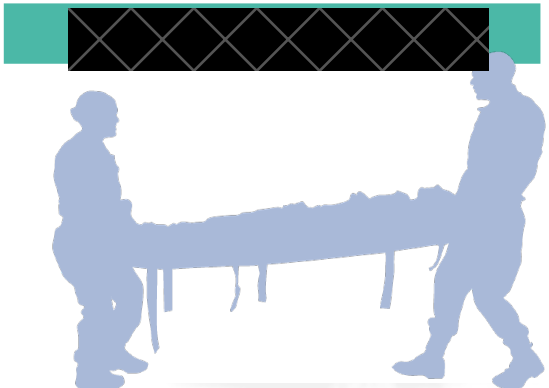
INTRA NASAL ROUTE FOR ANALGESIA ON THE BATTLEFIELD

CMC Oct 2022



Disclosure

The opinions or assertions expressed here in are the private views of the authors and are not to be considered as reflecting the views of the French military medical service.

Conflicts of Interest and Source of Funding

There was no conflict of interest for this article and no exterior or private source of funding.

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intranasal emergency department

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RESULTS BY YEAR

654 results

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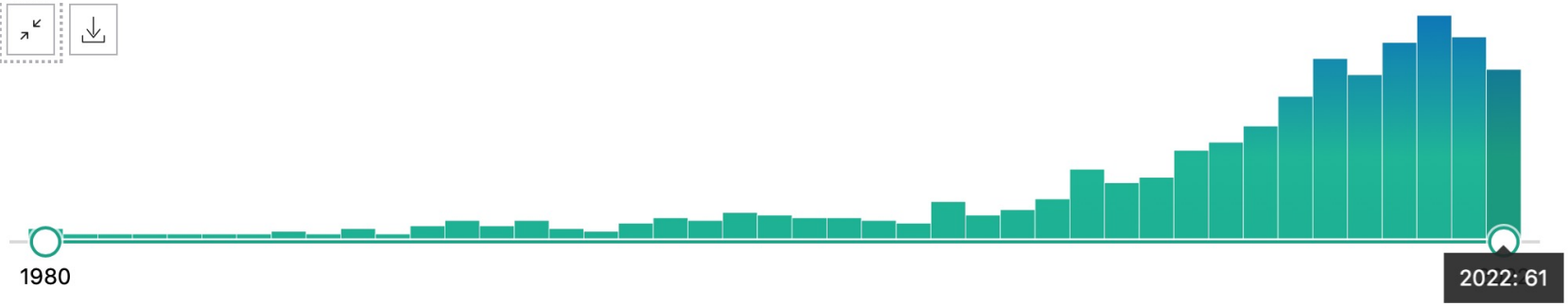
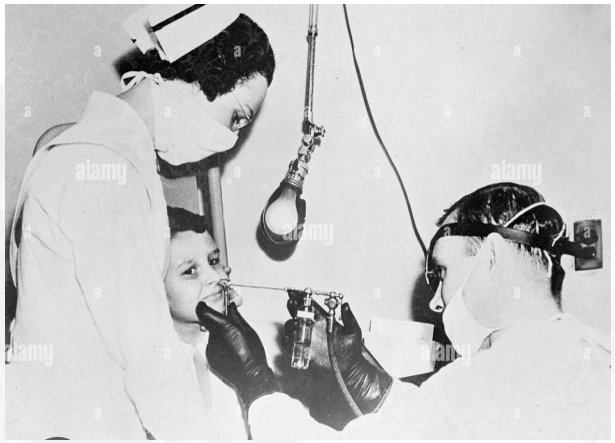


