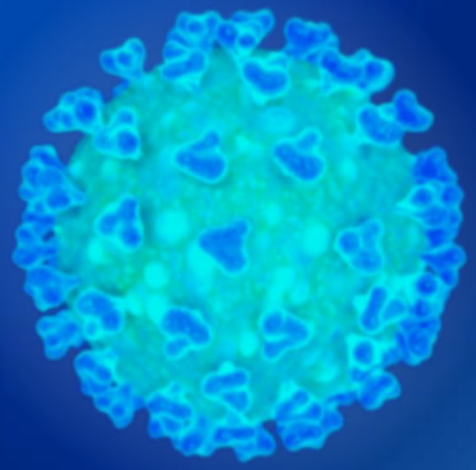
THE IMPORTANCE OF ORAL HYGIENE FOR INFECTION CONTROL WITH PVP-I GARGLE DURING COVID-19 OUTBREAK



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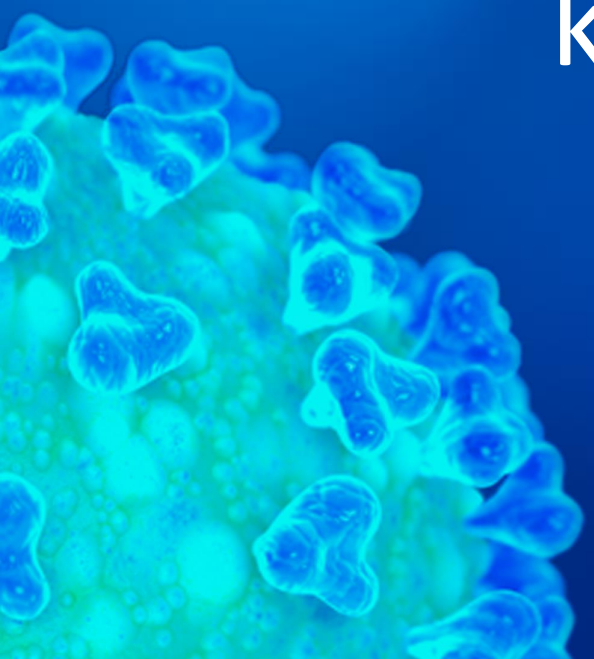
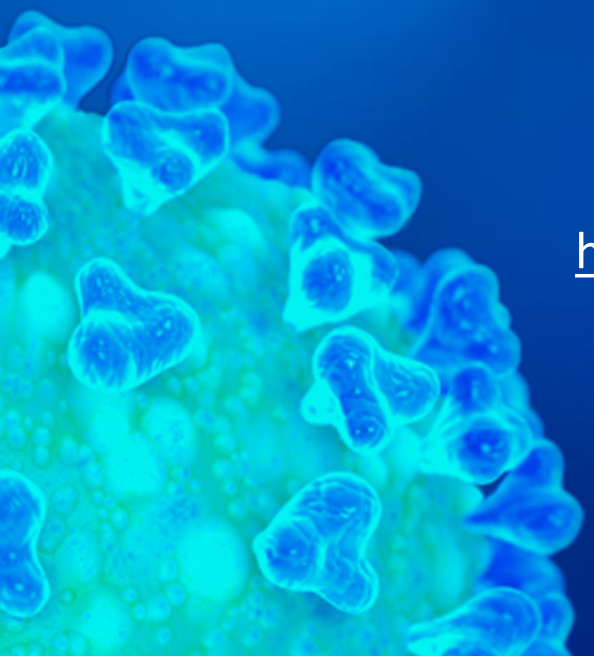
Departemen Ilmu Penyakit Mulut
Universitas Trisakti
SATGAS COVID-19 PB PDGI

Pandemik COVID-19 yang disebabkan karena coronavirus SARS-CoV-2 memberikan dampak luas bagi sistem kesehatan nasional, tidak hanya di Indonesia, tapi dunia





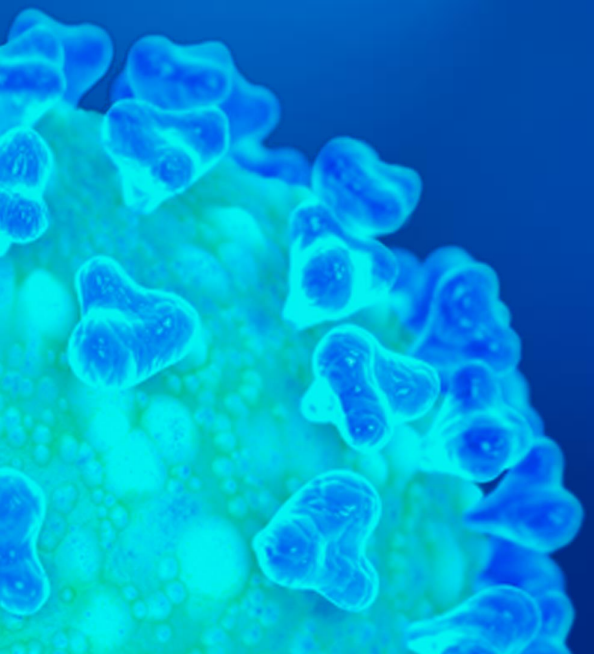
WHO mengeluarkan panduan bagi masyarakat untuk mengurangi paparan dan transmisi penyakit/infeksi melalui *personal hygiene* (kebersihan diri) yaitu kebersihan tangan dan saluran pernafasan serta keamanan pangan

https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public

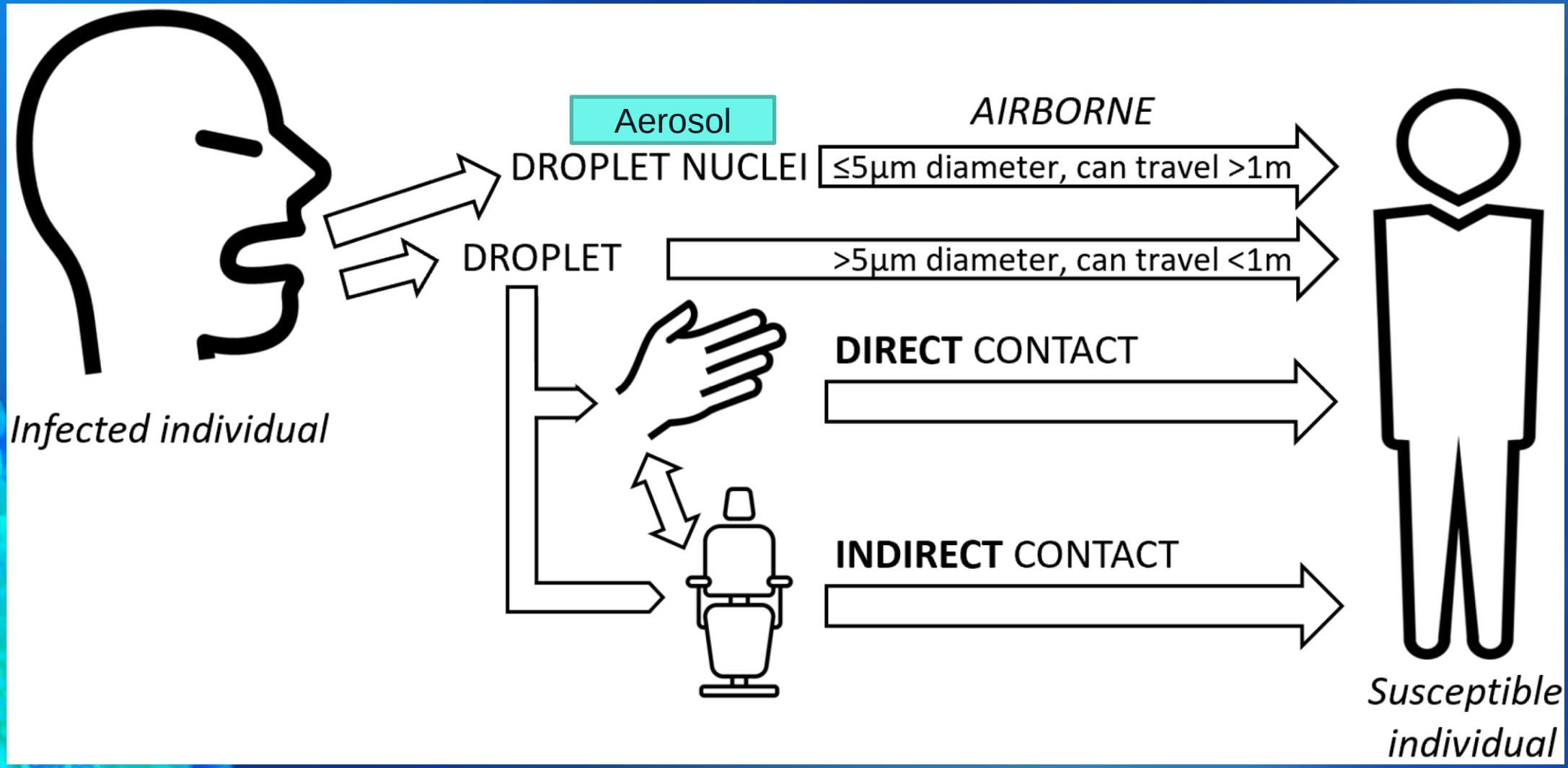
- Data per tanggal 15 Mei 2020 jumlah pasien mencapai 16.496 dan 1076 meninggal
- CFR 6,5%
- Pasien COVID -19 masih tetap menunjukkan peningkatan jumlah

- Laporan Wang dkk (2020), ditemukan 41% pasien mempunyai transmisi nosokomial dan disimpulkan oleh WHO-CDC bahwa penyebaran COVID-19 melalui droplet atau aerosol.

