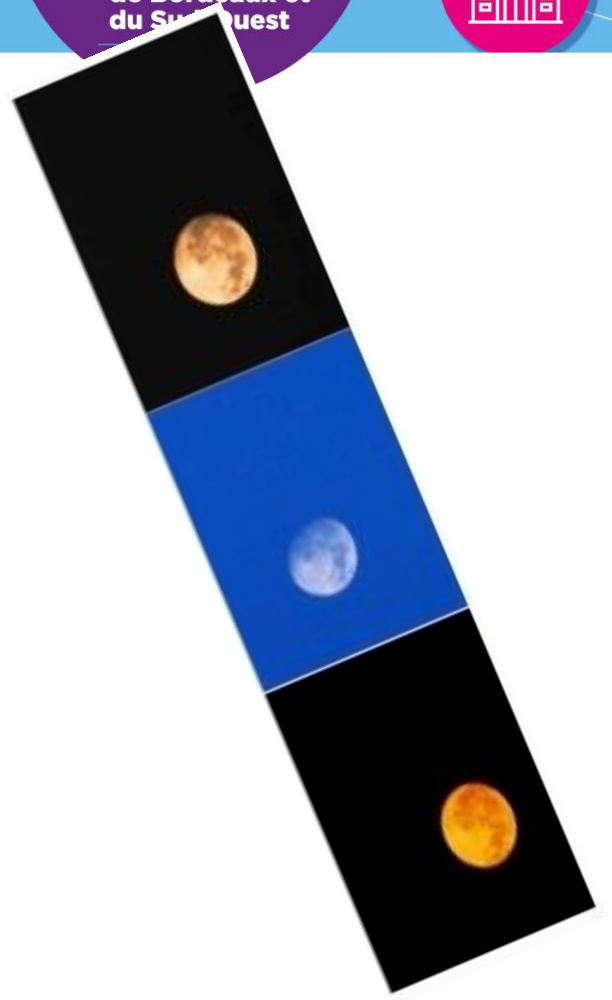


Pourquoi les infections sont plus fréquentes et plus graves chez les personnes âgées ?

Liens d’intérêt généraux

consultant, speaker, workshop and advisory boards : Pfizer/ BioMérieux/ Sanofi-Pasteur MSD/ Astellas /AstraZeneca/Sanofi / MSD/Novavax

As consultant National Public Health Institutes (Haute Autorité de Santé/ DGS/ANSM) / WHO

Reasearch, Education and Congress : Eisai, Pfizer, Sanofi Pasteur, Novartis, Pfizer, MSD, Public Health institutes

Pas de lien d’intéret pour cette présentation

Objectifs….

Le vieillissement lui même a-t-il un role dans la suceptibiltié

Reperer les facteurs qui majore le risque ?

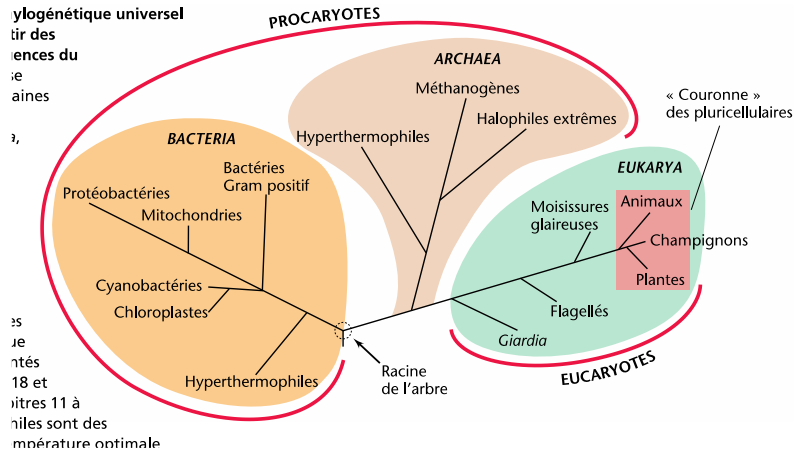
Reperer les facteurs qui augmentent la gravité ?

If Ageing is Universal, Intrinseque, Progressive and somehow Deleterious

Ageing is

Environment (comorbidites) → **HETEROGENEOUS** ← Genetic Epigenetic

80% OF >80 Y POP. AT HOME WITHOUT ADL DISABILITY



interaction Hote-micorbiote et ses evolutions / Epigenetique, Bio-Ageing, ?

Garder en mémoire

Ceux qui ne reçoivent pas d'ATB ne meurt pas tous

Osler and McCrae (1925), Cecil and Plummer (1933), and Ferguson and Lovell (1928) give the mortality percentages with the different types, as shown below :—

	Osler and McCrae	Cecil and Plummer	Ferguson and Lovell
Type I ..	24.1	28.2	26
„ II ..	37.7	48.9	20
„ III ..	53.7	42.7	*
Group IV ..	22.2	31.3	26.4

Napier E *Ind Med Gaz* 1935

The New England Journal of Medicine

Copyright, 1961, by the Massachusetts Medical Society

Volume 265 DECEMBER 28, 1961 Number 26

BACTERIOLOGIC FLORA OF THE LOWER RESPIRATORY TRACT*

GUSTAVE A. LAURENZI, M.D.,† ROBERT T. POTTER, M.D.,‡ AND EDWARD H. KASS, M.D., PH.D.§

TABLE 1. *Bacteria in the Expectorated, Pharyngeal, Tracheal and Bronchial Secretions of 10 Patients with No Evidence of Bronchopulmonary Disease.**

SOURCE OF SPECIMENS	"OROPHARYNGEAL COMMENSALS"†	*Diplococcus pneumoniae*	*Haemophilus influenzae*	COAGULASE-POSITIVE *Staphylococcus aureus* (*Micrococcus pyogenes*)	*Streptococcus haemolyticus*	COLIFORM RODS	ANY "POTENTIAL PATHOGEN"†
	no. of cases	*no. of cases*	*no. of cases*	*no. of cases*	*no. of cases*	*no. of cases*	*no. of cases*
Expectorated secretions	10	3	2	2	1	2	7
Pharynx	10	4	3	2	1	2	8
Trachea	10	2	1	2	0	0	4
Bronchi	0	0	0	0	0	0	0

*8 males, 2 females — mean age, 45 yr.
†See text for definition.

les poumons ne sont pas steriles : 1961

Le Vieillissement Physiologique ?

Tous les organes

Capacité maximale réduite

Homéostasie fragile

Adaptabilité diminuée

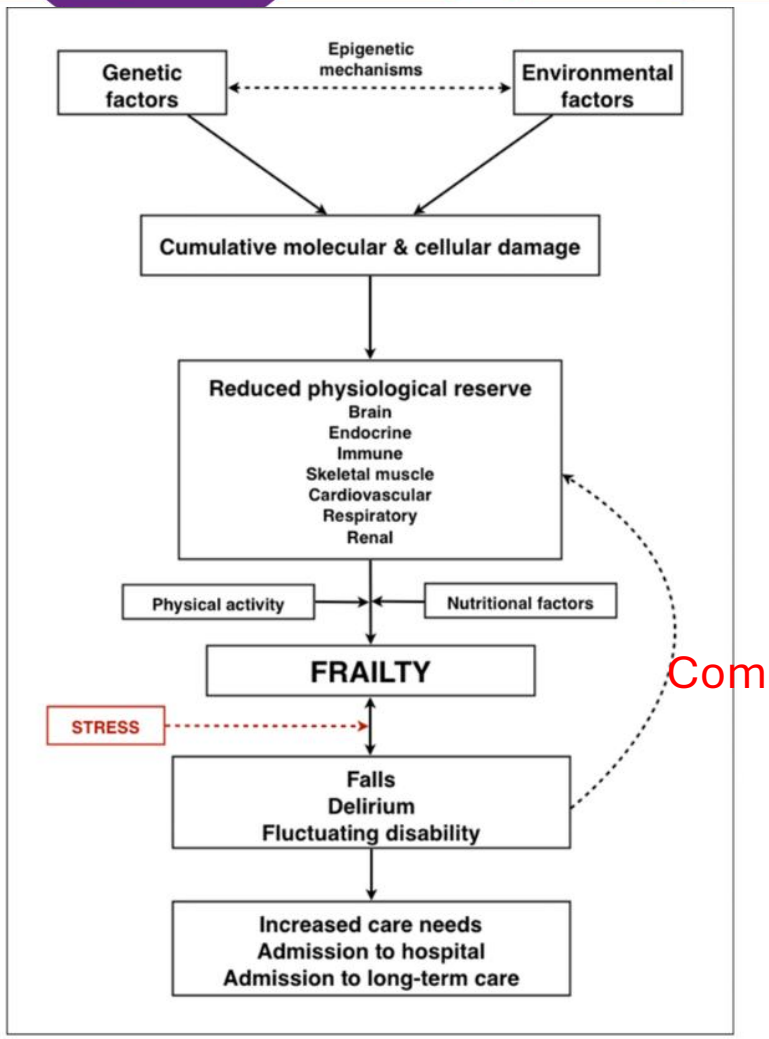
Lenteur et inadéquation des réactions

=

vulnérabilité face aux stress

Syndrome de fragilité

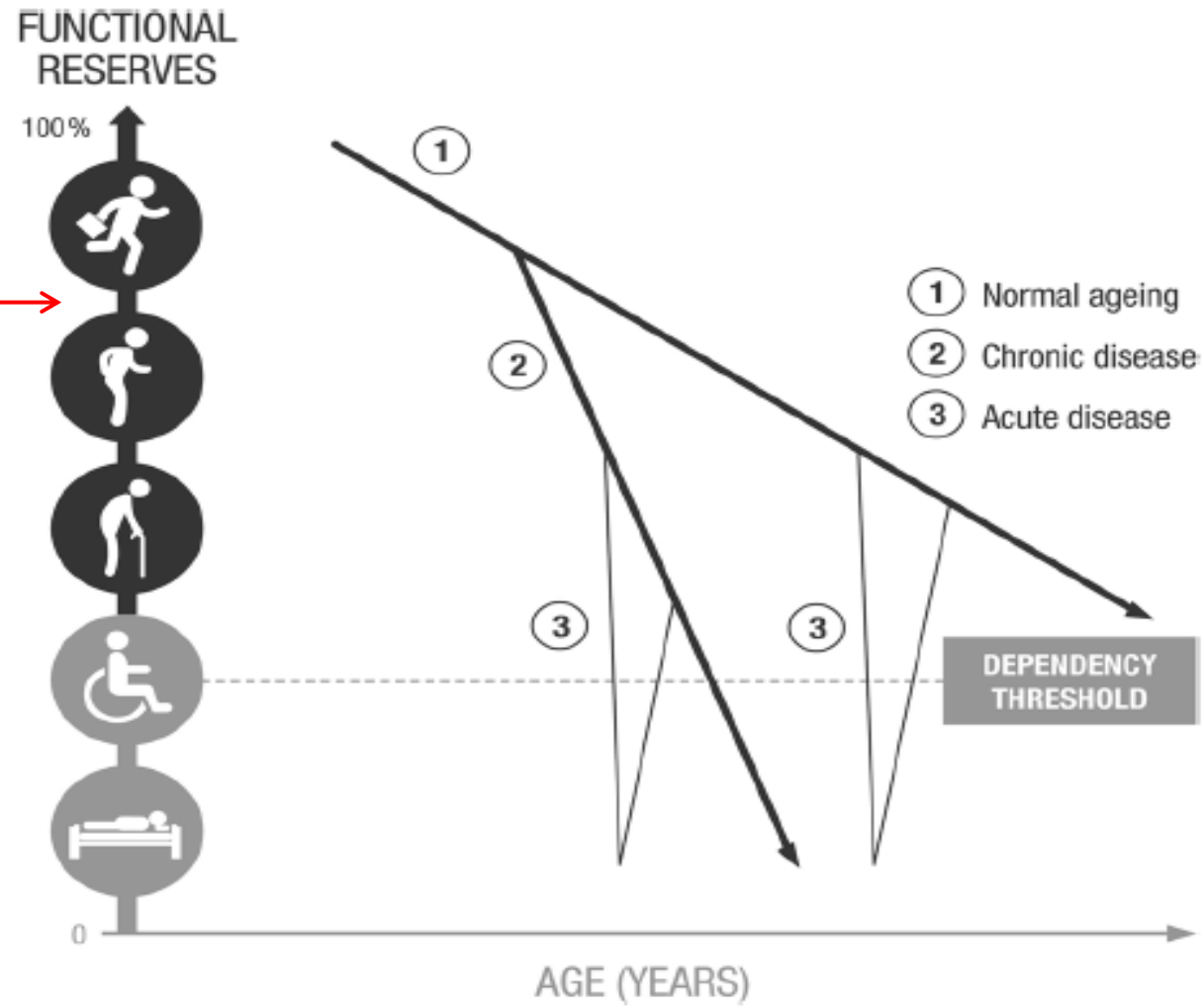
, **Walston J** JAGS 2006, **Fried L** J Gerontol 2001



Clegg A, et al. Lancet 2013

Fragilité →

Comorbidités



Herpes zoster consortium Gavazzi G *Aging Clin Exp Res 2016*

Pourquoi les infections sont plus fréquentes

.....

chez les personnes âgées ?