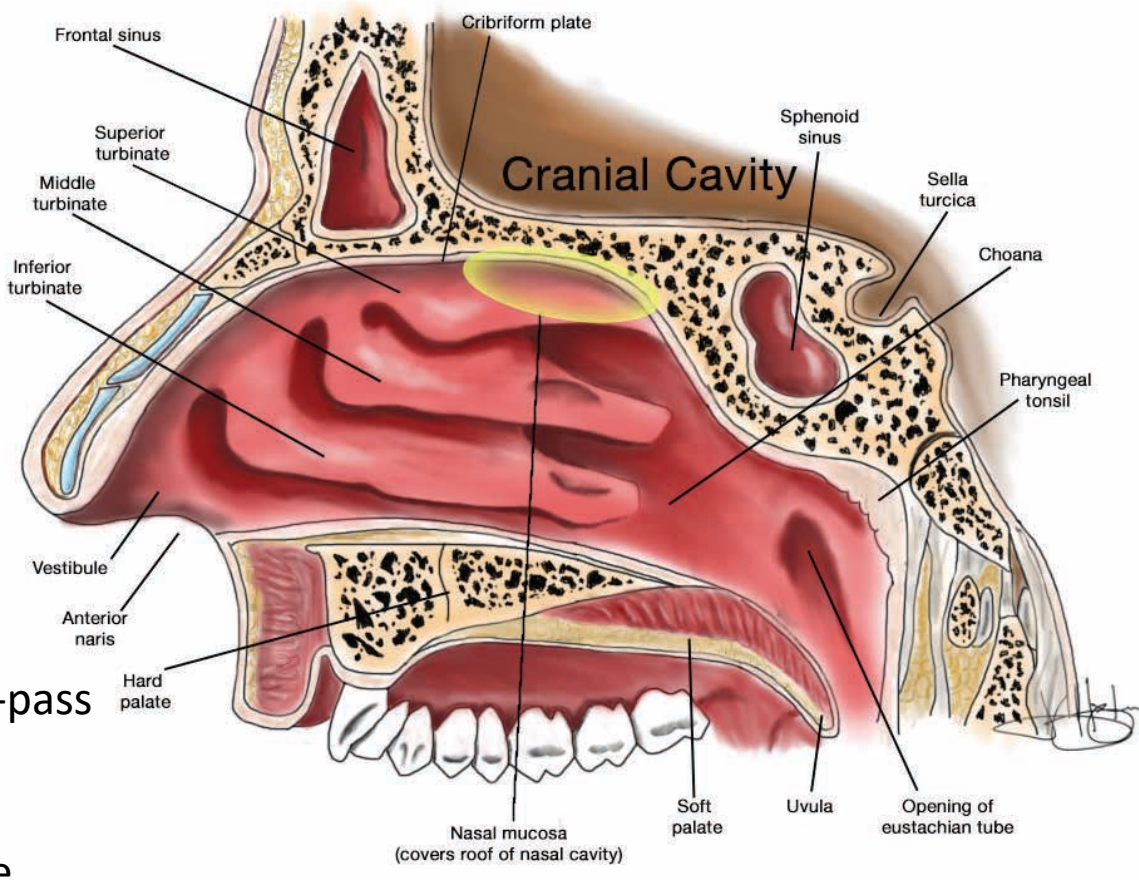


Why is it so sexy ?

- Perfect solution every time you can't/don't want insert an IV

- No needle, no risk of blood cross contamination
- Non invasive/Low risk of infection
- No need to be expert, Self administration

Anatomy physiopathology



➔Rich vascularisation

➔absorption-limiting effects of first-pass metabolism

➔Pathway to CSF via olfactory nerve

➔ Very effective for central acting medications

Rech and al, 2017

Few drawbacks ?

- Variation of Bio avaibility
- Limited dose due to low volume
- Some Contra indications
- No FDA CE aprovment for many drugs

What determine IN absorption?

- Molecular size
- pH of drugs
- Size of droplets
- liposolubility
- Possible enhancers: cyclo dextrins, chitosan

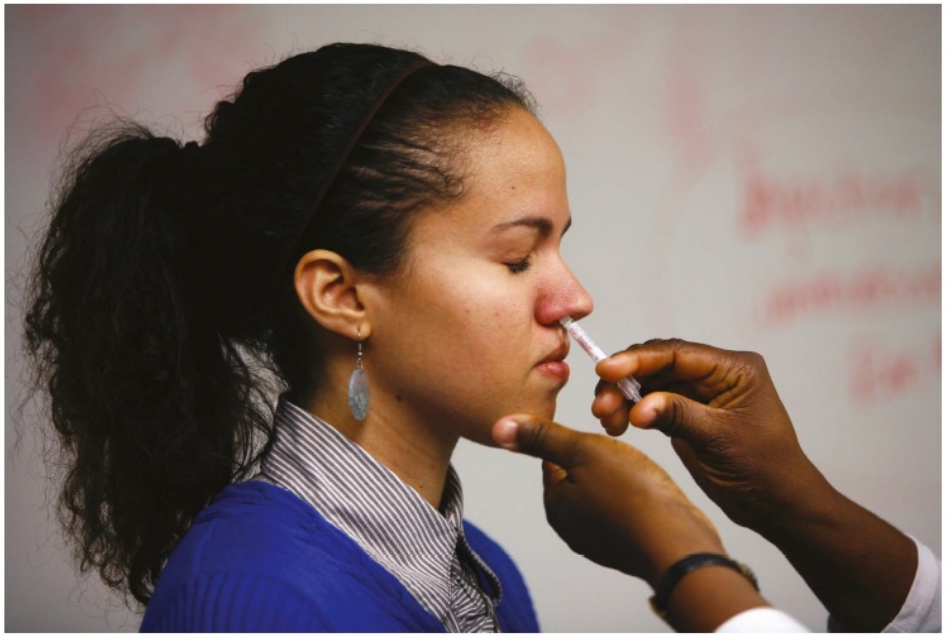
Which medications ?