  Saliva mengandung konsentrasi tinggi COVID-19 sebanyak 1,2 x 10^8 kopi/mL (To dkk, 2020).



COVID-19: Transmision



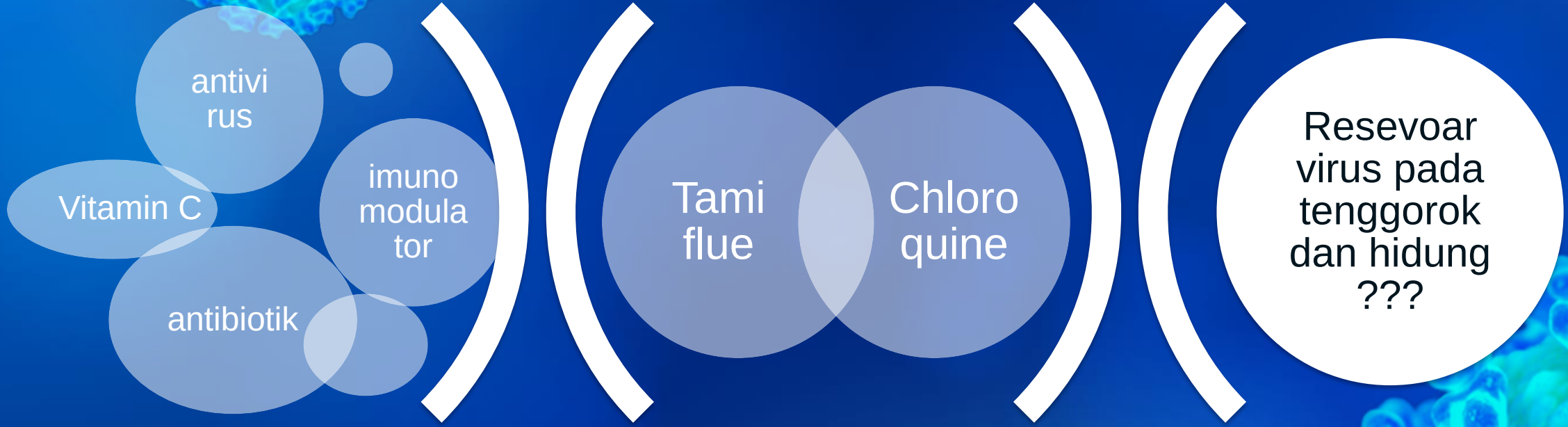
Rationale

Viral load terbanyak di **NASOPHARINK** dan **OROPHARINK** dan menjadi reservoir utama penyebaran droplet atau aerosol.[1]

Jumlah virus pada pasien OTG, OPD, PDP serupa.[1]

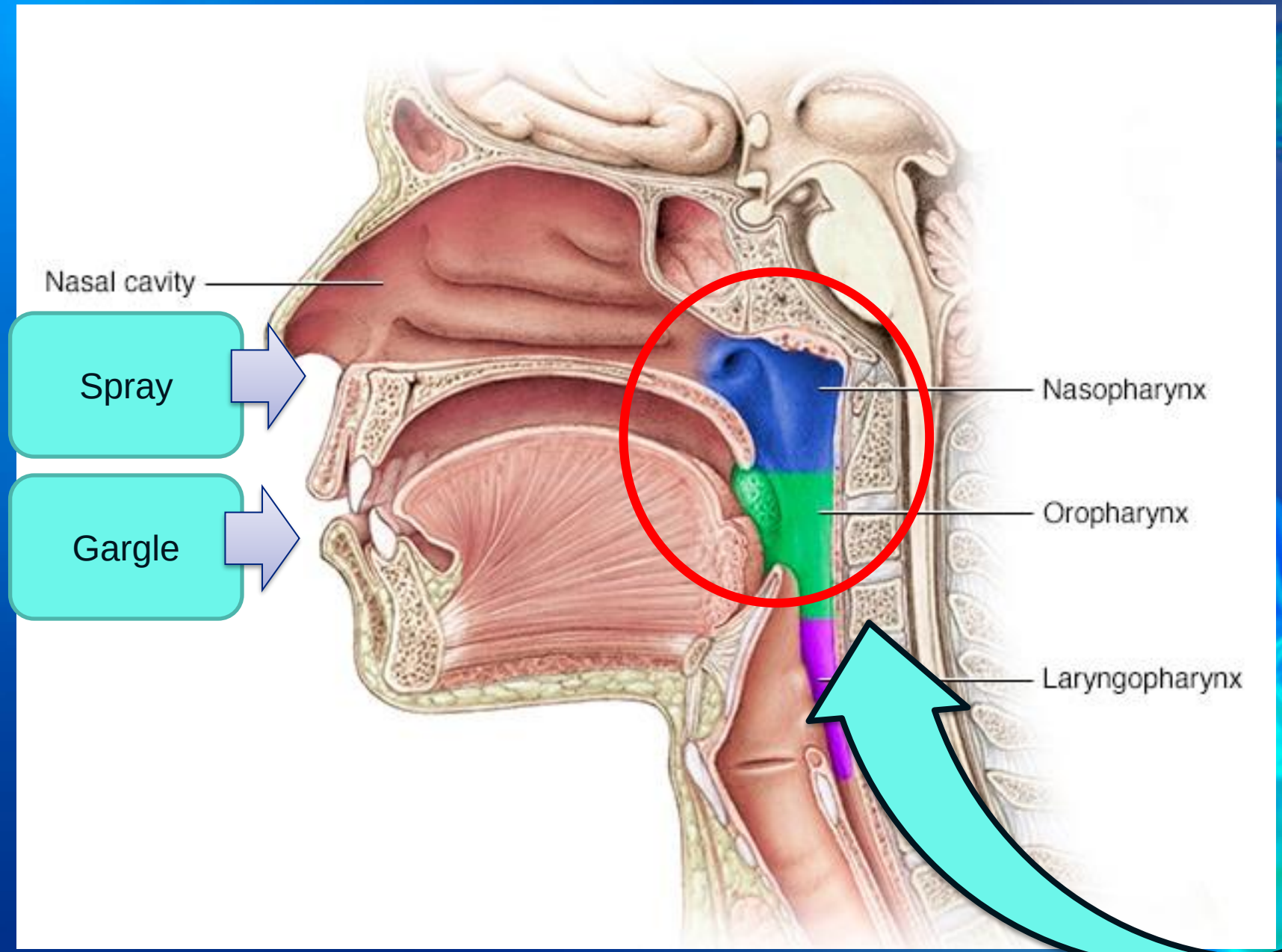
1 Leila JM et al, 2020. Consideration of povidone-iodine as a public health intervention for COVID-19: Utilization as“Personal Protective Equipment” for frontline providers exposed in high-risk head and neck and skull base oncology care. Oral Oncology. https://doi.org/10.1016/j.oraloncology.2020.104724.
2. To KK-W, Tsang OT-Y, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020; 361: 1319.

Rationale



Protap Covid dilakukan secara sistemik

Terlokalisir belum diintervensi


Nasal cavity
Spray
Gargle
Nasopharynx
Oropharynx
Laryngopharynx
Reservoir
Covid-19