Immunosenescence

Vieillissement des organes ?

comorbidités et FDR

Risk factors

General

Immunosenescence

Nutrition*

Anatomic / physiological organ modification

Disability *

Multimorbidity *

Polypharmacia

Specific

respiratory

Urinary

Skin/soft tissue

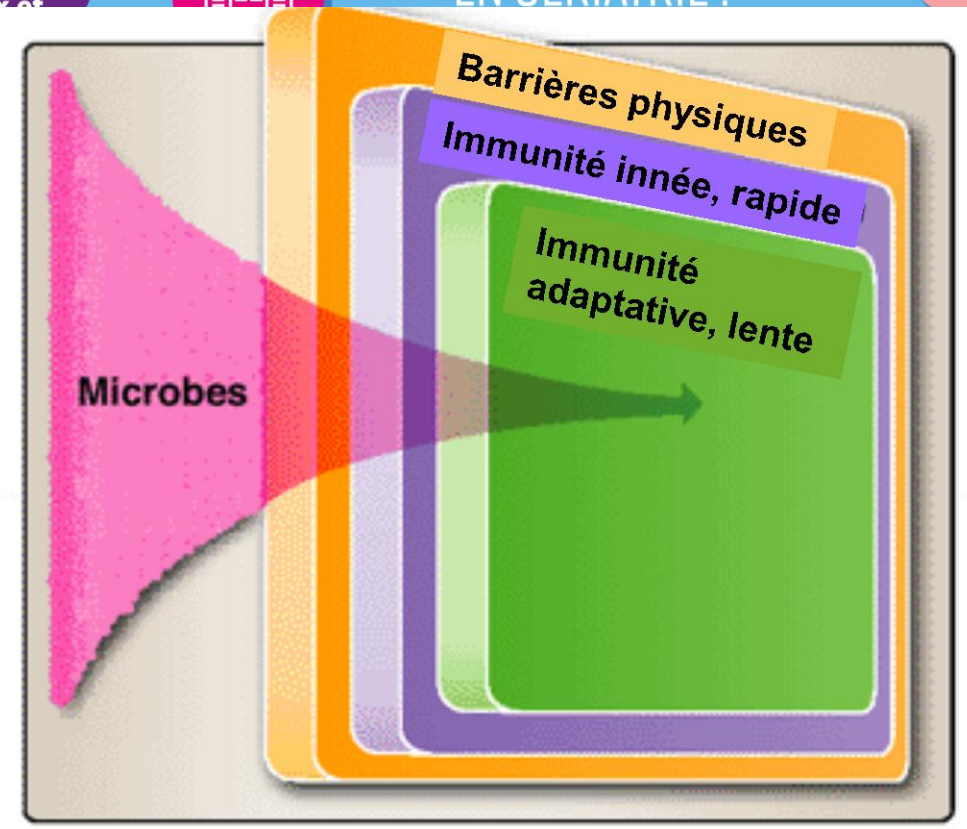
Digestive

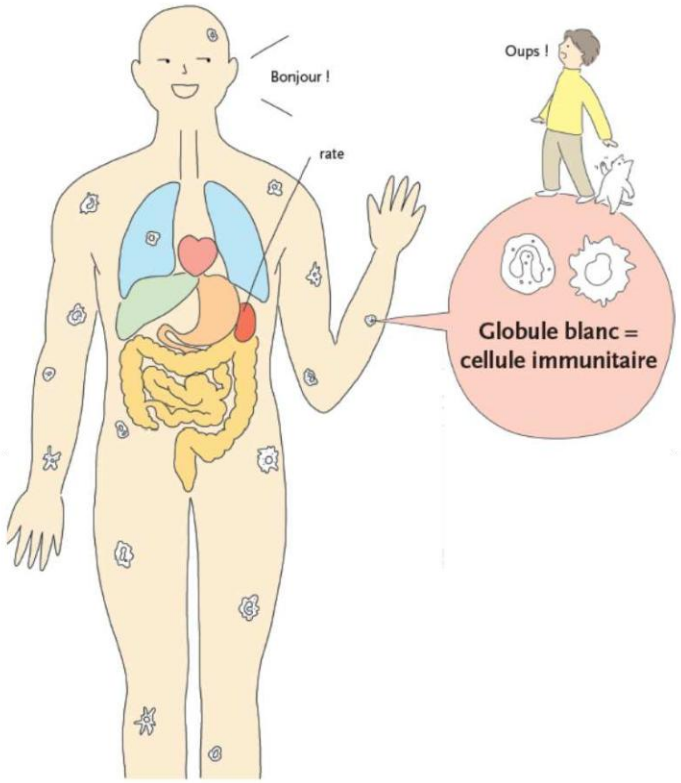
Implant Infection

Flu
Pneumoccocus
Zoster....

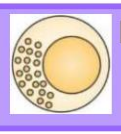
Loeb M Arch Intern Med 1999, **Gavazzi G** Lancet Infect Dis 2002,**Chandra RK** 2004, **El-Kadiki BMJ** 2005, **Paillaud E** Age and Ageing 2005, **Cretel E** Med Mal Inf 2010

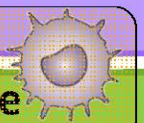
Immunité avant immunosenescence ?





Immédiate innée non-spécifique
→ Retarde la progression de l'infection

polynucléaires   Lymphocytes tueurs

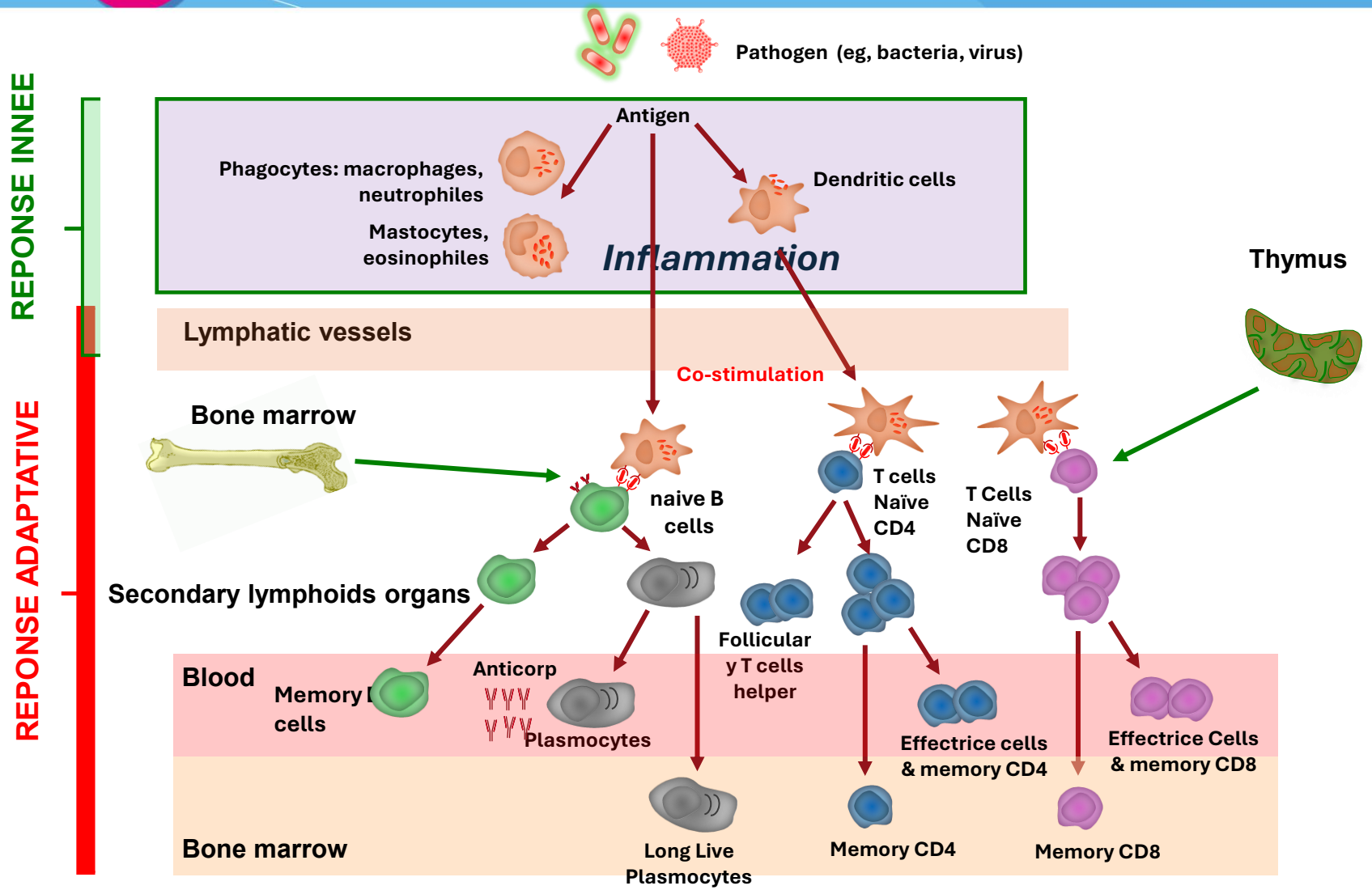
Cellule dendritique 

Immunité acquise spécifique
→ Elimination du pathogène
→ Génération d'une mémoire immunitaire