- Vaccine

Table 2. Clinical trials for intranasal immunization.

Type of vaccine	Sponsor institution	Stages	Clinical registration	Time
Live attenuated RSV/PIV3 vaccine	MedImmune LLC	Phase 1	NCT00345670[133]	2006
		Phase 1/2	NCT00767416[134]	2008
		Phase 1	NCT00493285[135]	2007
		Phase 1/2	NCT00686075[136]	2008
Live attenuated influenza vaccine	Beijing Chaoyang District Centre for Disease Control and Prevention	Phase 1	NCT02665871	2016
Live attenuated influenza vaccine	MedImmune LLC	Phase 1 Phase 2	NCT00112112 NCT00344305	2005 2006
Live attenuated influenza vaccine	PATH Vaccine Solutions	Phase 2	NCT01625689	2012
Live attenuated influenza vaccine	University of Colorado, Denver	Phase 2	NCT02474901	2015
Live attenuated *Bordetella pertussis* vaccine	GRIEMHMRF	Phase 1	NCT03137927	2017
Unmodified live attenuated Sendai virus vaccine	St. Jude Children's Research Hospital	Phase 1	NCT00186927	2005
Live attenuated *B. pertussis* vaccine	Institut National de la Santé Et de la Recherche Médicale, France	Phase 1, Phase 1	NCT01188512,[137-139] NCT02453048	2010 2015
Adenovirus-vectored influenza vaccine	Altimmune, Inc.	Phase 1	NCT00755703	2008
Adenovirus vaccine	NINAD	Phase 1	NCT01806909	2013
Live attenuated/inactivated influenza vaccine	St. Jude Children's Research Hospital	Phase 1	NCT00906750	2009
Inactivated influenza virus vaccine	NanoBio Corporation	Phase 1, Phase 1	NCT01333462, NCT01354379	2011 2011
Inactivated influenza vaccine	MedImmune LLC	Completed	NCT00808808	2008
RSV subunit vaccine	Mucosis BV	Phase 1	NCT02958540	2016
Pneumococcal subunit vaccine	Genocea Biosciences, Inc.	Phase 2	NCT02116998	2014
HIV gag peptides vaccine	Oslo University Hospital	Phase 1/2	NCT01473810[140]	2011
Recombinant RSV vaccine	Bavarian Nordic	Phase 1	NCT02864628	2016
Norwalk virus-like particle vaccine	Takeda	Phase 1/2	NCT00973284[141]	2009
Norwalk virus-like particle vaccine	LigoCyte Pharmaceuticals, Inc.	Phase 1	NCT00806962[142]	2008
Liposomal-based influenza vaccine	Hadassah Medical Organization	Phase 1/2	NCT00197301	2005
Proteosome-adjuvanted influenza vaccine	Hvivo	Phase 1/2	NCT02522754[143]	2015

RSV, respiratory syncytial virus; PIV3, parainfluenza virus type 3; GRIEMHMRF, Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation.



HYUNGWON KANG/BLOOMBERG

A student in Washington DC receives an influenza nasal-spray vaccine, in 2009. Intranasal and oral COVID-19 vaccines are now in development.

HOW NASAL-SPRAY VACCINES COULD CHANGE THE PANDEMIC

Vaccines inhaled through the nose or mouth might stop the coronavirus in its tracks, but there's little evidence from human trials so far. **By Emily Waltz**

Are sprays the future of COVID-19 vaccines? That's the hope of dozens of research groups and companies working on new kinds of inoculation. Rather than relying on injections, these use sprays or drops administered through the nose or mouth that aim to improve protection against the virus SARS-CoV-2.

This week, an inhaled version of a COVID-19 vaccine, produced by the Chinese company CanSino Biologics in Tianjin, was approved for use as a booster dose in China.