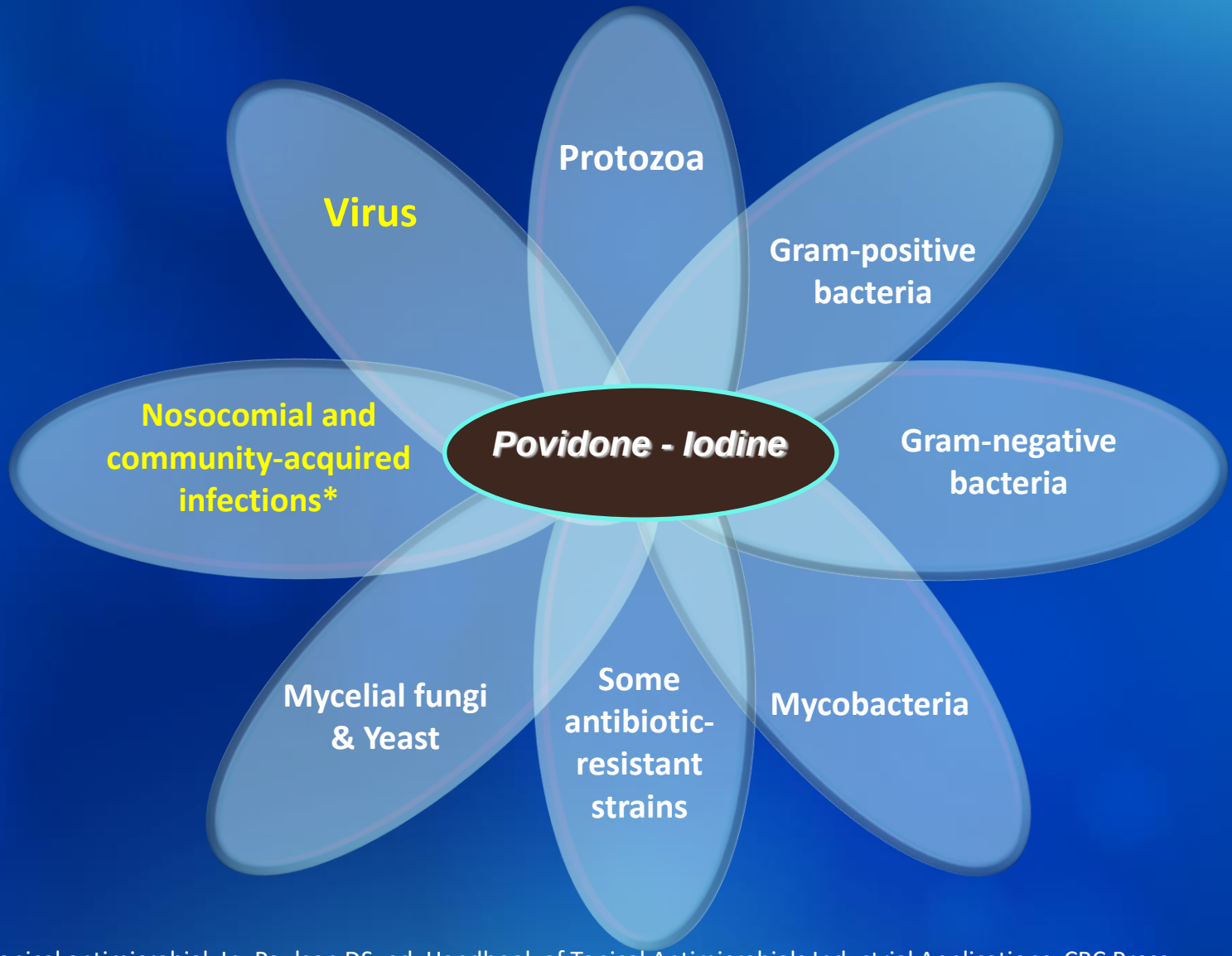
Gargle benefit - evidence based

- Pencegahan infeksi saluran pernapasan atas (ISPA) masih merupakan masalah utama kesehatan masyarakat.[1]
- Gargle air pada orang sehat menghasilkan penurunan 36% insidensi ISPA.[1]
- Gargle dengan air keran, teh hijau atau air fungsional menghasilkan penurunan *odds ratio* munculnya demam pada anak-anak.[2]
- Gargle dianggap sebagai suatu cara yang efektif dan tepat untuk menjaga higiene tenggorok dan mencegah demam pada anak.[2]
- Di Jepang, panduan menganjurkan gargle sebagai salah satu cara pencegahan ketika terjadi pandemi influenza.[1]

Sakai M, et al. BMC Health Serv Res. 2008;8:258. |
Noda T, et al. J Epidemiol. 2012;22(1):45–49.

Dari semua antiseptik rongga mulut yang beredar di pasaran, terdapat obat kumur yang sudah lama beredar (>60 tahun) dengan bahan dasar Povidone-Iodine

Efek *Broad-Spectrum* dari *Povidone - Iodine*



Referensi :

1. Ripa S, Bruno R, Reder R. Clinical applications of povidone-iodine as a topical antimicrobial. In: Paulson DS, ed. Handbook of Topical Antimicrobials Industrial Applications. CRC Press. 2002.
2. Tan E chua I, Muller S. Comparative Testing of Betadine and other commercially Available Antiseptics, Based on Current European Suspension Assay. Presented at: International Wound&Biotherapy Conference; 16-18 October 2015, Malaysia.

PVP-I: Antimikrobisidal spektrum luas

Gram Negative Bacteria[1]

- Acinetobacter sp.
- Aerobacter aerogenes
- Aeromonas sp.
- Bacteroides sp. (oralis)[1,11]
- Burkholderia cepacia
- Campylobacter jejuni
- Chlamydia trachomatis
- Citrobacter sp.
- Edwardsiella sp.
- Enterobacter aerogenes
- Escherichia coli[5]
- Haemophilus sp. (vaginalis)[1,11]
- Gardnerella vaginalis
- Herellea sp.
- Klebsiella pneumoniae
- Moraxella catarrhalis[10]
- Mima polymorpha[11]
- Morganella morganii
- Mycoplasma hominis
- Neisseria gonorrhoeae
- Proteus sp.
- Providencia sp.
- Pseudomonas sp.
- Salmonella sp.
- Serratia sp.
- Shigella sp.
- Ureaplasma urealyticum
- Vibrio sp.

Gram Positive Bacteria[1]

- Bacillus sp.
- Clostridium sp.
- Corynebacterium sp.
- Diphtheroides sp.
- Diplococcus pneumoniae[10]
- Enterococcus sp.
- Lactobacillus acidophilus
- Micrococcus sp.[1] incl. Micrococcus flavus[11]
- Peptostreptococcus
- Sarcina lutea
- Staphylococcus sp. incl. methicillin resistant (MRSA), Staphylococcus aureus, Staphylococcus epidermidis
- Streptococcus sp. incl. Streptococcus pneumoniae, Streptococcus faecalis, Streptococcus pyogenes
- Vancomycin resistant Enterococcus sp.

Mycobacteria[1]

- M. chelonae
- M. fortuitum
- M. tuberculosis

Fungi[1]

- Aspergillus sp.
- Blastomyces dermatitidis
- Candida sp.[1] incl. Candida albicans[5]
- Cladosporium sp.
- Cryptococcus neoformans
- Debaryomyces sp.
- Epidermophyton floccosum
- Microsporum audouinii
- Nocardia sp.
- Piedraia sp.
- Pityrosporum ovale
- Streptomyces sp.
- Torulopsis glabrata
- Trichophyton sp.

Protozoa & Other Organisms[1]

- Chlamydia trachomatis
- Entamoeba histolytica
- Mycoplasma hominis
- Trichomonas vaginalis
- Treponema pallidum

Viruses

- Adenovirus type 5[3]
- Bovine viral diarrhoea[3]
- Coronaviruses incl. MERS-COV[7] and SARS-COV[4]
- Coxsackievirus CA16[8]
- Cytomegalovirus[1]
- Ebola virus[6]
- Enterovirus 71[8]
- Herpes simplex virus type 1[1,2]
- Human Immunodeficiency Virus[1,2]
- Influenza A virus[4]
- Measles virus[2]
- Mumps virus[2]
- Norovirus[9]
- Polyomavirus SV40[3]
- Rabies virus[1]
- Rhinovirus[2]
- Rotavirus[2]
- Rubella virus[1]
- Vaccinia virus[6-7]

Spores[1]

- Spores of Aspergillus sp.
- Spores of Bacillus sp.
- Spores of Clostridium sp.
- Spores of Penicillium sp.

11 References

Perbandingan Aktivitas Beberapa Jenis Antiseptik

Zat Kimia/ Bahan	Bakteri			Virus		Jamur
	Gram +	Gram -	Spora	Lipofilik	Hidrofilik	
Alkohol (Etanol, Isopropanolol)	HS	HS	R	S	V	–
Aldehida (Formaldehida, Glutaraldehida)	S	HS	S	S	MS	S
Klorheksidin glukonat	HS	MS	R	V	R	–
Klorin natrium hipoklorit	HS	HS	S	**S**	**S**	MS
Hexachlorophene	S	R	R	R	R	R
Iodine (Povidone-Iodine)	**HS**	**HS**	**S**	**S**	**S**	**S**
Fenol	HS	HS	R	R	R	–
Oksidator/ hidrogen peroksida	HS	HS	S	V	V	S
Quaternary ammonium (benzalkonium chloride, cetylpyridinium chloride, benzethonium chloride)	HS	HS	R	S	R	

HS: highly susceptible; MS: moderately susceptible; S: susceptible; R: resistant; V; variable; – no data

Miller BF. Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing and Allied Health, 6th ed. Philadelphia, PA: Saunders, 1997.

PVP-I Versus Infeksi Saluran Nafas

- Kanagalingam dkk (2015), PVP-I juga efektif dalam mengurangi keparahan dan mempercepat durasi dari infeksi traktus respiratorius atas seperti *common cold*
- Influenza dan tonsilo-faringitis (Ludwig, 2013)
- PVP-I pada pasien penyakit kritis yang menggunakan ventilator untuk mencegah timbulnya *ventilator associated pneumonia* (Seguin dkk, 2006).

Dermatology

Oro-Buccal Antisepsis

Dermatology 2006;212(suppl 1):119–123
DOI: 10.1159/000089211

Inactivation of SARS Coronavirus by Means of Povidone-Iodine, Physical Conditions and Chemical Reagents

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Key Words
Severe acute respiratory syndrome · Coronavirus · Povidone-iodine · Infection control

Abstract
The efficacy of several povidone-iodine (PVP-I) products, a number of other chemical agents and various physical conditions were evaluated for their ability to inactivate the severe acute respiratory syndrome coronavirus (SARS-CoV). Treatment of SARS-CoV with PVP-I products for 2 min reduced the virus infectivity from 1.17 × 10^6 $TCID_{50}$/ml to below the detectable level. The efficacy

Introduction

Severe acute respiratory syndrome (SARS) was f
reported as an atypical pneumonia in Gangdong, Chi
in November 2002 [1]. The epidemic expanded rapic
to 26 regions and countries [2–4], and by the end of Ju
2003, 8,098 probable cases had been reported and mo
than 774 people had died [5]. Although the epidem
seemed to be controlled during the summer of 2003, lab
oratory-associated infections appeared in Singapore i
September 2003, in Taiwan in December 2003 and i
Beijing in April 2004. At the end of 2003, a new series of
probable SARS cases, which may have been unrelated to

Can oral disinfection with povidone iodine prevent viral respiratory infections?