Lymphocytes

 T CD8  T CD4  B  Ac

Mécanismes Immunitaires : rappels

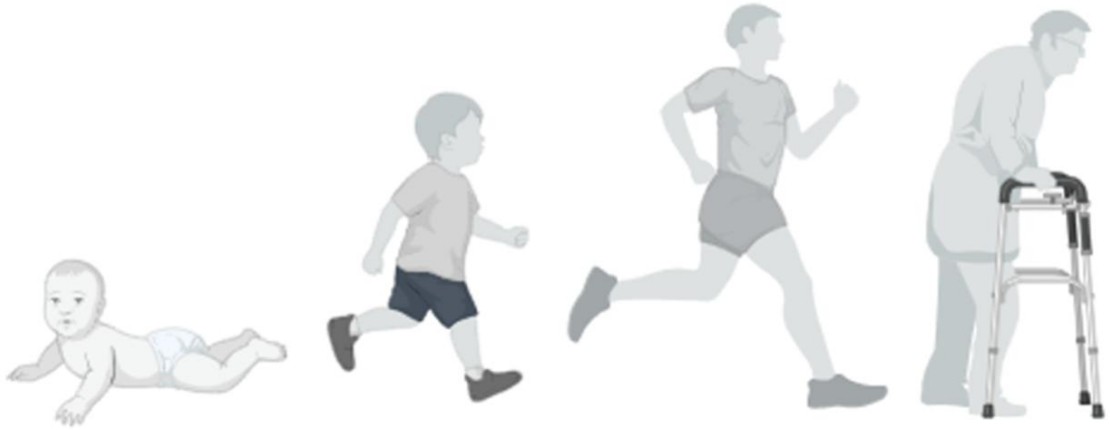


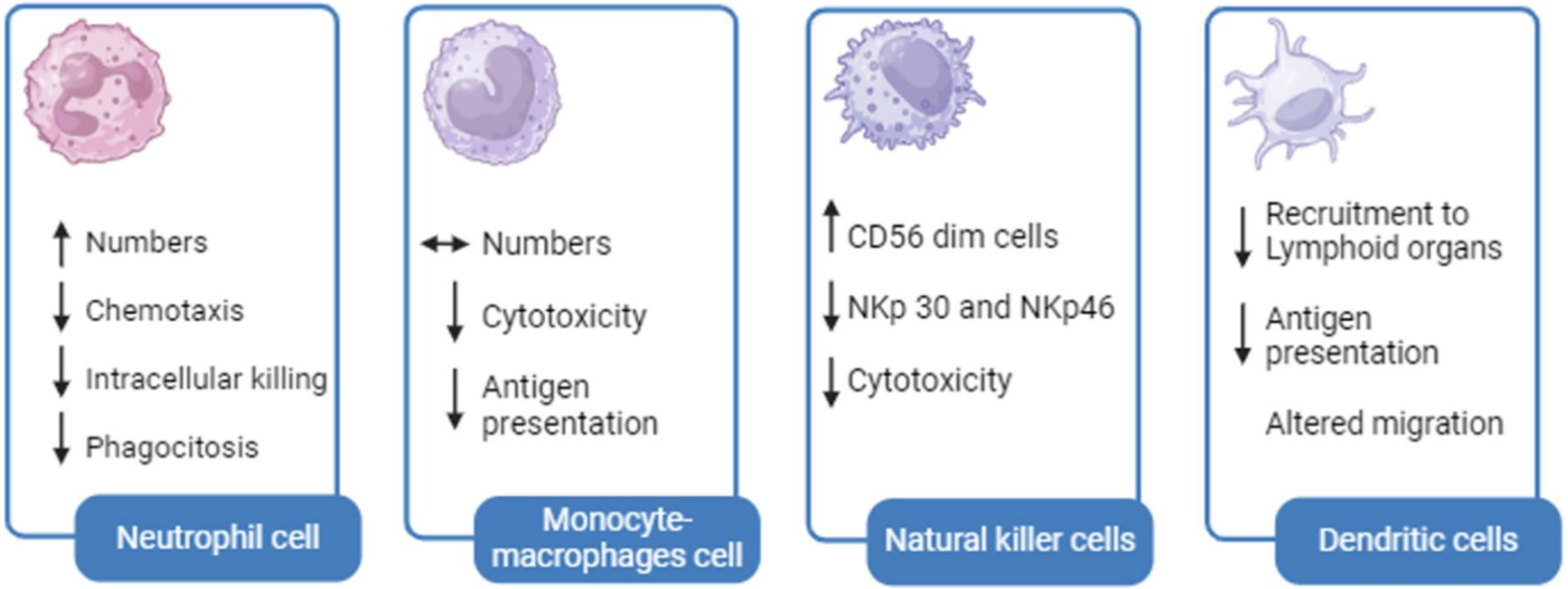
D'APRÈS B Combadières

Delves et al. Roitt's essential immunology. 11th ed. 2006. • Weinberger B et al. Clin Infect Dis. 2008;46:1078-84.

Le Vieillissement immunitaire

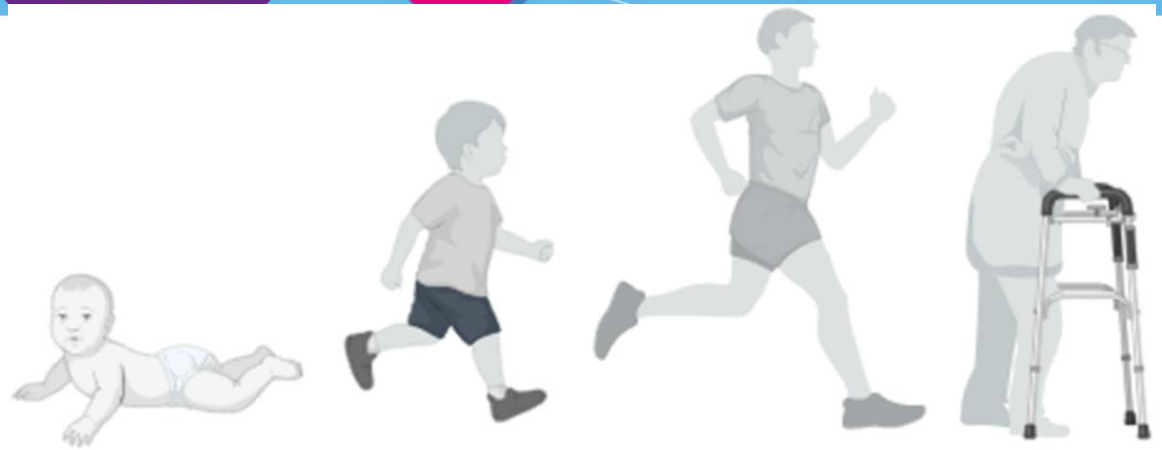
F. Mancinetti et al Mechanism Ageing Dev 2024 .

