabac. Mais elles constituent un rappel de ce que les vapeurs de propylène glycol détruisent bactéries et virus et ce ce que l'élévation de la température de l'air inhalé s'oppose au développement des virus. Ces effets, naguère solidement démontrés, sont quelque peu oubliés. L'apparition de la cigarette électronique peut ouvrir de nouvelles perspectives de recherches dans la prévention des épidémies bactériennes et virales.

Mots-clés:
Cigarette électronique – Propylène glycol – Épidémies – Virus – Bactéries.

Introduction

Since the numerous catastrophic outbreaks of plague, tobacco smoke has got a reputation for protecting against infections. A thesis of medicine cites the work of the Dutch physician Pr Diemerbroek, who reports that during a London epidemic the houses where tobacco was manufactured and sold were spared. He also escaped during the 1645 epidemic at Nijmegen, and became a strong supporter of the protective effect of tobacco smoke but, challenging himself, he admitted that Dutch tobacconists were not then specially protected. This reputation has been long living, so that the doctors who cared for the sick and wounded soldiers of Napoleon's wars in the pestilential atmosphere of the Pitié- Salpêtrière Hospital in Paris were smoking to protect themselves from contagion from all miasmas, as confirmed by Arvers, who started smoking for that reason [1].

When appeared the first electronic cigarettes, I thought they would be an ephemeral gadget, of which the only interest was to defy with impunity the restrictions on smoking in public places. Certainly their mere handling, issuing a pseudo-smoke and some oro-pharyngeal sensations (hit) are giving the *vaper** the behavioral illusion of smoking a real cigarette. The majority of e-cigarettes also deliver nicotine. Smokers recognize it and appreciate a cortical arousal, contrasting with a feeling of muscular relaxation from nicotine stimulation of the spinal Renshaw neuron [2], and a well-being, in relation to a rapid rise of

blood sugar, which might explain for some ones the precocity of their first cigarette in the morning. These are pharmacological properties, but there are strong reasons to believe that they do not summarize the powerful addiction to tobacco, as evidenced by the low success rate of nicotine replacement therapy (NRT) compared to placebo, and its relatively modest commercial success, contrasting with very active promotion campaigns and, in some countries such as France, its financial support by the Social Security Insurance [3].

Very serious prognosis error! E-cigarette market is developing quasi exponentially. From 5 millions $ en 2007, sales increased to 250 millions en 2011 to 500 millions en 2012, and are expected to get to one billion $ en 2013 [4]. This figure is difficult to evaluate in France, where 500,000 consumers might use it regularly [5]. Thus the e-cigarette is still and should remain a gadget. But as many vapers are vaping for fun, others use it as a tool to smoke less, and even to quit. It justifies a scientific and epidemiologic approach, regarding its toxicity and potential effects.

Everything is done to simulate a tobacco cigarette smoking. The shape of e-cigarettes often completely mimics it, but some resembles cigars, even pipes, as others have specific designs. As the vaper aspires, the resulting depression lightens a LED at the end of the e-cigarette and connects a battery to a resistor (atomizer) that heats at about 60°C a liquid that contains about 92% of highly hygroscopic molecules such as propylene glycol or glycerol, or a mixture of both. The rest is water, often 0.9% lactic acid (as a preservative?) and various flavorings, usually authorized in food. The heated air vaporizes all, and inhalation drives it with the other components of the liquid into the airways and lungs, where it gets full water vapor saturation in a humid atmosphere at 37° C. The exhaled air comes into contact with the usually cooler outside atmosphere, of which the saturation point of water vapor is lower. The excess vapor condenses in a visible cloud, giving the illusion of smoke. At each level of air humidity and temperature corresponds a critical point where such condensation occurs. This mist is more important if the outside temperature is lower. It dissipates quickly if the air is not saturated with water vapor.

Propylene glycol

One of the properties of propylene glycol (PG), which is the essential component of the liquid [6], is very interesting from an epidemiological point of view. In wartime, inexpensive protection of armies against epidemics was an essential aim, as well from airborne infections in barracks, as possibly from bacteriological weapons. The powerful antibacterial, antifungal and antiviral effect of PG aerosols was a stimulating approach. PG vapor is very active for the disinfection of air, by entering the germs carried by airborne droplets of Pflügge and perturbing their enzymatic equipment. This effect has been experimentally demonstrated in closed chambers, and the optimal conditions for this action have been defined [7, 8]. *"Under the experimental conditions employed, numerous kinds of bacteria, including pneumococci, hemolytic streptococci, staphylococci, H.influenzae, etc., as well of influenza virus, when sprayed into atmospheres containing such vapors, were killed so rapidly that no microorganisms or virus could be recovered from the test chamber"*. Test chambers were 10 feet square and 8 feet high. Droplets of bacterial cultures were atomized into them. PG vapors were obtained by heating between 70 and 80°C by a resistor device very similar to the one used in e-cigarettes. Mice were protected from pneumococcal infection. Rapid and complete sterilization occurs for vapor concentrations of 1g in 2 to 4 m^3 of air. Pneumococci and hemolytic streptococci were killed when PG concentrations as low as 1 g to 50m^3 of air were employed. (Figure 1 and 2)