ASN226

M. Eggers,[1] M. Eickmann,[2] J. Zorn[3]

[1]Labor Prof. Gisela Enders MVZ GbR, Stuttgart, Germany
[2]Institute for Virology, Philipps University of Marburg, Marburg, Germany
[3]Mundipharma Research GmbH & Co. KG, Limburg, Germany

Purpose

Nosocomial infections with respiratory tract viruses, particularly influenza and respiratory syncytial virus (RSV), can cause widespread and intractable outbreaks as the recent outbreaks of RSV in a haematology and transplant unit have shown.[1] Reported emerging and re-emerging viral outbreaks with serious implications on public health and nosocomial infections include Severe Acute Respiratory Syndrome (SARS) or Middle East respiratory syndrome (MERS).

Influenza viruses are spread via airborne dispersion of small particle aerosols. MERS, in contrast, seems to require closer contact, with virus passed on hands, fomites, or in large droplets inoculated into the eyes and nose at close range. SARS has two modes of transmission: aerosols of respiratory droplets and from contaminated surfaces, including direct person-to-person contact.

The virucidal efficacy of antiseptics and disinfectants can be determined using the European Standard EN 14476:2013/A1:2014.[2] Based on these criteria, the antiseptic povidone iodine (PVP-I) has been shown to be effective against the Ebola virus.[3]

The aim of this study was to investigate the *in-vitro* efficacy of four PVP-I formulations against enveloped

	Interfering substance
Clean conditions	0.3 g/L bovine serum albumen (BSA)
Dirty conditions	3.0 g/L BSA + 3.0 mL/L erythrocytes

Table 1. Interfering substances used to simulate clean and dirty conditions

The diluted test mixtures were added to plates containing indicator cells in cell culture medium. The cells were cultivated for the following number of days: influenza, 2; SARS and MERS, 3–5; and MVA, 6–8, then inspected microscopically for virus-induced changes in cell morphology. Virus titre was calculated from these observations using the Poisson formula. The virucidal activity was determined by the difference of the logarithmic titre of the virus control (mock treated cells) minus the logarithmic titre of the test virus ($\Delta \log_{10}$ $TCID_{50}$/ml). To demonstrate virucidal efficacy, disinfectant and antiseptic products are required to produce a log reduction in virus titre of at least 4.[2] As a validity control of the test system, formaldehyde was selected for inactivation of the reference virus.

Results

Figure 2. Virucidal activity of two different PVP-I preparations against SARS after 15 seconds

PVP-I Research Versus SARS

PVP-I efektif terhadap SARS-CoV yang menimbulkan infeksi SARS (Kariwa dkk, 2006),

MERS-CoV (Kirk-Bayley dkk, 2020),

Modified Vaccinia Virus Ankara (MVA) (Eggers dkk, 2015)

The new European test virus for enveloped virus (Eggers dkk, 2015), dan

Avian Influenza (Ito dkk, 2006).

PVP-I Research Versus SARS

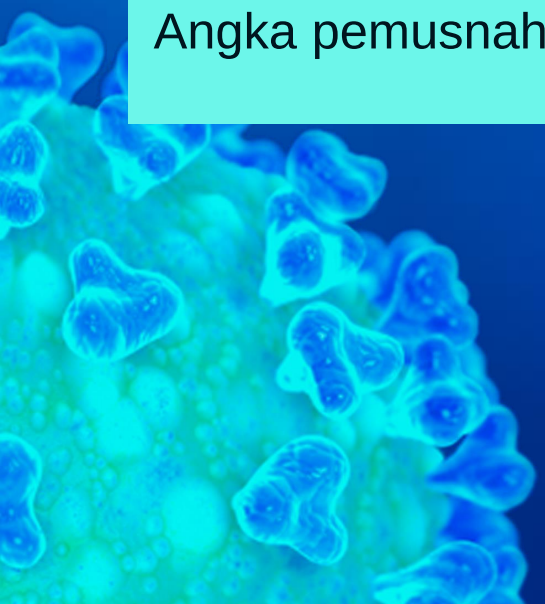
Penggunaan PVP-I 0,23% 0,23% selama 2 menit mampu menekan kuantitas SARS-CoV virus hingga kadar yang tidak terdeteksi lagi.

PVP-I konsentrasi 1% yang digunakan selama 30 detik, mampu menurunkan aktivitas virus MERS-CoV, 99,99%, (Eggers dkk, 2015).

PVP-I mampu menekan TNF-α yang berperan sebagai regulator inflamasi pada banyak penyakit kronik (König dkk, 1997).

Efektivitas PVP-I terhadap SARS-CoV

Aktivitas virusidal dalam 15 detik terhadap SARS-CoV	**PVP-I Gargle & Mouthwash 1%**	**PVP-I Surgical Scrub 7.5%**	**PVP-I Skin Cleanser 4%**
Faktor penurunan $\log_{10}$	> 4	> 4	> 4
Angka pemusnahan	>99.99%	>99.99%	>99.99%



Faktor penurunan $\log_{10}$ ≥4 (angka pemusnahan 99.99%) menunjukkan keampuhan virusidal yang efektif sesuai dengan Standard Eropa.[2]

Efektivitas PVP-I terhadap SARS-CoV

Reagent or treatment	Final PVP-I concentration, %	Virus titer after treatment, $TCID_{50}$/ml	
		60 s	120 s
Control	0	1.17×10^6	n.d.
Isodine	1	95.1	u.d.
Isodine Gargle	0.47	190	u.d.
Isodine Scrub	1	u.d.	n.d.
Isodine Palm	0.25	u.d.	n.d.
Isodine Nodo Fresh	0.23	u.d.	n.d.
Ethanol (final 35%)	–	u.d.	n.d.

n.d. = Not done; u.d. = under the detectable level.

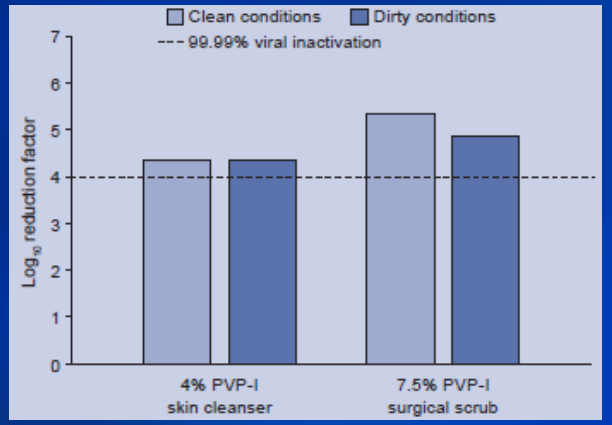
Studi invitro menunjukkan bahwa beberapa produk PVP-I efektif melawan SARS[1-3]

1. Eggers. Infect Dis Ther (2015) 4:491–501
2. Kariwa H. Dermatology. 2006; 212 Suppl 1:119-23
3. Eggers M et al. Can oral disinfection with povidone iodine prevent viral respiratory infections? Abstract & Poster ASN226 IMRP Singapore 2015.

Efektivitas PVP-I terhadap SARS-CoV

- Evaluasi efektvitas penggunaan *in vitro* berbagai produk PVP-I terhadap SARS-CoV.[1]
- Hasil: Aktivitas antiviral terhadap SARS-CoV tampak dalam 15 detik setelah paparan.

Aktivitas virusidal berbagai sediaan PVP-I terhadap SARS setelah 15 detik[3]



Log10 reduction factor ≥4

*Log10 reduction factor ≥ 4 (99.99% kill rate) demonstrate effective virucidal efficacy as stipulated in European Standard EN 14476:2013/A1:2014(2)

1. Eggers. Infect Dis Ther (2015) 4:491–501
2. EN14476:2013/A1:2014. Chemical disinfectants and antiseptics – Quantitative suspension test for the evaluation of virucidal activity in the medical area – Test method and requirements

Efektivitas PVP-I terhadap MERS-CoV

→ **PVP-I dapat berperan dalam membatasi penularan dan penyebaran MERS-CoV**

→ **PVP-I Mouthwash dapat menurunkan jumlah virus dalam ronggal mulut dan orofaring**

- **Studi *in vitro* pada 3 formulasi PVP-I terhadap MERS-CoV.**
- **Hasil: Produk berbasis PVP-I menunjukkan aktivitas virusidal cepat terhadap virus MERS-CoV dalam 15 detik setelah paparan.**

1. Eggers M, *et al*. Abstract IMRP Singapore 2015. |
2. EN14476:2013/A1:2014.

Ongoing journal review
NUS Duke Singapore, Mei 2020

Project title: Determining the efficacy of Povidone Iodine containing Betadine Products on the SARS-CoV-2 using in vitro viral kill time assays.