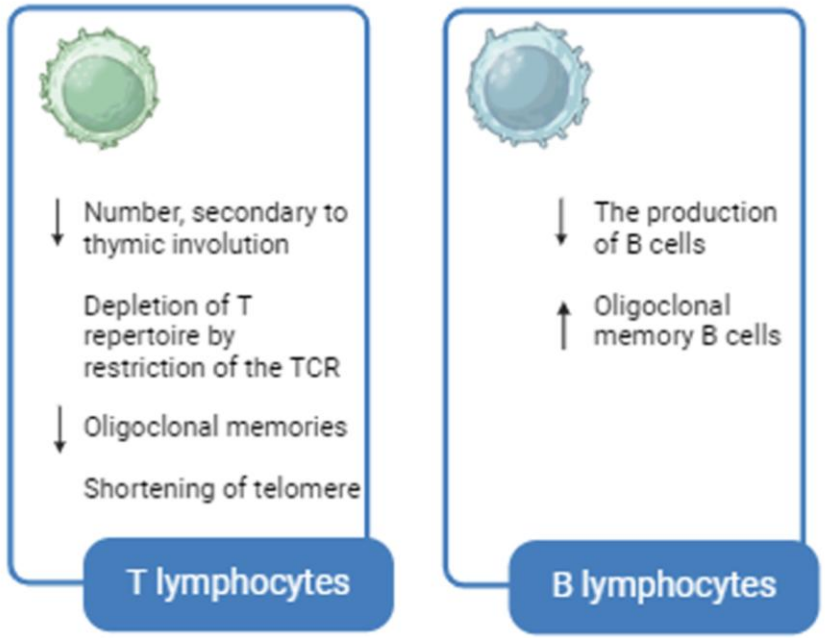




Cretel E Med Mal Infect 2011

Immunité Adaptative





=

Diminution du répertoire de réponse specifique

=

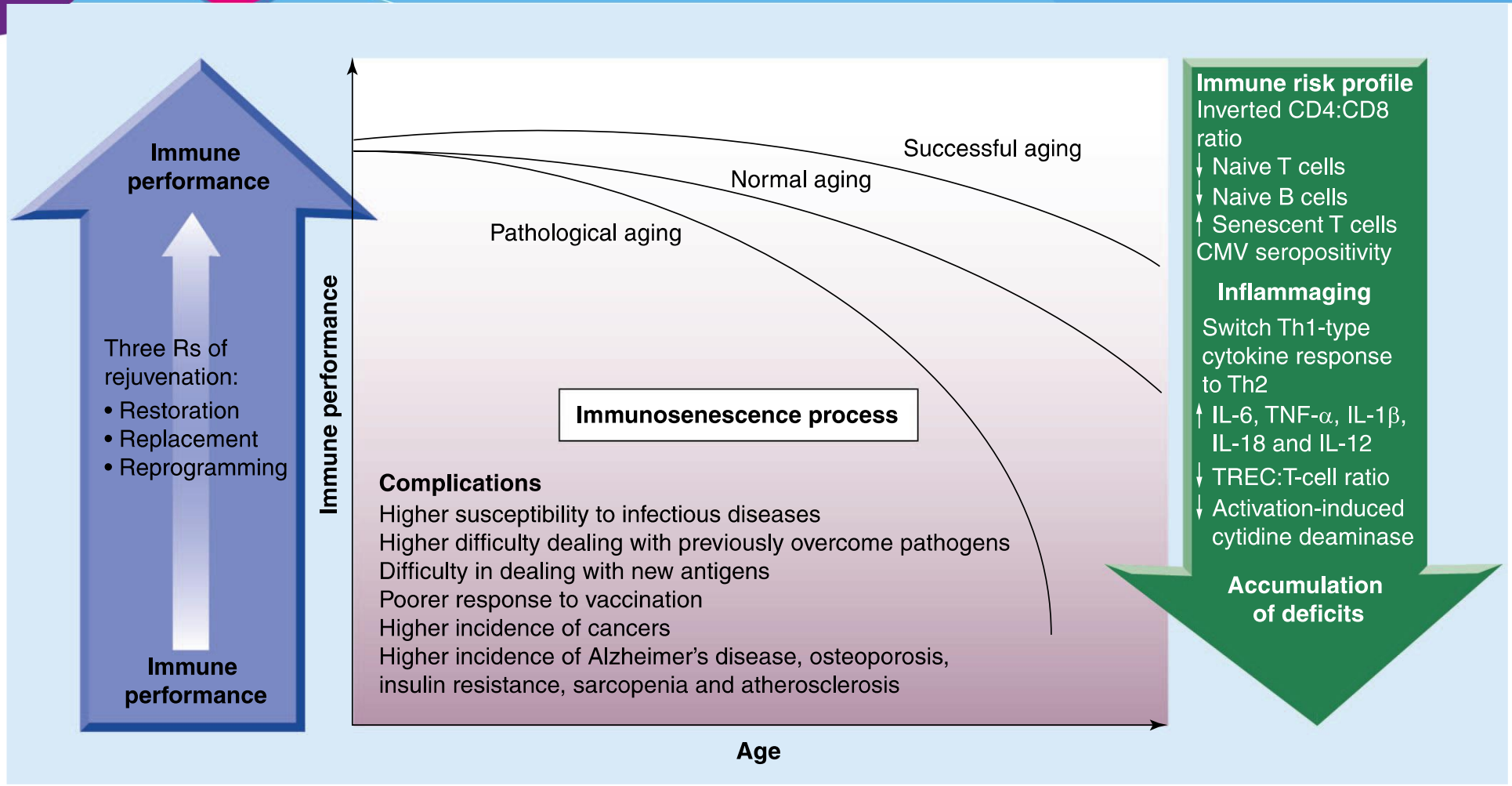
Diminution de l’expansion clonale

=

Moins bonne capacités à répondre aux nouveaux antigènes/ aux Ag connus

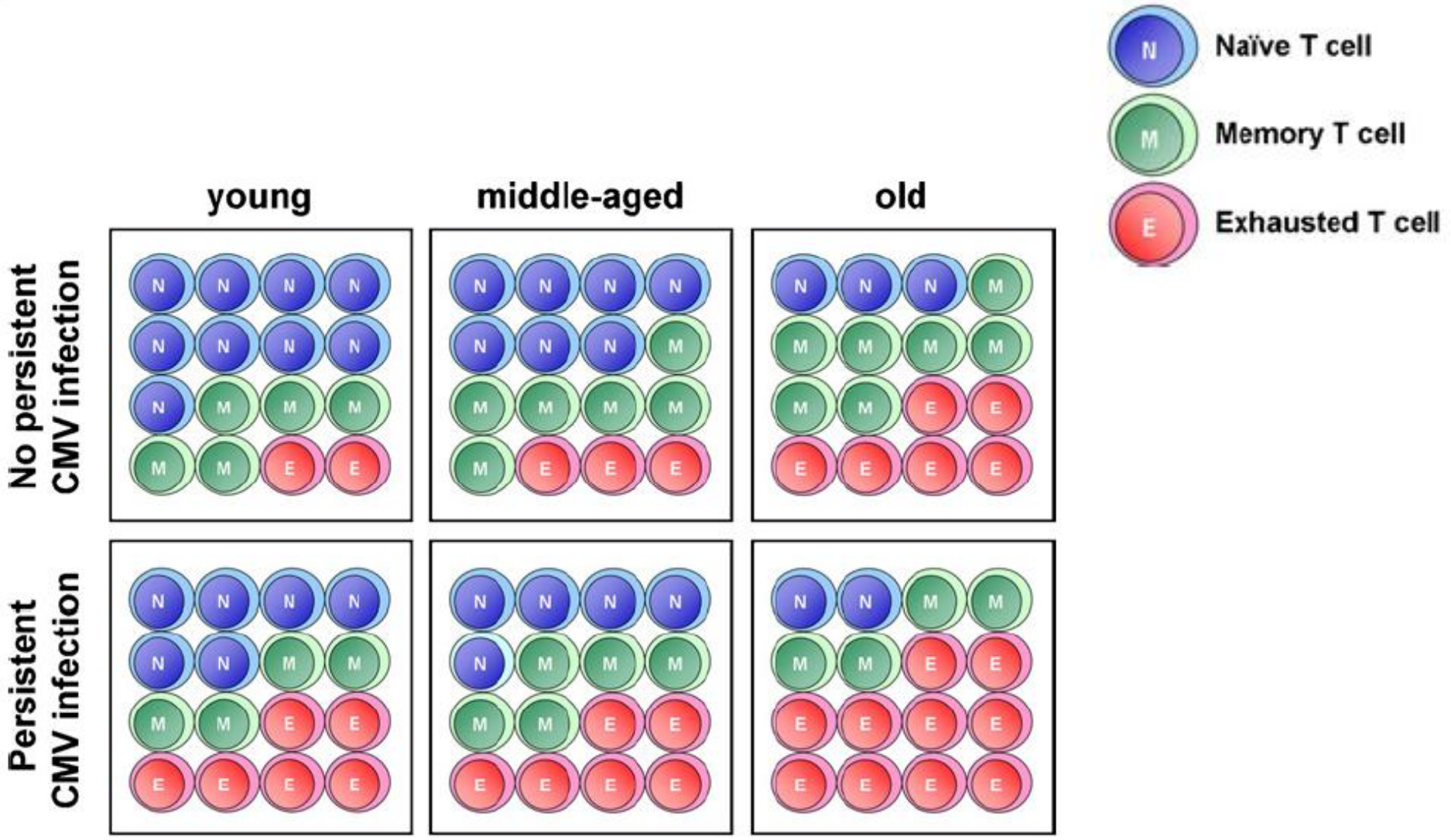
F. Mancinetti et al Mechanism Ageing Dev 2024 .

Immunosenescence : c'est tout !!!!



Lang PO Drug Aging 2014

CMV et Immunosenescence



S. Brunner et al. / Ageing Research Reviews 10 (2011) 362–369

Immunosenescence : biomarqueurs ?

Profile Immunosenescent

CMV + , Prolifération CD8

inflammation (IL6)

CD4/CD8 ratio < 1

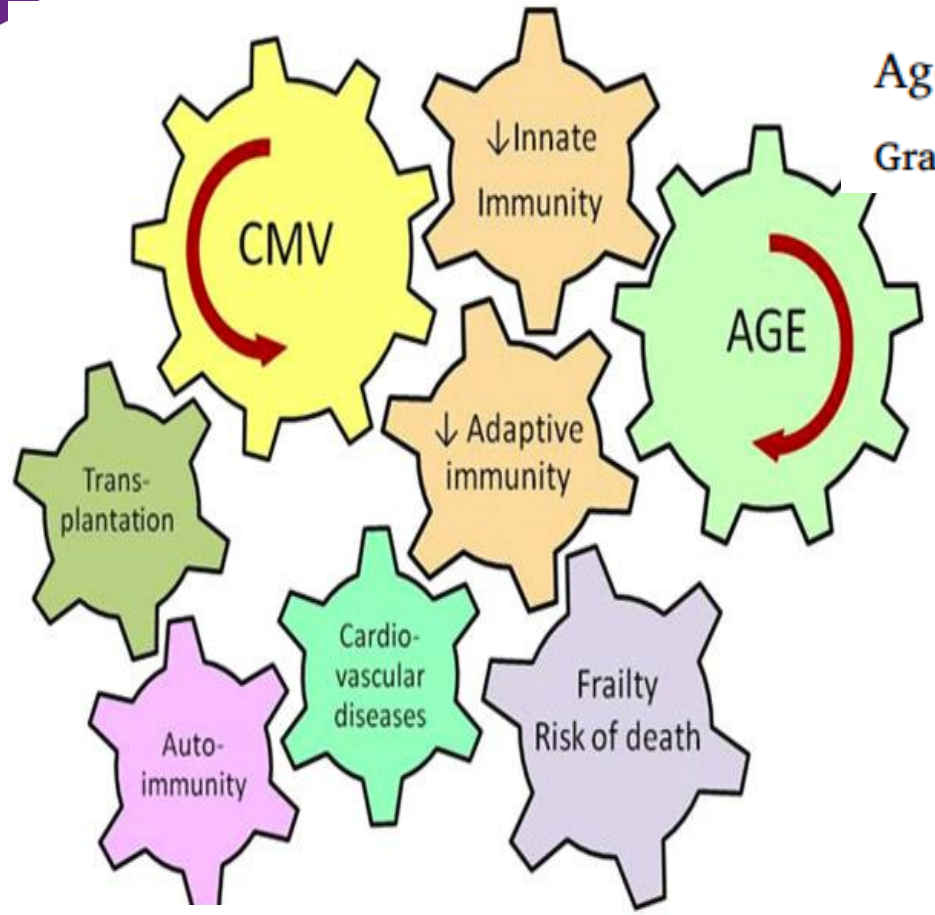
« Inflammaging »

↑ De la production d'IL-4, IL-6, IL-8, IL-10 et TNFα

↓ De la production d'IL-1 et d'IFN-γ

Lang PO Drug Aging 2014 , **McElhaney J** Aging res rev 2011, **Cretel E** Med Mal Infect 2011

Immunosenescence : Limites origine multifactorielle/



D'après B Combadières

Age and immunity: What is "immunosenescence"?

Graham Pawelec*

Etudes de cohortes limitées

Résultats contreversés
malgré SEINIEUR protocol

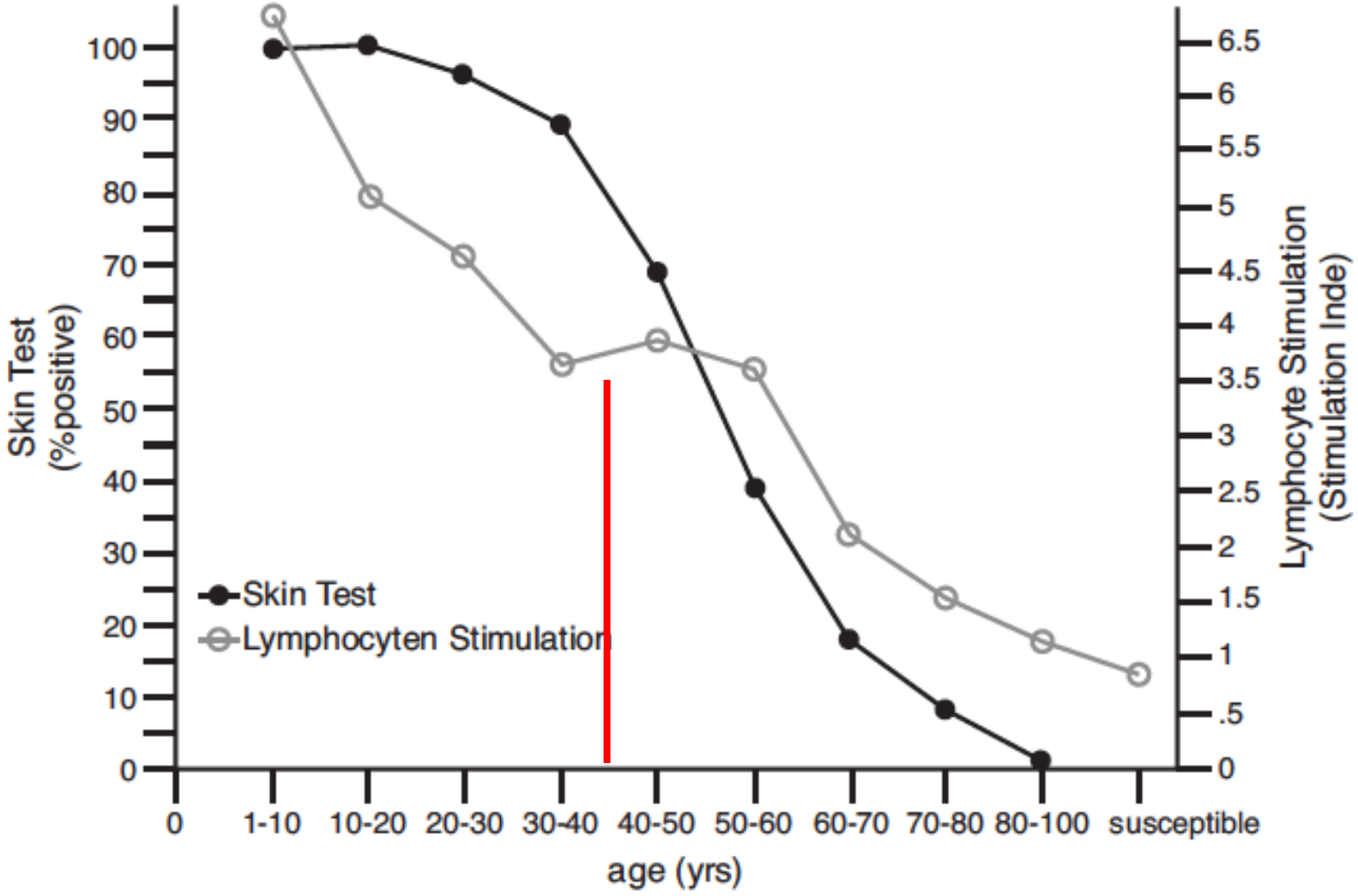
Association Modifications dans le temps
biomarqueurs Immuno variables

Rôle Epigénétique ?

liens avec des marqueurs cliniques non établis ....