Figure 1

Inoculation of Mice with Pneumococcus Type I Exposed to Propylene Glycol Vapor

(from Robertson et all.[6])

	Material introduced into chamber	Air samples		N° of pneumococcus colonies		Mice inoculated with 1cc of fluid from bead tower
		Time taken	Method of culture	On plate	In fluid from bead tower	
Test chamber	Propylene glycol vapour. 1/3,000,000 followed by pneumococcus spray	Immediatly after bacterial spray 10 mn later 30 mn later	Plate Bead tower Plate	0 0	0	10 mice. All remained well
Control chamber	Pneumococcus spray	Immediatly after bacterial spray 10 mn later 30 mn later	Plate Bead tower Plate	1128 484	1cc=228 Total=5700*	10 mice. All died from pneumococcus infection in 24 to 34 hrs

* The 2 liter air sample was drawn through 25cc of 50 per cent broth-water mixture

Figure 2

Relationship between Number of Bacteria Suspended in Air and the Effectiveness of Different Glycol Concentrations Employing Staphylococcus albus as the Test Microorganisms

(Total number of droplets of culture inoculum kept constant. Temperature 27-30°C. Relative humidity about 50 per cent) *(from Puck et all, [7])*

Amount of propylene glycol introduced: mg. glycol per liter of air	Calculated glycol concentration in chamber air	No. of bacteria on "immediate" control plate	Per cent reduction in No. of bacteria in glycol chamber* relative to control		
			Immediately (15 sec. after bacterial spray	5 min. later	15 min. later
0.66	Greater than saturation	4,000,13,000	per cent 99.3	per cent 100	per cent 100
0.4-0.45	Saturation (about) 1:2,500,000	500-6,000	96.7	99.8	100
0.32	Slightly below saturation 1:3,000,000	400-1,400 6,000	83.6 84.4	99.8 86	99.6 100
0.25-0.27	Unsaturated	73-199 450-1,300	72.7 11.6	99.0 36.2	97.8 85.7
0.16	1:6,000,000	36-122	0	0	0

* The percentages are based on comparison with the numbers of bacteria in samples taken simultaneously from control chambers; *i.e.,* Per cent reduction = (No. of bacteria from control chamber – No. of bacteria from glycol chamber) / No. of bacteria from control chamber

Glycerol has a 100 times much lower vapor pressure than propylene glycol. Its aerosol exhibited only a slight killing effect. PG antifungal effect has also been demonstrated [9]. Vapor is more active than the same amount of PG in aerosol. Paradoxically, germs grow well in broth containing 5 to 15% PG, retaining their vitality and virulence.

PG has fallen into disuse as an air-disinfectant, mainly because it was difficult to get sufficient concentrations in the ambient air of open premises. More, the advent of antibiotics, driven by industrial interests, made less crucial its development. Despite these obstacles, this application is still recognized to disinfect surfaces or indoors, and in solutions for hands disinfection, in combination with ethanol.

Temperature

Smoke from tobacco gets warm into mouth, sometimes burning as from pipe. When inhaled, the puff is often mixed with a part of cooler air. The temperature of the inhaled air may be of interest, because it interacts with the development of germs and virus.

According to the researches of the Nobel Prize A. Lwoff on viruses, an apparatus has been developed by joint teams of Pasteur and Weismann Institutes (*Rhinotherm*®). It allows inhaling through the nostrils humidified and heated air that increases the temperature of the nasal mucosa to 43°C, which may inhibit virus development. It was tested on 900 patients *vs* a placebo device. Three 30 min. sessions at 2-3 hours interval were enough to cure 72% of infective coryza *vs* 18% in the placebo groups [10]. (Figure 3)

Figure 3

Patients with infectious coryza treated with hyperthermia

from Yesushami A and Lwoff A [9]

			Post 1 day		Post 1 week	
			Cured	Not cured	Cured	Not cured
Group 1	Treated	23	17(74%)	6(26%)	16(70%)	7(30%)
	Placebo	18	4(22%)	14(78%)	4(22%)	14(78%)
Group 2	Treated	23	18(78%	5(22%)	18(78%)	5(22%)
	Placebo	2	0	2	0	2
Group 3	Treated	48	34(70%)	14(30%)	34(70%)	14(30%)
	Placebo	37	8(22%)	29(78%)	8(22%)	29(78%)
Total	Treated	94	69(73%)	25(27%)	68(72%)	26(28%)
	Placebo	57	12(18%)	45(82%)	12(18%)	45(82%)

A prolonged beneficial effect on persistent allergic rhinitis was also observed. Unfortunately, this apparatus did not success commercially as expected, perhaps because he weighed 3.5 kg and cost around $ 350.

Electronic cigarette

E-cigarette combines the propylene glycol and thermal effects. It might be much more efficient than PG aerosols, even sprayed in closed venues, because it leads concentrated vapor directly into the respiratory tract. More, its temperature might be close to the 43°C humid air delivered by the *Rhinotherm*® device. Lactic acid might participate to the antibacterial effect,

but also to the "*hit*", an irritation of the throat that vapers appreciate. However, its very low pH greatly limits nicotine diffusion and absorption.