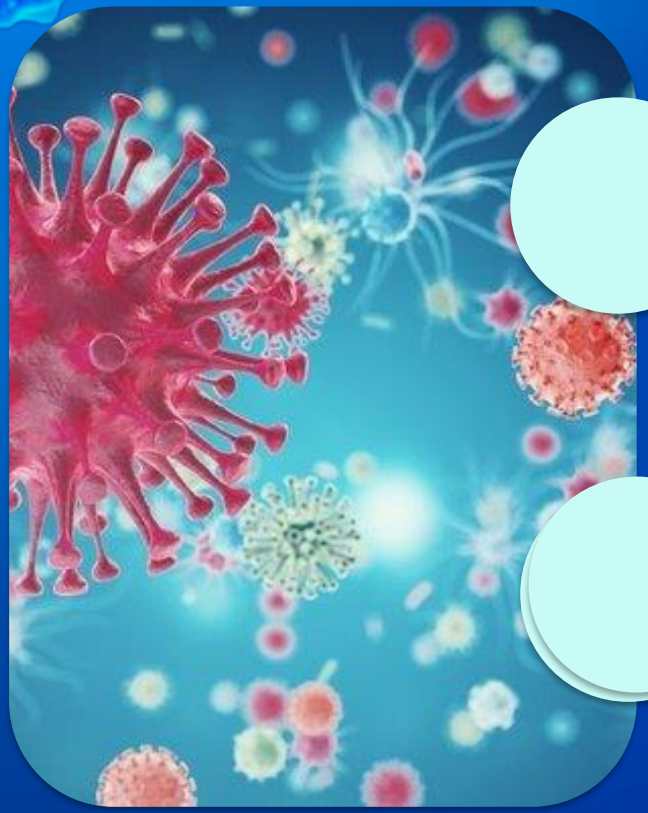
Methodology:
A total of 4 products (Antiseptic solution, Throat spray, Skin Cleanser and Mouthwash) were tested for viricidal activity on SARS-CoV-2 in my laboratory at Duke-NUS Medical School.
All procedures strictly adhered to Duke-NUS biosafety procedures and approved protocols.

Viricidal Activity Assay
The efficacy of 4 products; 10% Antiseptic Solution, 7.5% Skin Cleanser, 1% Gargle and Mouthwash and 0.45% Throat Spray against SARS-CoV-2 were tested in a suspension assay. Viricidal activity was performed taking into account the cytotoxicity of the product. Viricidal activity of all 4 products were tested in triplicate with a 30 second kill time.

Results and Conclusions:
The summarized results are attached.

The efficacy of four (4) Betadine PVP-I products; 10% Antiseptic Solution, 7.5% Skin Cleanser, 1% Gargle and Mouthwash and 0.45% Throat Spray against SARS-CoV-2 were tested in a suspension assay. In conclusion, all 4 tested Betadine products demonstrate viricidal activity (>4 log reduction of viral titre) against SARS-CoV-2 in 30 seconds.

PVP-I Mengendalikan Penyebaran Infeksi

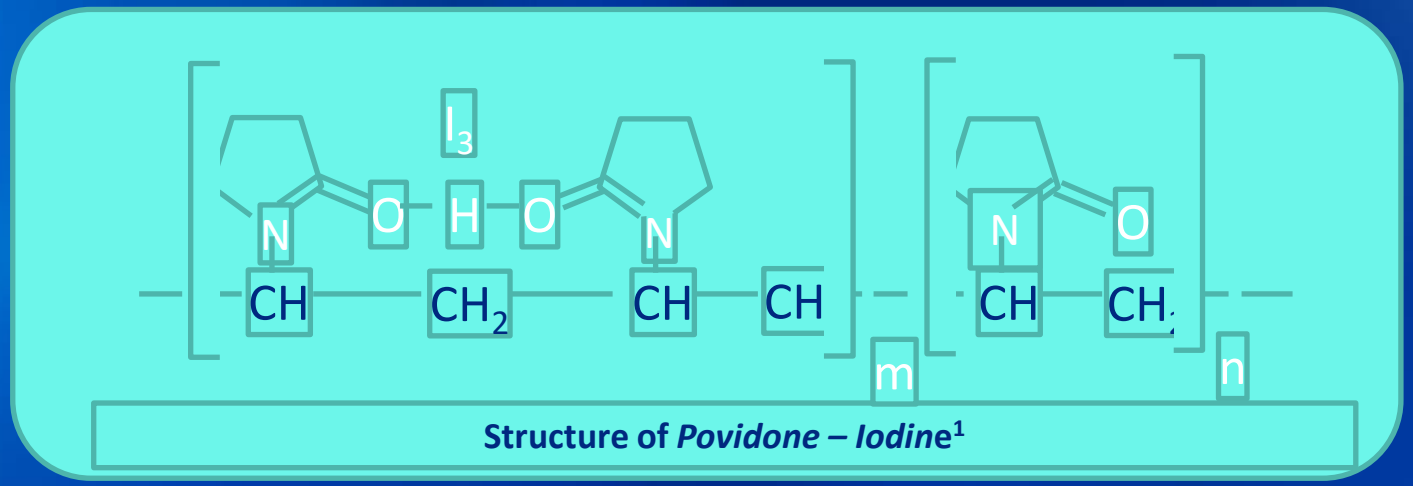


SARS-CoV-2 rentan terhadap oksidasi sehingga mouthwash yang lebih tepat digunakan adalah hidrogen peroksida atau povidone iodine.[1]

PVP-I memiliki aktivitas virusidal yang lebih tinggi dibandingkan antiseptik lainnya seperti chlorhexidine dan benzalkonium chloride.[2]

1. Peng X, et al. Transmission routes of 2019-nCoV and controls in dental practice. International Journal of Oral Science (2020) 12:9.
2. Kirk-Bayley J, Challacombe S, Sunkaraneni VS, Combes J. The use of Povidone Iodine nasal spray and mouthwash during the current COVID-19 pandemic may protect healthcare workers and reduce cross infection. (March 28, 2020). Available at SSRN: https://ssrn.com/abstract=3563092

Povidone -iodine: Struktur Kimia



Structure of *Povidone – Iodine*[1]

$$(PVP \bullet H^+)\, I^-_3 \longleftrightarrow (PVP \bullet H^+) + I^- + I_2 \rightarrow \text{Iodine Aktif}$$

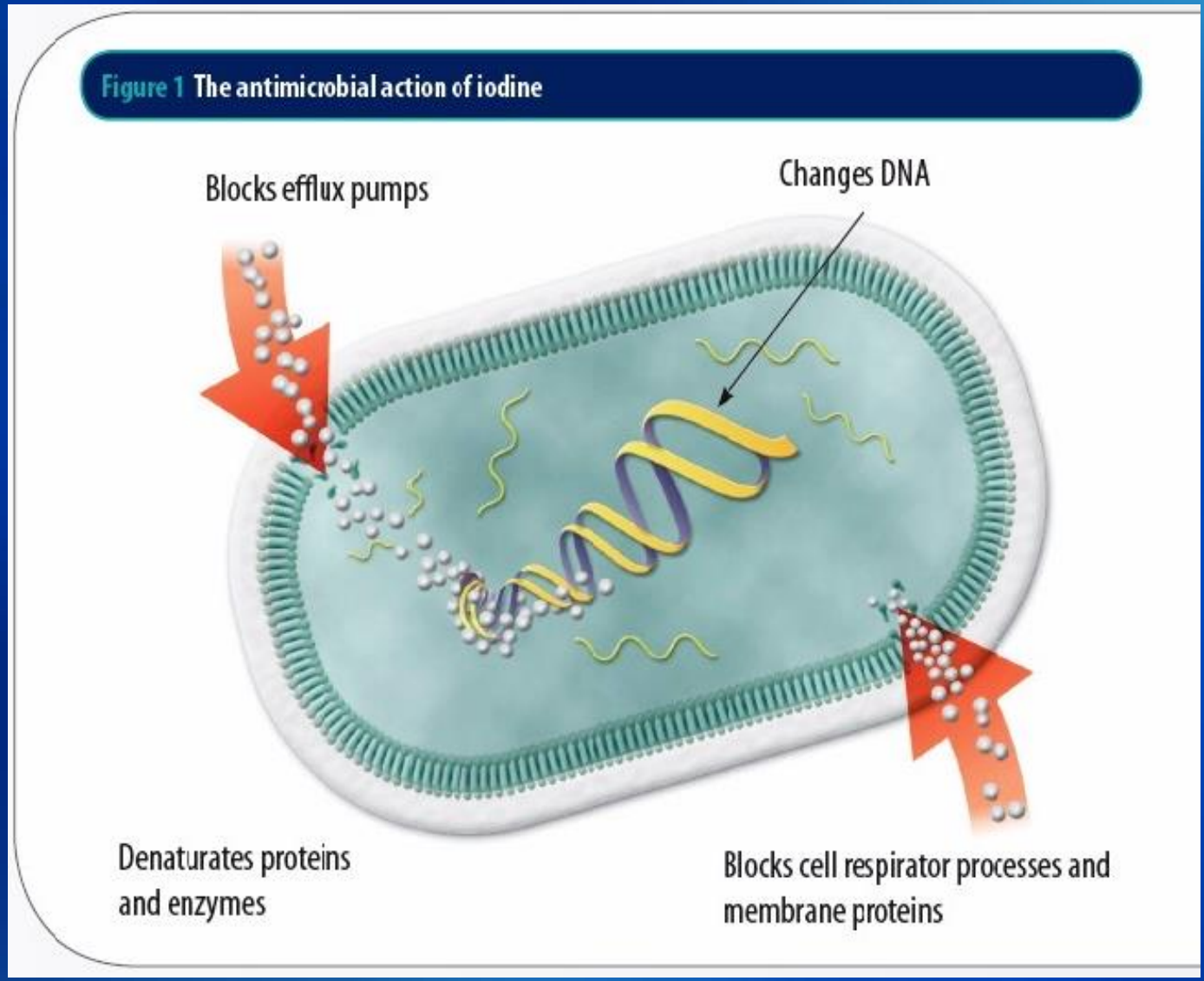
Ekuilibrium kimiawi Povidone-Iodine di dalam medium air[2]