Pawelec G Exp Gerontol 2018

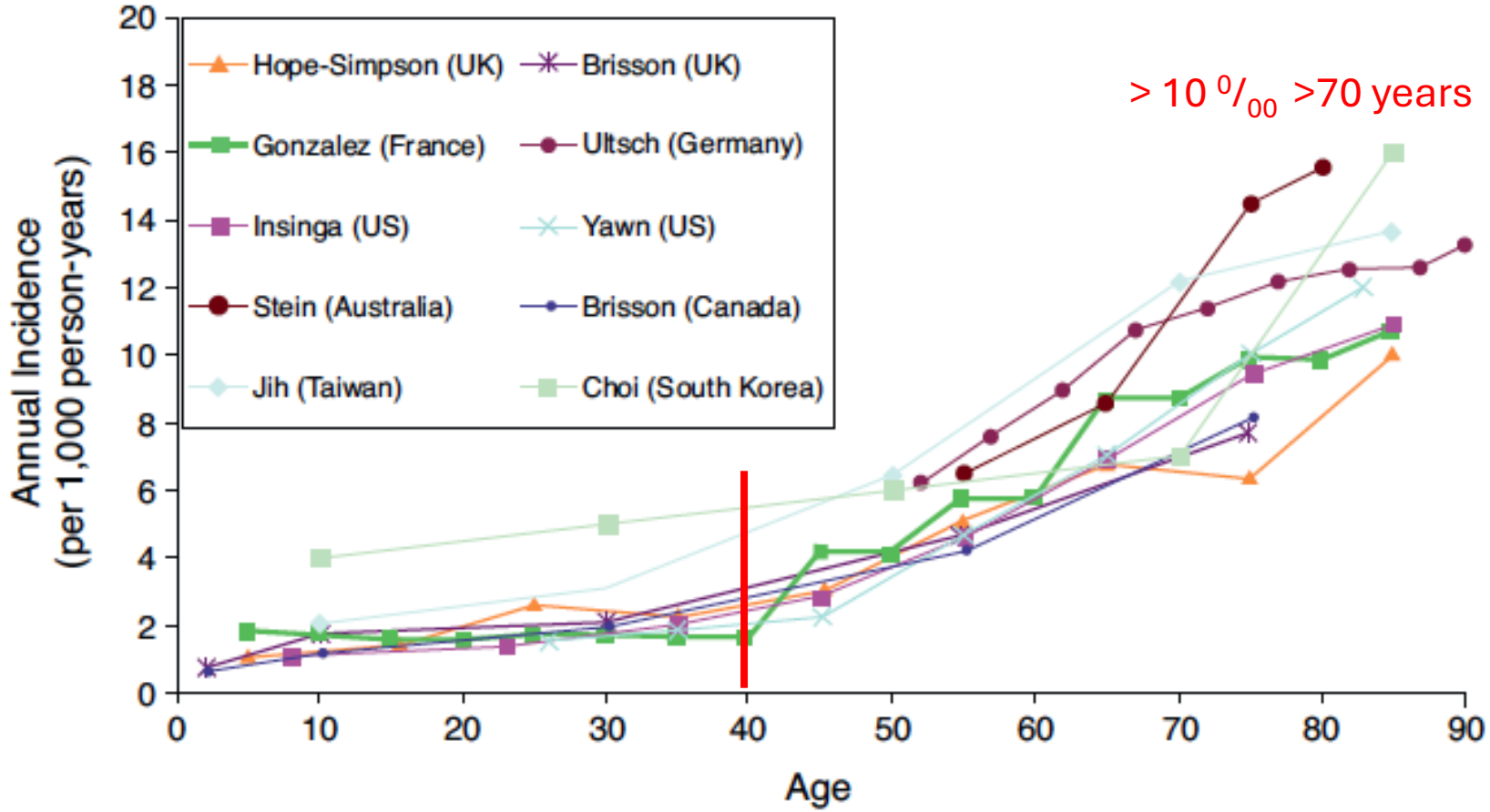
Réponse Immunologique à AgVZV selon l'âge



Levin MJ , *Cur Op IMmunol 2012*

Incidence Zona selon âge

Exemple in France : 300 000 cases /y an > 50% >60 years



> 10 $^{0}/_{00}$ >70 years

1 out of 4/5 individual
will experiment Zoster over his life

Levin MJ , *Cur Op IMmunol 2012*

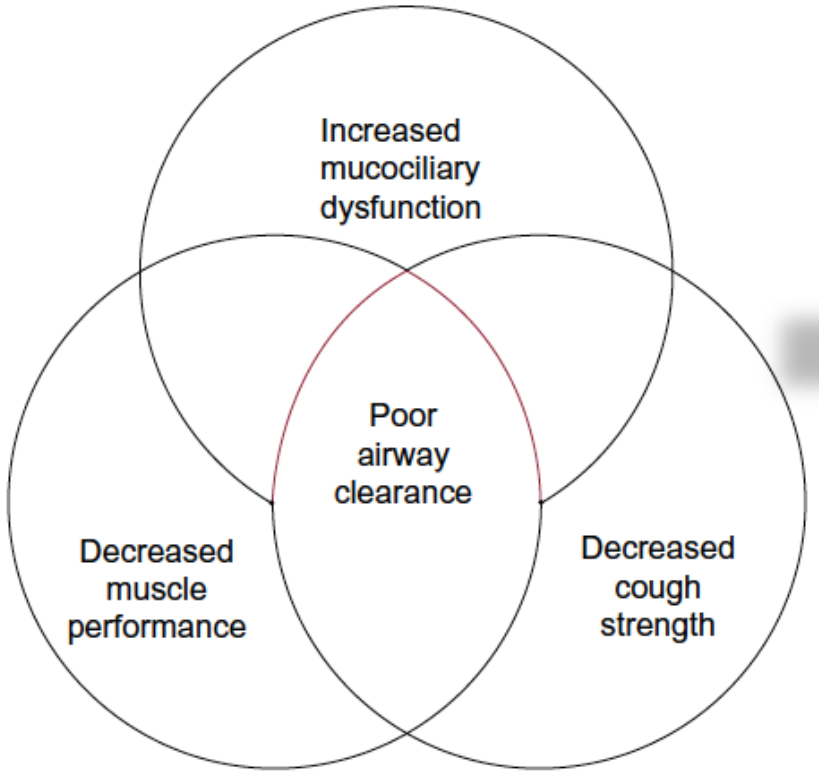
Immunosenescence

Vieillissement des organes ?

comorbidités et FDR

Vieillissement pulmonaire
Défenses immunitaires ?

Défenses locales



Défenses systémiques = Immuno-sénescence

- Diminution activité phagocytaire des PNN sur Pneumocoque avec l'âge
- Diminution des capacités d'opsonisation des anticorps

Est ce l'IS systémique qui joue le rôle majeur ?

Lowery EM et al. Clin Interv Aging. 2013;8:1489-96. • Simell B et al. Vaccine. 2011;29(10):1929-34.

Rôle de la colonisation bactérienne Vieillissement bucco dentaire ?

Majoration de la charge bactérienne avec vieillissement et Mauvaise hygiène bucco dentaire

Types de colonisant changent :

En Plus… du Streptococcus pneumoniae

Staphylococcus aureus,
Pseudomonas aeruginosa,
Klebsiella pneumoniae,
Enterobacter cloacae,
Escherichia coli
+ anaérobies

Majorés par les parondotopathies

Facteurs de risque de Mauvaise hygiène dentaire

Poor diabetic control
Advanced malignancy
Impaired swallowing reflex
Dementia
Cerebrovascular accident
Parkinson's disease
Radiation therapy
Human immunodeficiency virus
Poor functional status
Drug-induced xerostomia

El lSoh AA Lung 2011: 173-180; Quagliarello V Clin Infect Dis 2005 40:1-6

Vieillissement pulmonaire colonisation bactérienne *Streptococcus pneumoniae* ?

Table 1. Subject Characteristics and Pneumococcal Colonization Rate

Characteristic	Total N = 503	Community n = 109	Nursing Home n = 296	Hospital n = 98	*P*-Value
Age, mean ± SD	80.3 ± 10.0	66.2 ± 4.5	84.3 ± 7.4	83.8 ± 6.4	.001
Male:female	0.52	0.43	0.54	0.58	.57
Comorbidities, mean ± SD	2.5 ± 1.8	1.0 ± 1.1	2.7 ± 1.4	3.6 ± 2.4	.001
Antibiotic use within the previous 3 months, n (%)	139 (27.6)	8 (7.3)	93 (31.4)	39 (39.8)	.001
Hospitalization within the previous year, n (%)	162 (32.2)	11 (10.1)	102 (34.5)	51 (52)	.001
Influenza vaccine within the previous year, n (%)	376 (73)	43 (39.4)	258 (87.2)	66 (67.3)	.001
Pneumococcal vaccine, n (%)	187 (37.2)	14 (12.8)	148 (50)	25 (25.5)	.001
Katz score, mean ± SD	14.7 ± 7.2	8.0 ± 0.2	16.4 ± 7.1	17.6 ± 6.8	.001
Pneumococcal colonization, n (%)	21 (4.2)	6 (5.5)	12 (4.1)	3 (3.1)	.69

Taux de colonisation bas <6% quel que soit le lieu de vie
MAIS

During the 3-month follow-up, more than one-quarter of nursing home residents carried a pneumococcus. It is likely

Flamaing J et al. J Am Geriatr Soc. 2010;58(2):396-8.

Bactériémie germes /age

Type of Infection	40-59	60-79	≥80
Escherichia coli			
Female	47.5 (26)	161.4 (39)	403.6 (36)
Male	11.6 (6)	101.4 (21)	249.9 (10)
Total	29.9 (32)	133.7 (60)	356.0 (46)
Staphylococcus aureus			
Female	18.3 (10)	78.7 (19)	145.8 (13)
Male	30.8 (16)	111.0 (23)	424.8 (17)
Total	24.4 (26)	93.6 (42)	232.2 (30)
Gram-positive cocci			
Female	40.2 (22)	169.7 (41)	470.9 (42)
Male	100.2 (52)	318.5 (66)	1149.5 (46)
Total	69.4 (74)	238.4 (107)	681.1 (88)
Gram-negative bacilli			
Female	80.3 (44)	186.2 (45)	594.2 (53)
Male	50.1 (26)	188.2 (39)	749.7 (30)
Total	65.6 (70)	187.2 (84)	642.4 (83)
All BSIs			
Female	124.1 (68)	372.5 (90)	1143.7 (102)
Male	158.0 (82)	593.6 (123)	2149.1 (86)
Total	140.6 (150)	474.6 (213)	1455.0 (188)