It's one of more than 100 oral or nasal vaccines in development around the world. In theory, these vaccines could prime immune cells in the thin mucous membranes that line cavities in the nose and mouth where SARS-CoV-2 enters the body, and quickly stop the virus in its tracks — before it spreads. Vaccine developers hope that these 'mucosal' vaccines will prevent even mild cases of illness and block transmission to other people, achieving what's known as sterilizing immunity. A few mucosal vaccines are already approved for other diseases, including a sprayable vaccine against influenza.

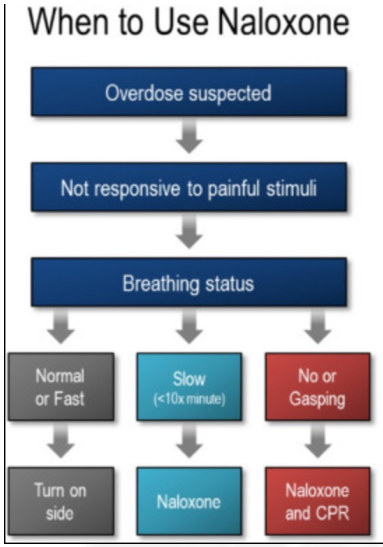
Evidence in animals supports the idea that sterilizing immunity can be induced against COVID-19, although data from humans are scant. *Nature* explains why mucosal vaccines might help to quash SARS-CoV-2, and what the latest findings mean.

Why might mucosal vaccines be better than conventional shots?

The COVID-19 vaccines currently in use do a good job of reducing disease severity and preventing hospitalization, but don't block

Which medications ?

- antidots



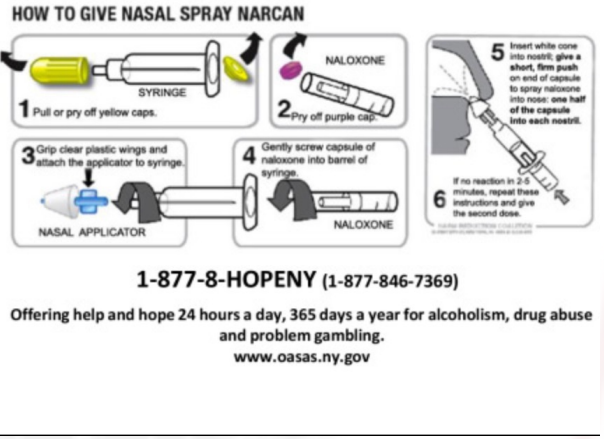
Review > Harm Reduct J. 2022 Sep 19;19(1):102. doi: 10.1186/s12954-022-00682-w.

Naloxone administration by law enforcement officers in New York State (2015–2020)

Elham Pourtaher [1], Emily R Payne [2], Nicole Fera [2], Kirsten Rowe [2], Shu-Yin John Leung [2], Sharon Stancliff [2], Mark Hammer [2], Joshua Vinehout [3], Michael W Dailey [4]

Affiliations + expand

PMID: 36123614 PMCID: PMC9483860 DOI: 10.1186/s12954-022-00682-w



Which medications ?

- Anti seizure

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Recommandations Formalisées d'Experts

Prise en charge des états de mal épileptiques en préhospitalier, en structure d'urgence et en réanimation dans les 48 premières heures

(A l'exclusion du nouveau-né et du nourrisson)

Les BZD constituent la référence pour le traitement de première ligne de l'EME en IV, à défaut en IM, IR ou intra-nasale). En l'absence de lorazépam en France, les BZD de première ligne à retenir sont le

Which medications ?

- Sedation

Original

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Diego Palao Vidal[a,b]
José Antonio Monreal Ortiz[a,b]
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Efficacy and safety of intranasal haloperidol in an acute Psychiatry Unit: a pilot study on schizophrenic patients with mild-modedate agitation

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ABSTRACT

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Which medications ?

- Analgesia

Review > Am J Emerg Med. 2018 Feb;36(2):310-318. doi: 10.1016/j.ajem.2017.11.043. Epub 2017 Nov 20.