- PVP-I merupakan suatu kompleks polimer sintetik *polyvinylpyrrolidone (povidone)* yang berikatan hidrogen dengan unsur iodium (I_3).[3]
- Di dalam larutan air, ekuilibrium kimiawi yang terbentuk membuat hanya sedikit iodine yang dilepas sebagai iodine bebas (I_2).[4]

1 Schwarz W, *et al.* PVP-Jods. In Hierholzer G, Gortz G (eds): *PVP-Jod in der operativen Medizin.* Berlin: Springer. 1984:1–6. 2 Fleischer W, *et al. Dermatology.* 1997;195(suppl 2):3–9; 3 Gottardi W. Iodine and iodine compounds. In: Block SS, ed. *Disinfection, Sterilization, and Preservation*; 4th ed. Philadelphia: Lea & Febiger. 1991:152–166 4 Reimer K, *et al. Zent.bl Hyg Umweltmed.* 1997/98;200:423–434;

Mekanisme Kerja PVP-I

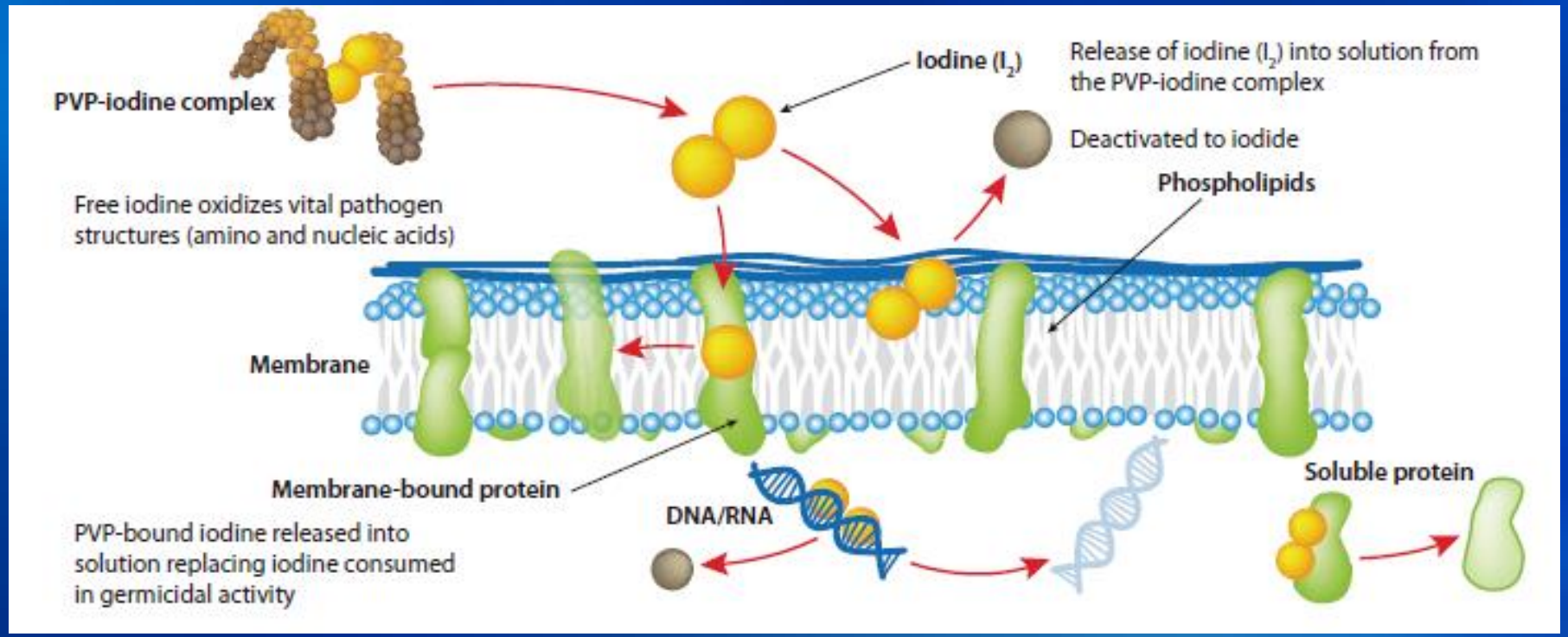
- Aktivitas mikrobisida dari *povidon-iodin* diakibatkan oleh pelepasan iodin bebas (I_2) dari kompleks *polyvinylpyrrolidone.*
- Saat *povidon-iodin* melepaskan iodin, ion *povidon-H* terbentuk, mengubah kompleks tersebut menjadi 'polielektrolit' yang berikatan dengan dinding sel mikroorganisme yang bermuatan negatif.
- Iodin kemudian mendenaturasi protein-protein yang sensitif pada membran, sehingga berakibat lisis dan kematian sel.



Sibbald RG1, Leaper DJ2, Queen D3. Iodine made easy. Wounds international. Vol.2 ; Issue 2.2011.

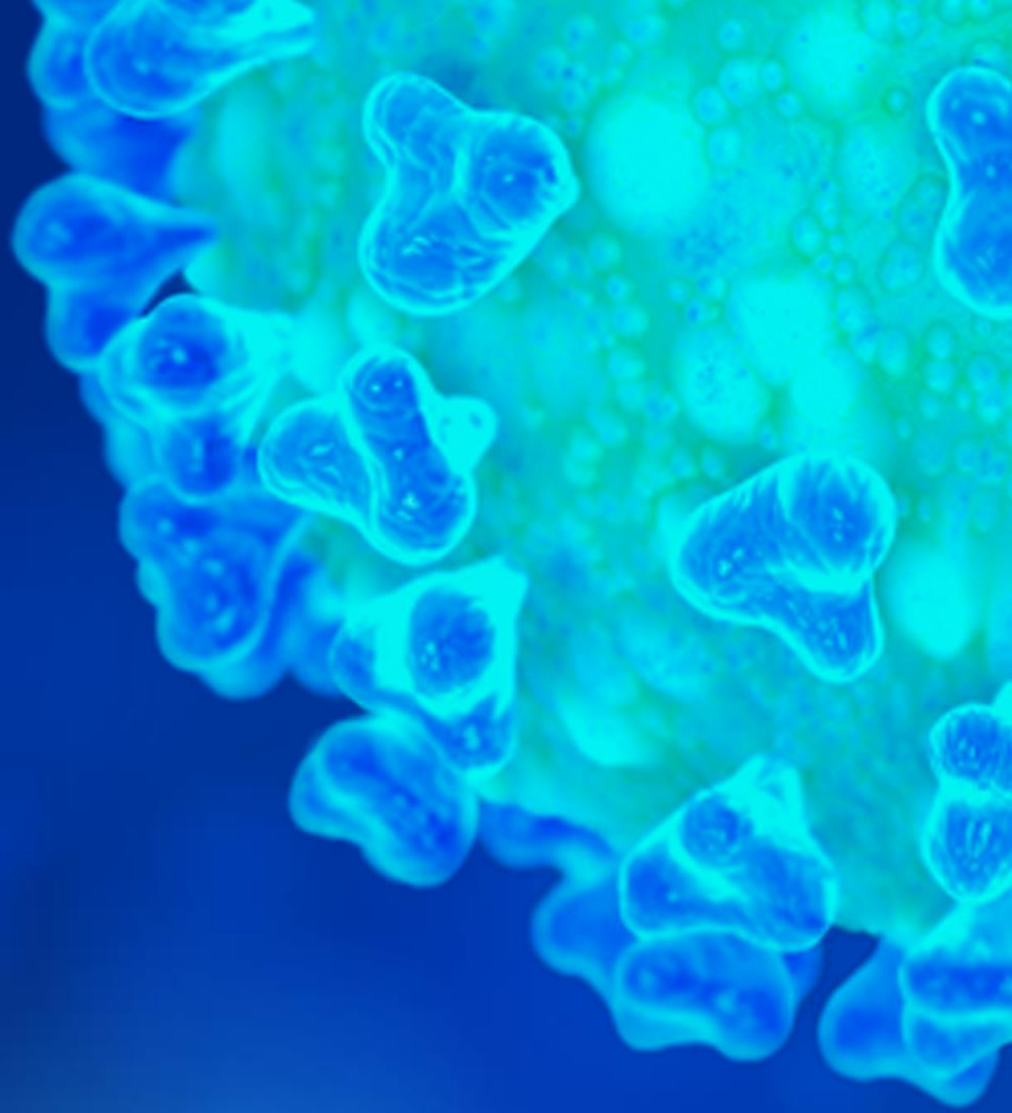
Mekanisme Kerja PVP-I

I_2 membunuh mikroorganisme dengan cara mengoksidasi struktur penting patogen (protein, DNA/RNA).



BETADINE® Product Monograph

Protap Pemakaian Obat Kumur PVP-I yang benar



MEDICAL USE OF POVIDONE IODINE AGAINST COVID-19. WHY NOT?