X 20

X 10

X 10

Pas de diminution par 10 ou par 20 de activité anti E coli/ Anti Staph…

Uslan DZ Arch Intern Med. 2007

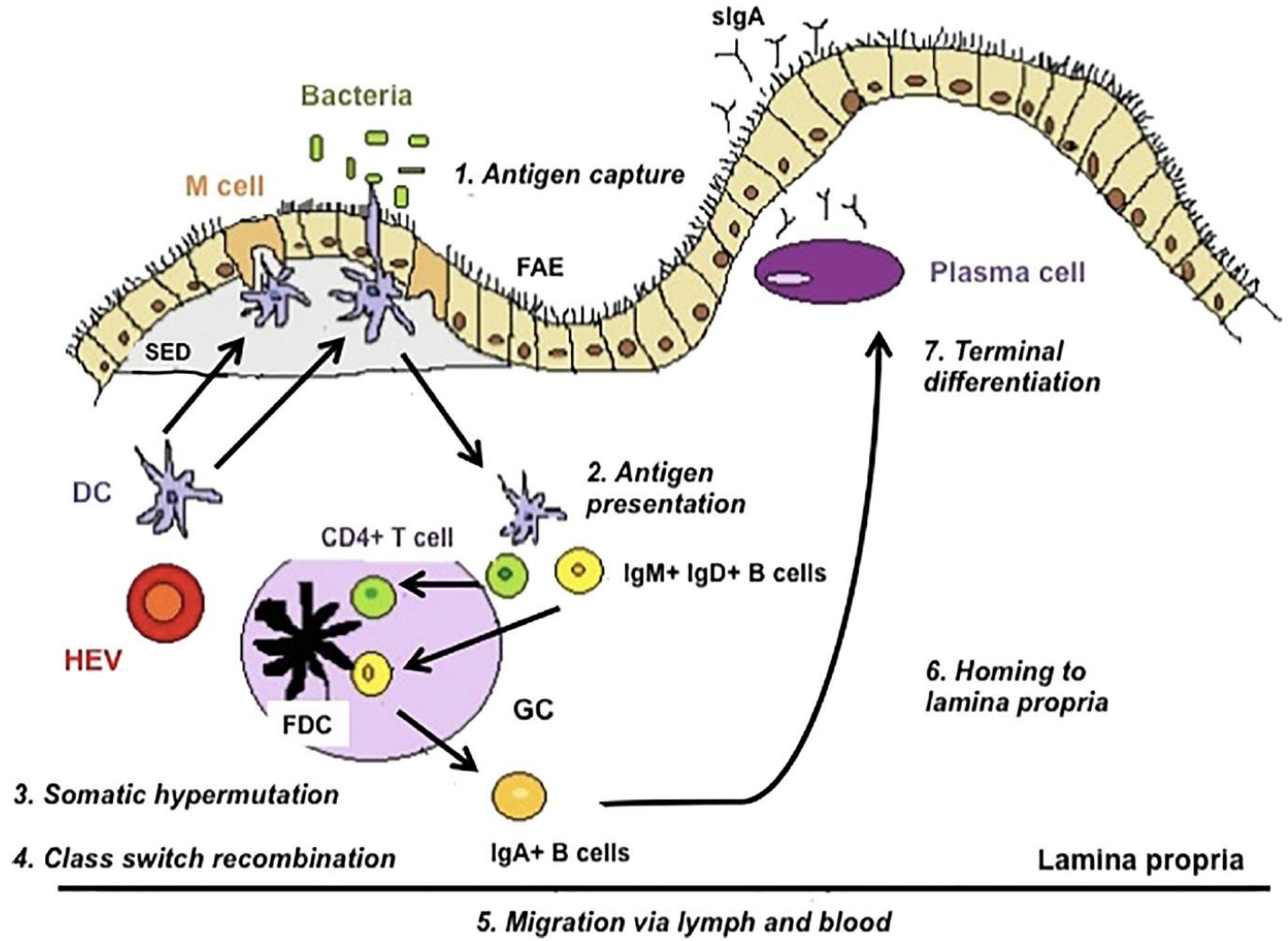
Vieillissement des premières barrières

Peau (Epaisseurs: élasticité, cel Dend, Macrophages..)
Tractus digestif (Cel Dend, Macroph, Ig A....)
Tractus Uro-génital (Obstacle, Immunité locale, Résidu PM)
Tractus respiratoire (... vu..)

Dysfonction motrice....
Modifications anatomiques
Modifications de l'immunité muqueuse
Modifications des microbiomes (Intestinal +++)

Martelli S *BioGerontol* 2016, Gavazzi G *Lancet Infect Dis* 2002

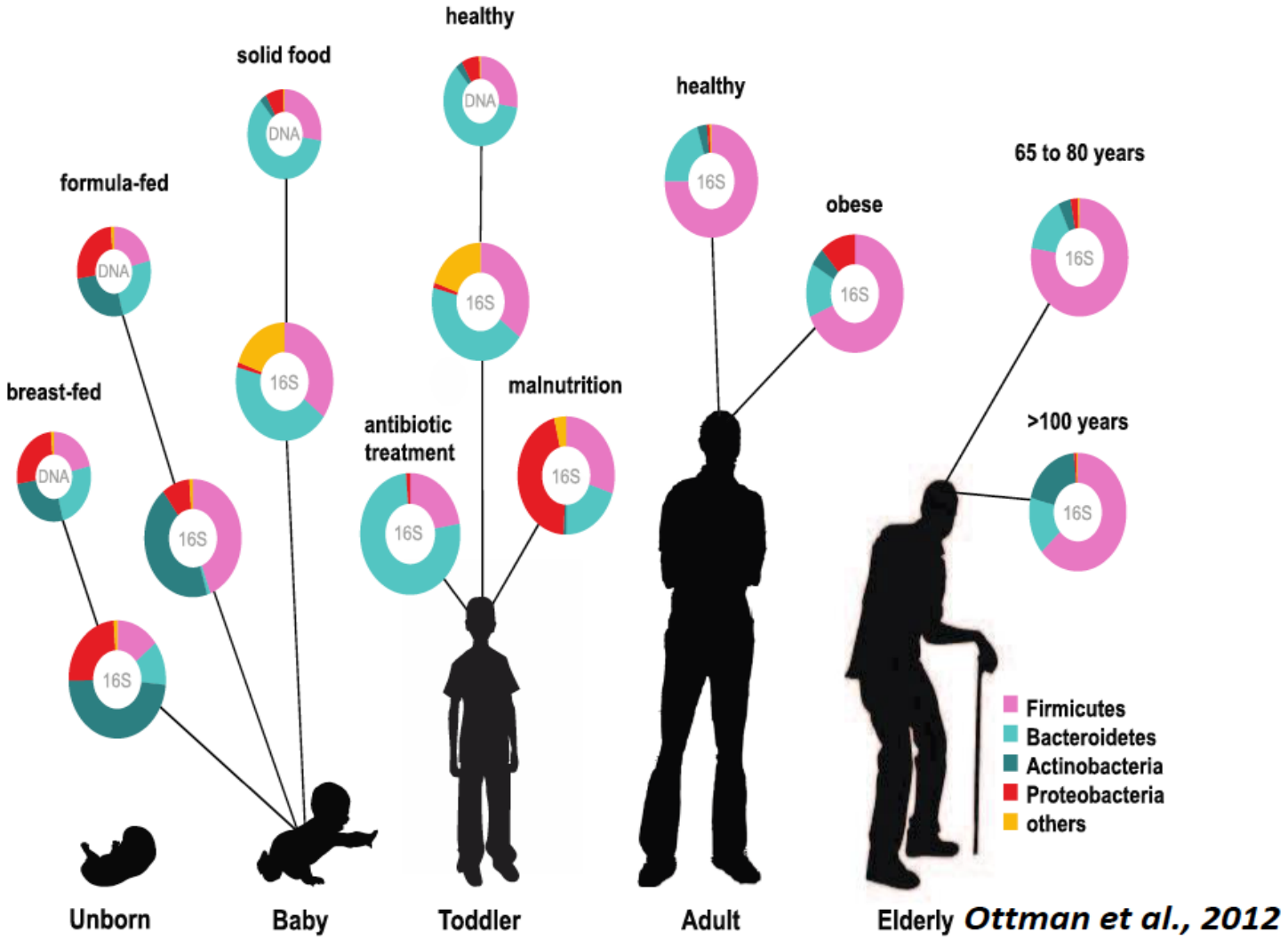
Immunité muqueuse : gut



Martelli S Biogerontology (2016) 17:159–176

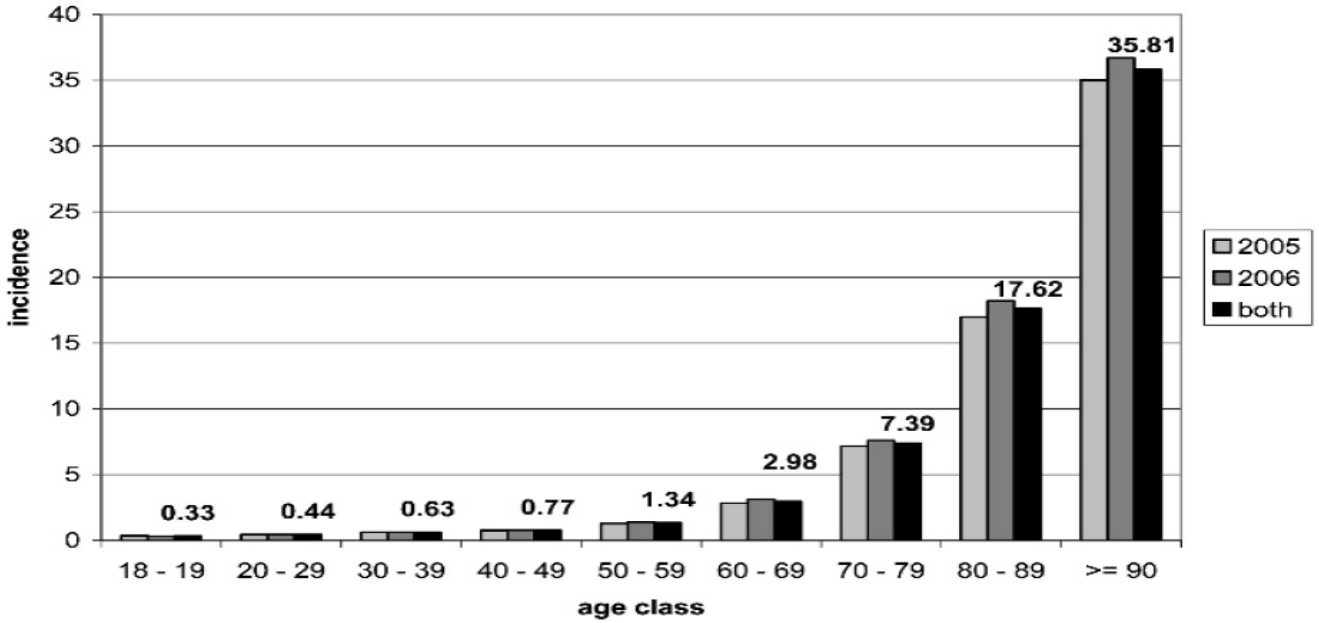
majorations
des translocations
bacteriennes