Controversies

Everything about tobacco smoking causes violent ideological and financial controversies. Most vapers use e-cigarette to diminish or stop smoking. Thus e-cigarette becomes a concurrent for the tobacco industry. But these firms realize that smokers trying to stop are a tremendous market. As a consequence, about all the big tobacco companies, *Imperial Tobacco, Philip Morris, BAT, Altadis*, begin to manufacture e-cigarettes, or did buy existing brands. It would be a good thing for health. But e-cigarette is also competing with nicotine medications. Here, the battle is fierce. After a period where each one was tinkering with his secret formula, composition of e-cigarettes should be declared and controlled, as for any product. Propylene glycol has nothing to do with the very toxic ethylene glycol. However, some samples of PG available on the market might contain toxic impurities. Merchants themselves realize that, for credibility reasons, they have to strictly control the purity of their supplies. Pharmaceutical lobbies are asking for interdiction of e-cigarettes, arguing that their total safety has not been demonstrated. Manufacturers of electronic cigarettes do not agree with this. In fact, propylene glycol is considered as safe, widely used as a food additive and in medicines and cosmetics [11], No toxicity of it has been demonstrated, even by long term inhalation [12]. But already a proposal of the European Commission for a Directive on tobacco products wants to limit nicotine content of all products at the level of patches and gums [13]. But their attitude is ambiguous, because they clearly are also interested in taking control over e-cigarettes, and even perhaps selling them. This is the reason why they would like that they were classified as drugs for smoking cessation and therefore undergo strict pharmaceutical controls. E-cigarettes makers consider that the proposal of the European Commission is flawed, especially with regard to the limitation of the nicotine content, for the sole purpose of limiting the spread of e-cigarettes.

Discussion

One may question the antibacterial effect of tobacco smoke, although the combustion produces compounds like formaldehyde. It is more likely that the idea was carried out by the symbolic purification by fire, and helped to tolerate stinking hospital wards.

E-cigarettes deliver PG vapors in a warm humidified air. There is a growing tendency to use glycerol to produce steam, for irrational fear of PG. But, as far as antibacterial and antiviral action is concerned, only PG seems efficient. Most e-liquids contain 0.9% lactic acid, probably as a preservative to prevent propylene glycol degradation of. The result is a very high acidity, which can irritate the throat. It is present in e-cigarettes that do not contain nicotine and are available on the market. This low pH may also lower spreading and absorption of nicotine, which does not have any interest regarding the disinfectant effect, and participate with it to the "hit" sensation. Others components such as aromas are not necessary but, even if some adverse effects were demonstrated on long term use, it would concern the regular vapers only.

Adding PG vapors to increased temperature, E-cigarettes might be more efficient than the Pasteur Institute device. More, they are light and easily available everywhere. Some are disposable and not very expensive, which is an advantage for the short time necessary to cure a common cold. But they lead the puff into the mouth, whose temperature is 37°C. From a

small questionnaire I put on a vaper's forum, I got 88 answers. Subjectively, 53 regarded the temperature of the vapor as tepid, 21 as warm, 2 as hot. But, at another question, 9 inhaled it directly into the lungs, as users of narghileh do, but 68 reported they were vaping the same way as they smoke or had been smoking, by mixing the puff with external air. Such a behavior would annihilate the increase of temperature, making this item inefficient in the usual e-cigarette use.

According to Lwoff, the temperature of nasal mucosa lies between 31 to 36°C, which favors viral replication. To get the best effect, e-cigarettes vapors should thus be inhaled through the nose. More, this way leads the puff directly to le trachea and the lung. This does not represent a real problem. However, his device increases the temperature to 43°C at 2.5 cm inside the nostrils. This limit prevents burning of the nasal mucosa. In a hammam atmosphere, saturated with water vapor, the temperature can reach 50°C without causing lesions. However, there is a potential risk of burning with e-cigarette, especially when used with low resistance atomizers, which can reach 100°C. Vapers should be warned about it.

Antibacterial and antiviral actions of propylene glycol and of the temperature increase, as they are grouped in a system such as electronic cigarette deserve scientific evaluation. However, the conventional randomized controlled trials are complex, expensive, and difficult to apply to groups of healthy subjects without personal clinical benefit. On the other hand, vapers groups are very reactive on the web. An on-line study on 1347 subjects could describe their behavioral profile after few months only [14]. Rather than traditional trials, it would probably be more effective, if vapers were aware of this possibility, that they assess themselves the effects of their e-cigarette on the frequency and duration of their seasonal colds.

*To vape, vaping, vaper are neologisms that are now well established concerning the use of electronic cigarettes.

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Conflicts of interest

I declare that I have no links of interest, neither with the pharmaceutical or tobacco industries, nor with the fabricants and traders of electronic cigarettes.

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Legends

Figure 1.- Mice exposed to Pneumococcus cultures spray in two chambers. One of them was filled with propylen glycol vapor

Figure 2.- Antibacterial effect of propylen glycol

Figure 3.- Effect of nasal inhalation of humidified air heated at 43°C on evolution ofinfectious coryza