Luis Mendoza, MD, PhD
Sr Medical Advisor
IQVIA
Czech Republic

Povidone-iodine (PVP-I) is an old antiseptic used in practice of medicine as a surgical scrub; for pre- and post-operative skin cleansing; for the treatment and prevention of infections in wounds, decubitus ulcers, cuts, and burns; in gynecology for vaginitis associated with candidal, trichomonal or mixed infections. For these purposes, PVP-I has been formulated at concentrations of 7.5–10.0% in solution, nasal and throat spray, surgical scrub, ointment, swab dosage forms, eye drop, and vaginal suppositories. The safety profile of PVP-I at such concentrations is well established and many available products in the market are over the counter. The most well-known brand for PVP-I is BETADINE.

PVP-I has been reported as a broad-spectrum microbicide with potency to inactivate bacteria, fungi, protozoans, and several viruses. After searching the medical database "PubMed" and entering the keywords: povidone-iodine and virus, I have found that there 101 scientific publications connect with PVP-I against viruses. The first publication about the efficacy of PVP-I was reported in 1975 where the PVP-I can reduce the titers of herpesvirus type 2 by 92% (1).

Recent in vitro studies have demonstrated virucidal activity of PVP-I against a wide range of

The use of Povidone Iodine nasal spray and mouthwash during the current COVID-19 pandemic may reduce cross infection and protect healthcare workers.

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Abstract

In late 2019 a novel coronavirus, SARS-CoV-2 causing Coronavirus disease 2019 (COVID-19) appeared in Wuhan China, and on 11th March 2020 the World Health Organisation declared it to have developed pandemic status. In early SARS-CoV-2 infection, viral titres of greater than 10^7/mL in saliva and nasal mucous can be found; minimisation of these titres should help to reduce cross infection. Povidone-iodine (PVP-I) disinfectant has better anti-viral activity than other antiseptics

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Letter to the editor

Consideration of povidone-iodine as a public health intervention for COVID-19: Utilization as "Personal Protective Equipment" for frontline providers exposed in high-risk head and neck and skull base oncology care

Letter to the Editor

In response to the novel coronavirus SARS-CoV-2, healthcare systems have been challenged to allocate scarce resources while striving to achieve distribution justice to meet the critical needs of the communities they serve. Though there are ongoing randomized trials evaluating the utility of systemic therapies, post-convalescent serum, and vaccine development, these interventions are costly and time intensive. Alternative therapies and preventative measures are needed now, not only to accelerate the flattening of the epidemiologic curve, but also safeguard providers and patients as we re-evaluate tiered surgical responses and operational processes moving forward.

Early investigations in China have suggested that cancer patients harbored a higher risk of infection compared with the overall population and that infected cancer patients, particularly those who received chemotherapy or underwent surgery within a month of infection, were more susceptible to the need for critical care, respiratory support, and mortality [1]. In the viral hotspot of Wuhan, nosocomial spread was suspected in 12% of

centrations (e.g. 0.001%). A detailed review of its virucidal activity against a wide range of common viruses, including SARS-CoV and MERS-CoV coronaviruses, is beyond the scope of this article [6]. As a word of caution, *in vitro* studies using 10% and 5% PVP-I have demonstrated cilotoxicity on human respiratory cells [7]. However other investigations demonstrate continued virucidal effects of diluted PVP-I concentrations, without evidence of respiratory cilia toxicity, diminished olfactory function, or changes in mucosal appearance [8]. In *vitro* studies of 0.23% PVP-I mouthwash (1:30 dilution) can inactivate both SARS-CoV and MERSCoV following a 15-second exposure [6]. Though rare, prolonged use of topical 10% PVP-I solution (weeks-months) may increase the risk of iodine toxicity [9]. Allergy, contact sensitivity, and skin reactions are rare [10].

Here we present a novel intervention strategy utilizing topical applications of PVP-I to attenuate nosocomial transmission of COVID-19 surrounding head and neck and skull base oncology care. Given that frontline providers exposed

Untuk pasien/ nakes yang asimtomatik atau berada di tempat yang high-risk: hingga 4 kali sehari.[2]

1 Kirk-Bayley J, Challacombe S, Sunkaraneni VS, Combes J. The use of Povidone Iodine nasal spray and mouthwash during the current COVID-19 pandemic may protect healthcare workers and reduce cross infection. (March 28, 2020). Available at SSRN: https://ssrn.com/abstract=3563092 or http://dx.doi.org/10.2139/ssrn.3563092

2 Consideration of povidone-iodine as a public health intervention for COVID-19: Utilization as “Personal Protective Equipment” for frontline providers exposed in high-risk head and neck and skull base oncology care. Oral Oncology. Accepted 15 April 2020. https://doi.org/10.1016/j.oraloncology.2020.104724

SIAPA YANG PERLU BERKUMUR

Menjalani prosedur berisiko tinggi

Pasien (+) COVID 19

Berada di atau berasal dari area berisiko tinggi COVID 19

adanya sekresi dari nasal, mukosa, oral, pharingeal dan paru

Gunakan nasal dan oral (kumur dan gargle) dg PVP-I setiap 2-3 jam sekali sampai 4 kali/hari

SIAPA YANG PERLU BERKUMUR

Tenaga kesehatan yang terlibat langsung dalam penanganan pasien yang diduga/terlah terkonfirmasi positif terinfeksi SARSCoV-2

Terlibat langsung dalam prosedur penanganan pasien di daerah berisiko tinggi COVID-19

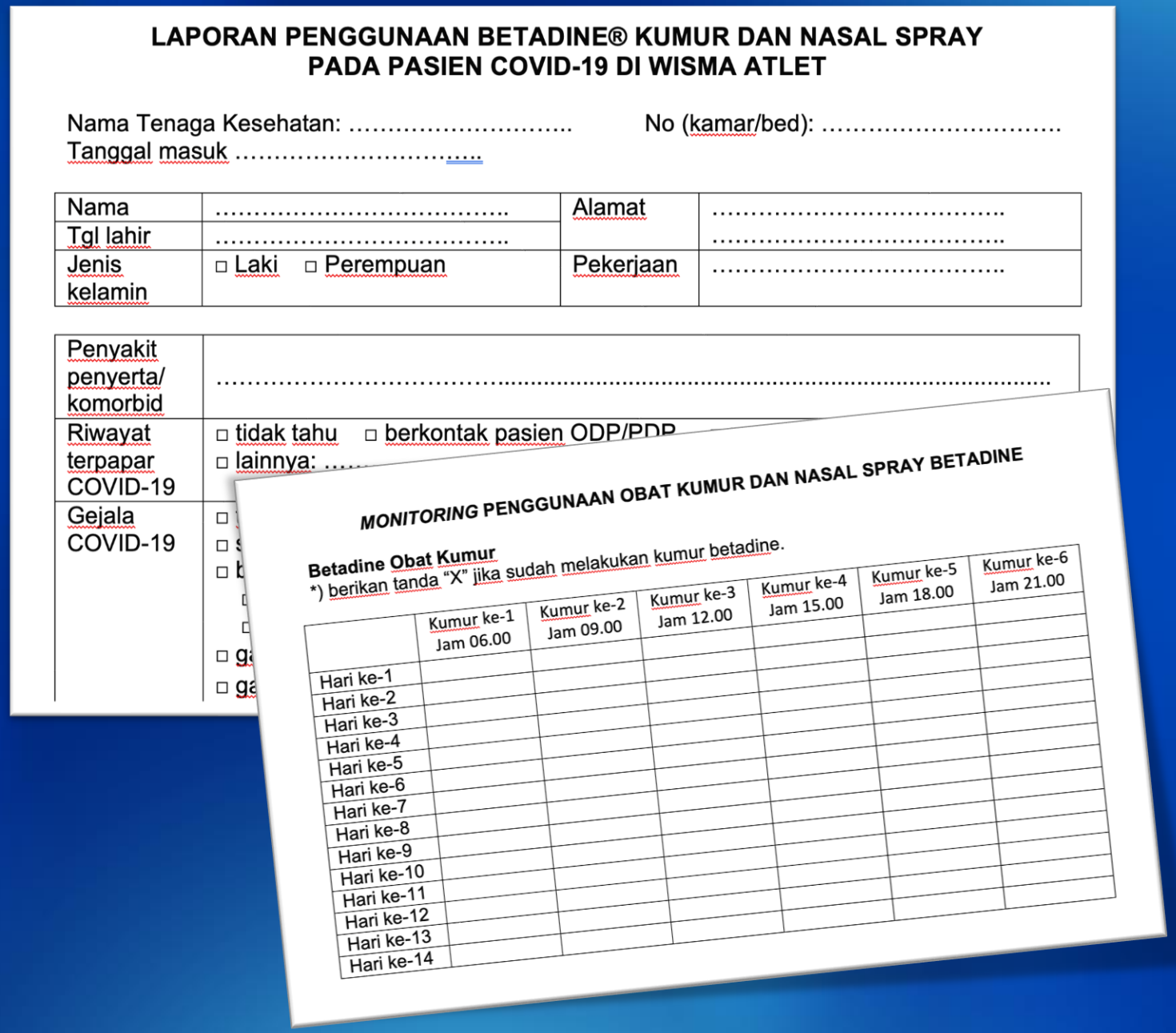
Sebelum dan setelah kontak dengan pasien

Mengalami keterbatasan APD(PPE)

Menangani prosedur berisiko tinggi pada pasien tak bergejala

Gunakan nasal dan oral (kumur dan gargle) dg PVP-I setiap 2-3 jam sekali sampai 4 kali/hari

Usulan masuk dalam Protap pasien OPD/PDP di Wisma Atlet



LAPORAN PENGGUNAAN BETADINE® KUMUR DAN NASAL SPRAY PADA PASIEN COVID-19 DI WISMA ATLET

Nama Tenaga Kesehatan: …….. No (kamar/bed): ……
Tanggal masuk ……

Nama	……..	Alamat	……..
Tgl lahir	……..		……..
Jenis kelamin	□ Laki □ Perempuan	Pekerjaan	……..