Vieillissement et microbiote

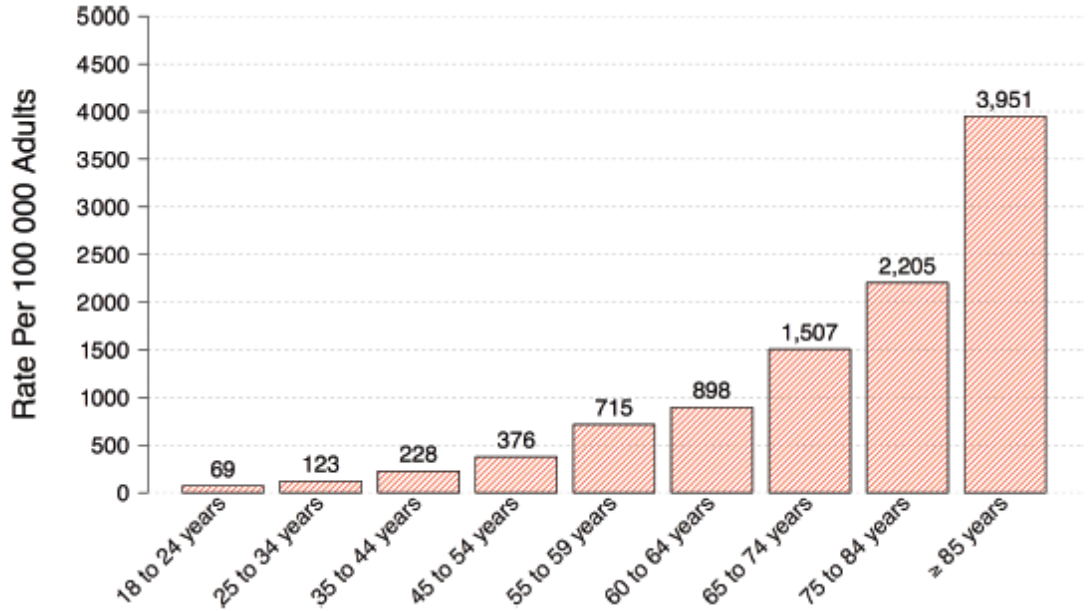


Pneumonies

Pneumonie communautaire

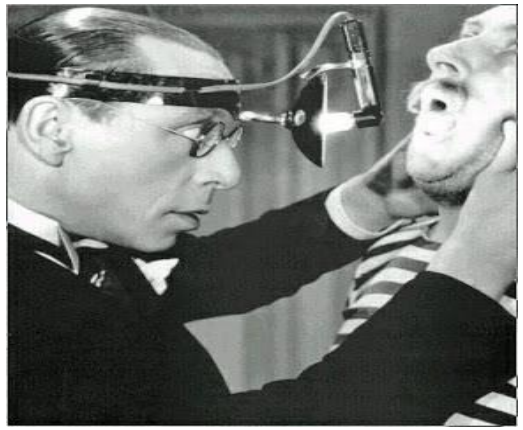


Pneumonie communautaire Hospitalisée



Jeunes / vieux : De x 10 à x 50

Ewig S et al. Thorax 2009;64:1062-69. Ramirez CID 2017



soit 1.000 à 5.000/100.000

Prévalence	>65 ans	>80 ans
Pneumonie communautaire	1‰	10‰
Pneumonie nosocomiale	1%	à 5%
Pneumonie en EHPAD	1%	à 4,6%

incidence 0.3- $2/_{1000}$RJ

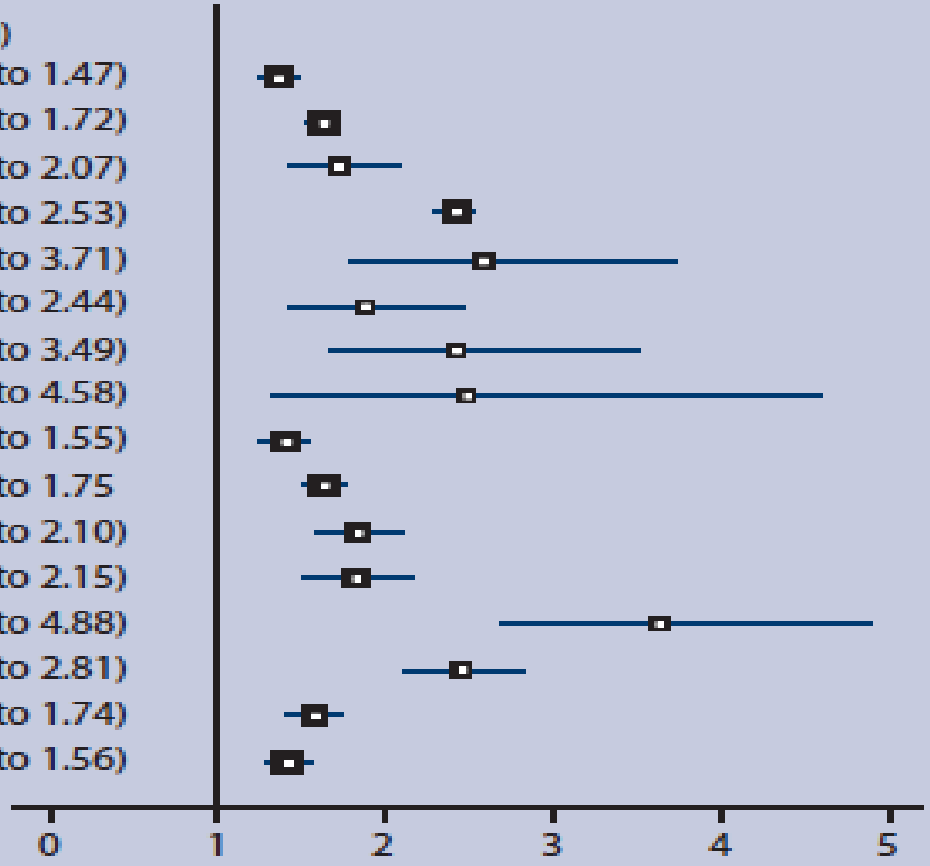
France: Incidence annuelle en EHPAD : 21% (Incur)

Kelaiditi E et al. J Am Med Dir Assoc. 2014;15(8):588-92. • Ewig S et al. Thorax 2009;64:1062-69. • Kaplan V et al. Am J Respir Crit Care Med. 2002;165(6):766-72. • Enquete EPIPA. http://cclin-sudest.chu-lyon.fr/EHPAD/EHPAD_prevalence/auvergne/rapport.pdf • Chami K et al. J Hosp Infect. 2011;79(3):254-9.; Mylotte JM Clin ger Med 2007, ; Ramirez Clin Infect Dis 2017

Pneumonie et comorbidités

Adjusted odds ratios and 95% confidence intervals

Diagnosed with	N cases/controls	OR (95%CI)
Diabetes	1334/3847	1.36 (1.27 to 1.47)
Heart disease	3239/8585	1.63 (1.54 to 1.72)
Renal disease	203/386	1.72 (1.43 to 2.07)
Respiratory disease	4468/8843	2.42 (2.31 to 2.53)
Asplenia	55/81	2.58 (1.80 to 3.71)
Chronic liver disease	94/17	1.87 (1.43 to 2.44)
Sickle cell/Coel. disease	55/85	2.42 (1.68 to 3.49)
HIV/AIDS	22/31	2.48 (1.34 to 4.58)
Immunosuppressed	776/2910	1.40 (1.26 to 1.55)
Stroke or TIA	1454/3583	1.63 (1.52 to 1.75
Rheumatoid athritis	387/821	1.84 (1.62 to 2.10)
Parkinson's disease	230/513	1.82 (1.53 to 2.15)
Multiple sclerosis	85/112	3.63 (2.70 to 4.88)
Dementia	385/674	2.45 (2.13 to 2.81)
Osteoporosis	650/1578	1.57 (1.41 to 1.74)
Any cancer	1151/2976	1.42 (1.30 to 1.56)



Adjusted for deprivation, smoking, all diseases, use of vaccines,

Immunodépressions : ~1,8 millions

Vinogradova Y et al. Brit J Gen Pract. 2009;59:716-17. *Wyplosz B, Fernandes J, Infect Dis Now 2021;51*

des risques + spécifiques

Risk Factor		(OR) IC (95%)
Gender	1.710	1.223–2.391
Sputum suctions	4.477	2.901–6.909
Daily oxygen therapy	5.719	1.908–17.145
Nutrition support (nasogastric tube o	3.362	2.227–5.077
Urinary Catheterisation	1.850	1.122–3.052
Deterioration of swallowing function	4.783	3.310–6.911
Fever with acute infectious diseases	2.020	1.410–2.894
Dehydration	4.163	2.583–6.711
Dementia	1.545	1.121–2.129
Deterioration of swallowing function	3.584	1.948–6.592

Trouble de la déglutition / Sonde de nutrition / Deshydratation / Oxygene/ Dépendance fonctionnelle.....

Manabe T et al. PLosONE 2015 :1-12 . Rothan-tondeur J Am Ger Soc 2003 , Loeb M Arch Intern Med 1999

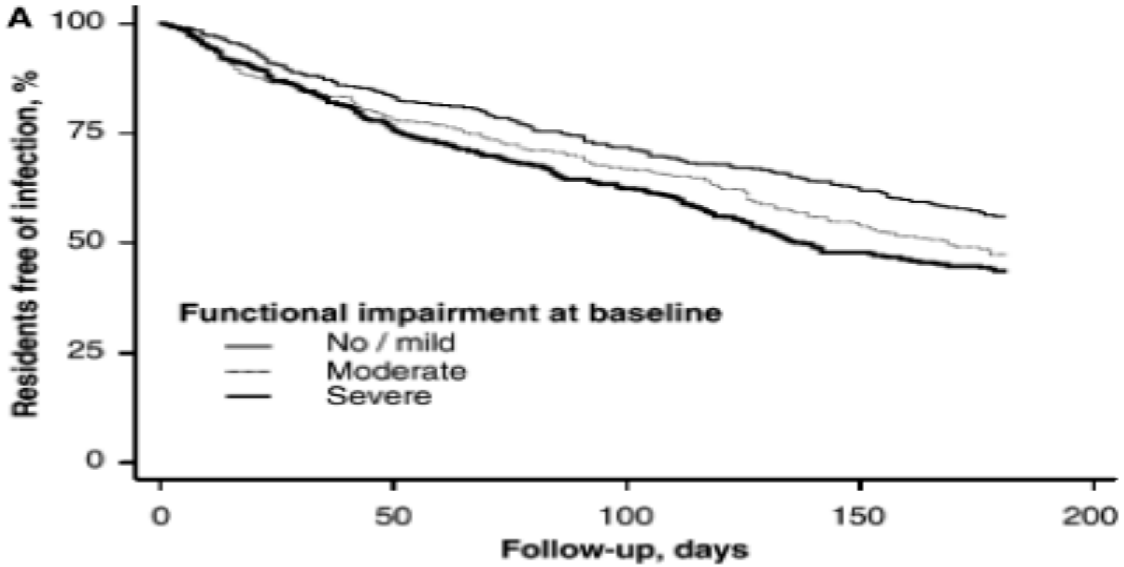
FDR pneumonie: Statut fonctionnel

Loeb M Arch Intern Med 1999

(prospective study, 85 y, 254 à 79 patients 3y)

Respiratory tract infection in « Nursing home »

- ↘ Functional status = ↗ incidence x 2.6(1.8-3.8)



Bula *JAGS* 2005

prospective study, Infections in « Nursing home »

3 niveaux d'ADL, 85 y, 1070 patients

6 month follow up

Dépendance/ Nutrition

FDR de Pneumonie ?

- Pop âgé > 65 ans
- Plus on est vieux plus les FDR dependance/ nutrition élevés

Variable	Full Population
No lung disease	Reference
Lung disease, no medication or oxygen	2.0 (1.5–2.7)
Lung disease with medication but not oxygen	2.5 (2.2–3.0)
Lung disease, using oxygen	8.3 (5.5–12.7)
No heart disease	Reference
Non-CHF heart disease	1.2 (1.1–1.4)
Mild CHF	1.9 (1.5–2.5)
Severe CHF	3.3 (2.3–4.7)
Middle quintile of sex-specific weight	Reference
Lowest quintile of sex-specific weight	1.5 (1.3–1.9)
Second quintile of sex-specific weight	1.1 (0.9–1.3)
Fourth quintile of sex-specific weight	1.1 (0.9–1.3)
Highest quintile of sex-specific weight	0.9 (0.7–1.2)
Weight missing	0.4 (0.2–0.7)
<10% weight change	Reference
>10% weight loss during baseline	1.9 (1.3–2.6)
>10% weight gain during baseline	1.1 (0.7–1.8)
No functional impairments	Reference
One impairment	1.3 (1.0–1.6)
Two or more impairments	2.1 (1.2–3.5)
Nonsmoker or no smoking data	Reference
Former smoker	1.3 (1.1–1.5)
Current smoker	1.8 (1.4–2.3)
Any use of home health services	1.6 (1.3–1.9)

Jackson ML et al. J Am Geriatr Soc. 2009;57(5):882-8.