The use of intranasal analgesia for acute pain control in the emergency department: A literature review

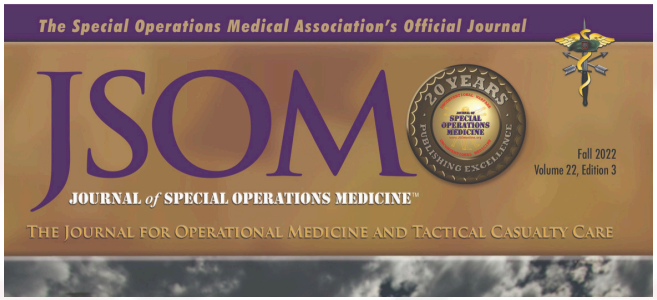
Billy Sin [1], Jennifer Wiafe [2], Christine Ciaramella [3], Luis Valdez [4], Sergey M Motov [5]

Table 2. Intranasal medication pharmacokinetics and adverse effects.[8,36,55,56,62,63,69,79,81,82]

Medication	Bioavailability, %	Onset, Minutes	Duration, Minutes	Dosing	Intranasal Adverse Effects
Midazolam	50	10–15	30	Procedural sedation: Pediatric: 0.1–0.5 mg/kg Adult: volume limits adequate dose Seizures: Pediatric: 0.2 mg/kg Adult: 10 mg Maximum single dose based on volume: 10 mg	Nasal burning, bitter taste
Fentanyl	89	6–7	30–60	Analgesia: Pediatric: 1–2 μg/kg per dose Adult: 100 μg Maximum single dose based on volume: 100 μg	Respiratory depression, lightheadedness, euphoria, nausea/vomiting
Naloxone	4–30	8–13	30–120	Opioid reversal: Pediatric: no data; recommend 0.2 mg/kg Adult: 2–8 mg Maximum single dose based on volume: 2 mg using IV solution for IN administration; 8 mg using new 4 mg/0.1 mL product	Nasal dryness, edema, congestion, and local inflammation
Ketamine	40–50	5–23	72	Procedural sedation: Pediatric: 3–9 mg/kg Adult: volume limits adequate dose Analgesia: Pediatric/adult: 0.5–1 mg/kg Maximum single dose based on volume: 100 mg (50 mg/mL solution); 200 mg (100 mg/mL solution)	Sore throat, bad taste

French expérience of Intra nasal Ketamine on the battlefield

Combat casualties treated with intranasal ketamine for prehospital analgesia: A case series



In Press, JSOM

- 8 months deployement
- War casualties
- Mean ISS 22
- Wawes from 1 to 15 casualties at a time

Localisation	Proportion
Head/neck	25%
Thorax	27%
Abdomen	17%
Extremities	66%
Burns	5%
Neck	5%

259 patients

243 soldiers (94%), 16 civilians (6%)
6 women (2%), 5 children (2%)

Lack of information => 48 patients excluded

211 patients

W-BFPRS < 7, or no analgesia done => 71 patients*

140 inclusions

NATO Categorisation of these 140 Patients

	T1	T2	T3	T4	Total
N	50	79	8	3	140
%	35,7	56,4	5,7	2,1	100

IN Group
N =76

Opiate SC/IV Group***
N=64

*W-BFPRS : Wong–Baker Faces Pain Rating Scale from 0 to 10

** IN Group : Patients treated by intranasal ketamine

***Opiate SC/IV Group : Patients not treated by intranasal ketamine

IN group : 76 patients

- 50 mg of IN ketamine, which could be repeated
- Done by any medic or soldier under supervision
- 72% received only IN Ketamine + 10 mg S/C Mophine for analgesia in the first hour
- 1 side effect : psychodyslepsia

➔67/76 (88%) in IN group did’nt nedd IV for analgesia in the 1st hour

➔Those needing IV needed lower doses of Morphine and ketamine

➔No major side effect

➔Very quick and easy to use in triage

French Health service central pharmacy device

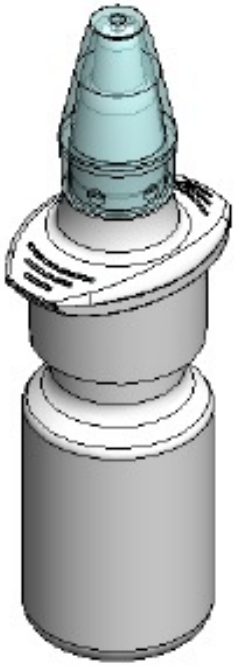
- IN Ketamine with individual device,

available 2023

- 10% ketamine, 5 mg per pulverisation, up to 40 mg

- For health care provider in 2023,

➔ Maybe in the IFAK for self administration in the futur



Conclusion

➔No more 0,5 cc / nostril

➔Use concentrated Drugs

➔Use an Atomisor device

➔keep in mind few contra indications: face trauma, epistaxis

➔Many applications in disaster medicine, triage

QUESTIONS ?

CMC Oct 2022