Penyakit penyerta/ komorbid	……..
Riwayat terpapar COVID-19	□ tidak tahu □ berkontak pasien ODP/PDP □ lainnya: ……
Gejala COVID-19	□ □ □ b □ □ □ g □ g

***MONITORING* PENGGUNAAN OBAT KUMUR DAN NASAL SPRAY BETADINE**

Betadine Obat Kumur
*) berikan tanda "X" jika sudah melakukan kumur betadine.

	Kumur ke-1 Jam 06.00	Kumur ke-2 Jam 09.00	Kumur ke-3 Jam 12.00	Kumur ke-4 Jam 15.00	Kumur ke-5 Jam 18.00	Kumur ke-6 Jam 21.00
Hari ke-1						
Hari ke-2						
Hari ke-3						
Hari ke-4						
Hari ke-5						
Hari ke-6						
Hari ke-7						
Hari ke-8						
Hari ke-9						
Hari ke-10						
Hari ke-11						
Hari ke-12						
Hari ke-13						
Hari ke-14						

Penggunaan *Povidone Iodine* Jangka Panjang

- Tidak ada masalah keamanan yang baru yang dilaporkan pada penggunaan harian untuk:
  - Sariawan parah akibat radioterapi[1] - 6 minggu
  - Sariawan parah akibat kemoradiasi[2] - 9 minggu
  - Pencegahan gingivitis[3] - 24 minggu
  - Stomatitis pada leukemia mielogenus akut[4] - 1-3 tahun

Referensi: 1. Madan PD, *et al. J Cancer Res Ther.* 2008;4:3–8. 2. Rahn R, *et al. Dermatology.* 1997;195(Suppl 2):57–61. 3. Ader AW, *et al. J Clin Endocrinol Metab.* 1988;66:632–635. 4. Tsuzura Y, *et al. Gan To Kagaku Ryoho.* 1992;19:817–822.

Efek Samping Penggunaan dan Profil Keamanan PVP-I ® Obat Kumur Antiseptik

- Penggunaan BETADINE® Obat Kumur Antiseptik tidak menunjukkan *staining* pada enamel gigi.
- Iritasi *idiosyncratic mucosal* dan reaksi hipersensitif.
- Absorbsi berlebihan dapat menyebabkan efek samping sistemik seperti metabolik asidosis, *hypernatremia* dan gangguan fungsi *renal*.
- Walaupun ada risiko *hyperthyroidism* atau *thyrotoxicosis* akibat pemaparan *Iodine*, hormon *thyroid* yang tidak normal bukan merupakan masalah utama.

Walaupun absorbsi sistemik *Iodine* dapat terjadi pada penggunaan jangka panjang, tetapi manifestasi kliniknya (gangguan fungsi *thyroid*) jarang terjadi.

Perhatikan *safety precaution pada* penggunaan BETADINE® Obat Kumur Antiseptik

Referensi: 1. Produk informasi Betadine Obat Kumur antiseptik. 2016. 2. Ripa S, *et al.* Clinical applications of povidone-iodine as a topical antimicrobial. In: Handbook of Topical Antimicrobials Industrial Applications. Industrial applications in consumer products and Pharmaceuticals. 2002. CRC Press; Print ISBN: 978-0-8247-0788-0 3. Tut O K, et *al. J Public Health Dent.* 2010; 70:(3)249-252. 4. Fine P D. *J Hosp Infect.* 1985; 6(suppl):189-193.

Keamanan Povidone-Iodine Gargle

- **Pengobatan dengan PVP-I Mouthwash & Gargle 1% tidak boleh melebihi 14 hari**[1]
  - ➢ Jika gejala tidak membaik setelah 14 hari, pasien harus menghubungi dokter.
- Namun, **beberapa studi menggunakan Povidone-Iodine for Oral & Throat Care selama periode panjang** tanpa ditemukannya masalah keamanan:

Meskipun **tidak ada masalah keamanan baru yang dilaporkan terhadap penggunaan jangka panjang Povidone-Iodine** Mouthwash & Gargle[2-5], **lakukan tindakan pencegahan keamanan.**

(1) **BETADINE**® Gargle and Mouthwash 1% Prescribing Information (Cyprus SPC)package insert/leaflet, (2).Madan PD, *et al. J Cancer Res Ther*. 2008;4:3–8, (3).Rahn R, *et al. Dermatology*. 1997;195(Suppl 2):57–61, (4). Ader AW, *et al. J Clin Endocrinol Metab.* 1988;66:632–635, (5). Tsuzura Y, *et al. Gan To Kagaku Ryoho*. 1992;19:817–822

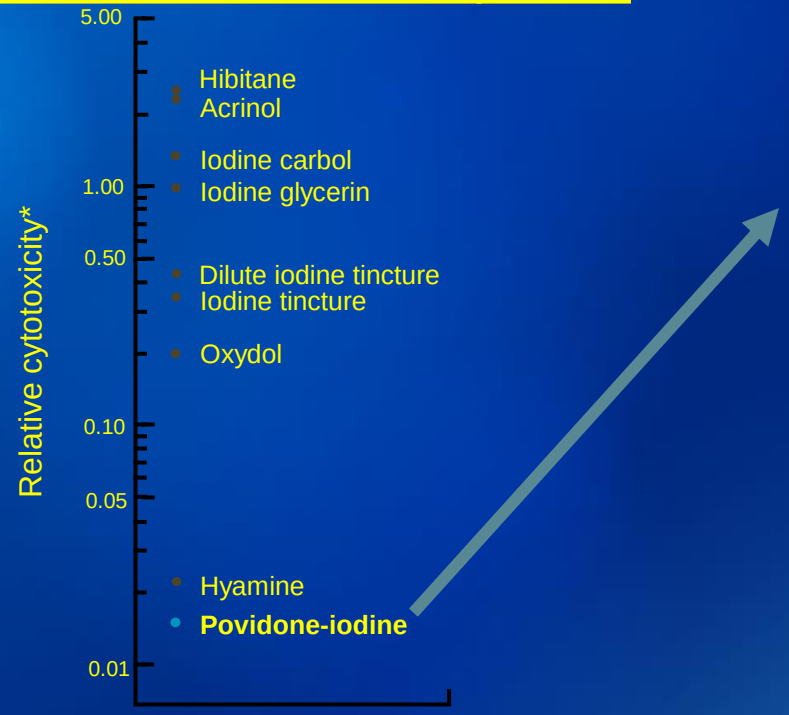
Keamanan Povidone-Iodine Gargle

Studi	Penggunaan Povidone-Iodine Mouthwash & Gargle
Madan PD, dkk.[2]	PVP-I Mouthwash **dua kali sehari selama 6 minggu** pada manage radiotherapy-induced Oral Mucositis → PVP-I tidak menyebakan iritasi atau kerusakan mukosa mulut
Rahn R, dkk.[3]	PVP-I Mouthwash **4 kali/hari selama 6 minggu** pada radiochemotherapy-induced Oral Mucositis → PVP-I tidak menyebakan iritasi atau kerusakan mukosa mulut
Ader AW, *et al*.[4]	Penilaian keamanan dan fungsi tiroid selama penggunaan PVP-I Mouthwash & Gargle **setiap hari selama 6 bulan** → Nilai marker tiroid tetap dalam kisaran normal → Ttidak ada buki berkembangnya disfungsi tiroid
Tsuzura Y, dkk.[5]	PVP-I Gargle **8-10 kali/hari selama 1 hingga 3 tahun** untuk pencegahan stomatitis pada pasien leukemia akut

Efek *Cytotoxic Povidone-Iodine* Lebih Rendah Dibanding Antiseptik lain pada Rongga Mulut

- **Evaluation of the cytotoxicity of antiseptics used in oral care** on human keratinocytes from gingival tissues[1]

Relative cytotoxicity of antiseptics at concentrations used in dental practice[1]



*Concentration of antiseptic that resulted in a 50% decrease in neutral red uptake when compared with the untreated control X dilution coefficient.

PVP-I was less cytotoxic than other antiseptics used on mucous membranes in the oral cavity[1]

Another *in vitro* study found that **PVP-I was less cytotoxic and better tolerated** than chlorhexidine, octenidine, and polyhexamethylene biguanide[2]

1. Tsutsui T, *et al. Toxicol In Vitro.* 1994;8(6):125-128.
2. Muller G, et al. *Dermatology.* 2006;212(Suppl1):91-93.

Summary

- Oral hygiene penting dijaga saat wabah COVID-19, terkait reservoir berada di dalam mulut
- Salah satu upaya untuk menjaga oral hygiene adalah dengan pembersihan rongga mulut secara mekanik dan obat kumur
- Studi menunjukkan bahwa PVP-I gargle efektif mengatasi coronavirus MERS-CoV dan SARS-CoV1 dan 2 sehingga dapat menjadi pilihan dalam menekan penyebaran infeksi COVID-19

CEGAH RANTAI PENYEBARAN COVID-19 UNTUK INDONESIA SEHAT

Terima Kasih
Semoga Bermanfaat