Infection associée aux soins, et dépendance

infection Nosocomiale

level of ADL, 85 y, 214 patients

↘ Functional status = ↗ prevalence NI

	Non adjusted		Adjusted	
	OR (CI 95 %)	**p**	**OR (CI 95 %)**	**p**
Urinary tract indwelling	5,8 (2,5-13,9)	<0,01	4,4 (1,6-12,3)	<0,01
ADL<3 at admission	6,5 (2,4-17,3)	<0,01	4,4 (1,8-11,1)	<0,01
New functional decline	2,3 (1,1-4,7)	0,02	-	-
Pressure sore	3,3 (1,4-7,7)	<0,01	-	-
Pneumonia	3,3 (1,6-7,2)	<0,01	-	-
Life threatening diagnosis	3,1 (1,3-7,1)	<0,01	2,7 (1,1-6,6)	0,03

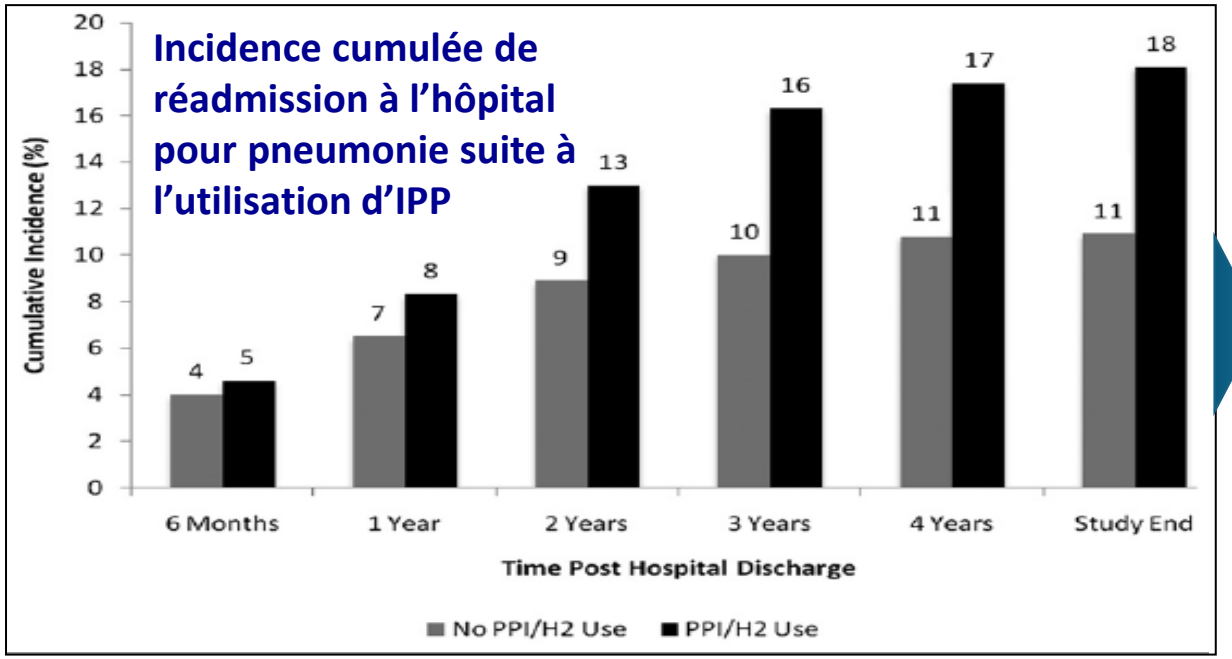
Independant de : recente surgery, ATBique, catheter…

Maziere S, Gavazzi G, *JNHA 2013*

Médicaments et Pneumonie :

les inhibiteurs de la pompe à protons (IPP)

IPP	Nbre de cas (%)	Témoins (%)	OR non ajusté	OR ajusté (IC95%)
Oméprazole	68 (14,3%)	470 (9,5%)	1,80	1,74 (1,28-2,35)
Pantoprazole	25 (5,3%)	132 (2,7%)	2,47	2,29 (1,43-3,68)
Lansoprazole	5 (1,1%)	70 (1,4%)	0,91	0,91 (0,35-2,34)

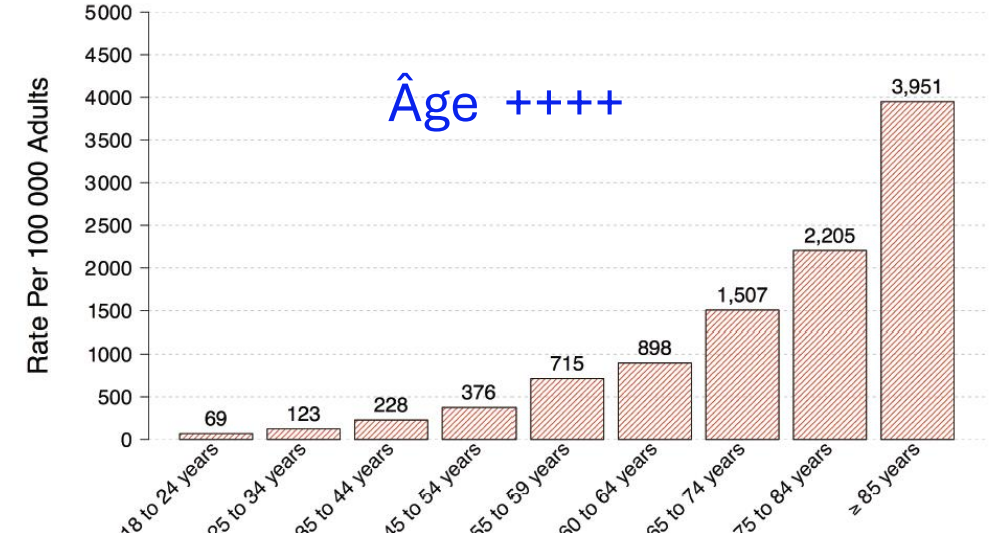


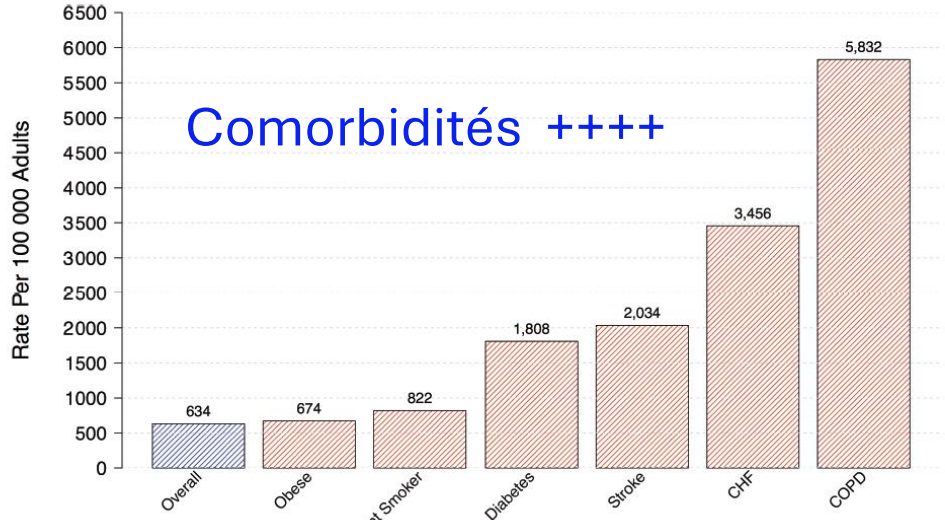
Augmentation dès les 12 premiers mois (jusqu'à près de 60% à 4 ans)

Laheij RJF et al. JAMA. 2004;292(16):1955-60. • Eurich DT Am J Med. 2010;123(1):47-53.

1 Marqueur > tous des P. Communautaires

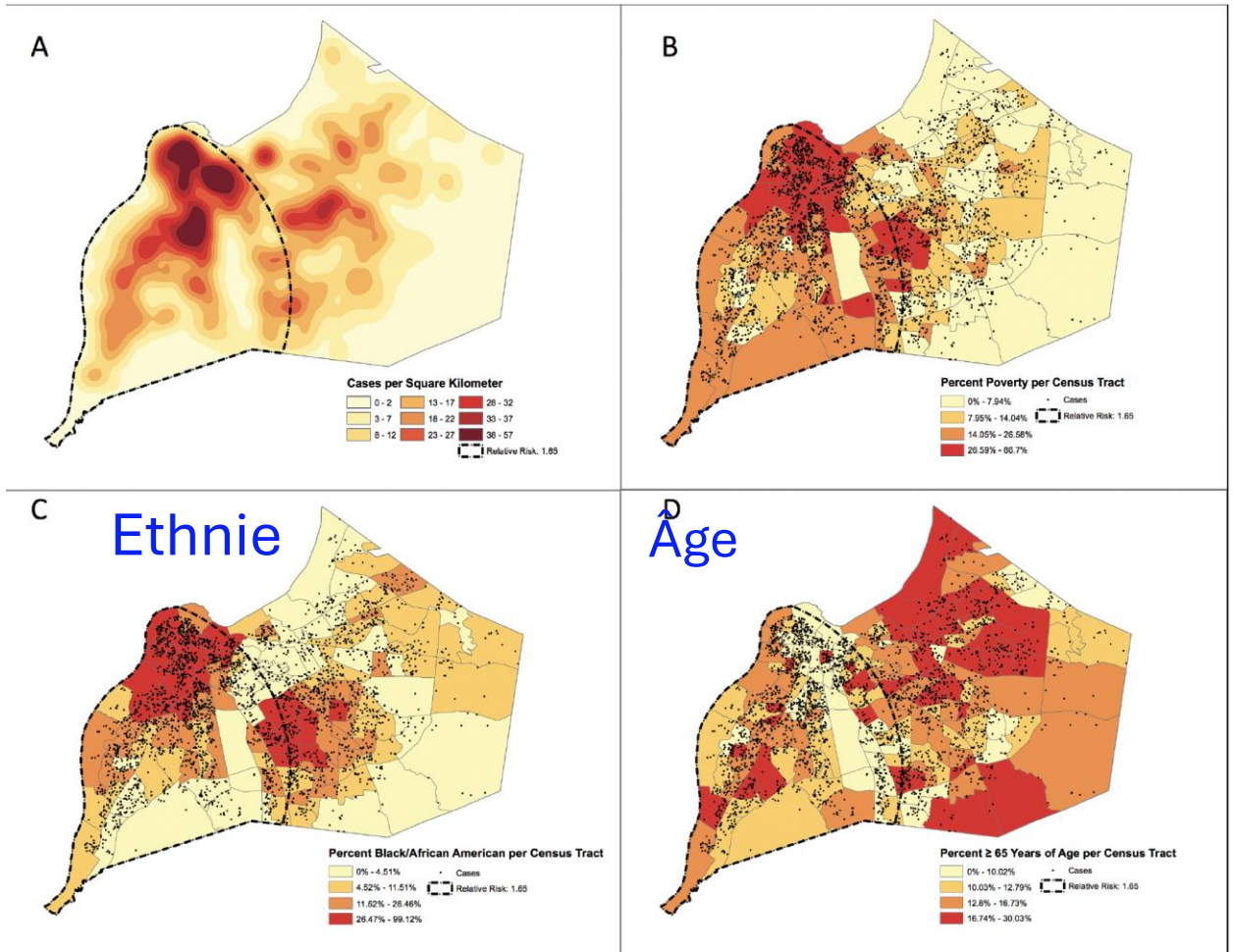
Ramirez et al CID 2017:65





Niveau Socio-Economique

TOUT



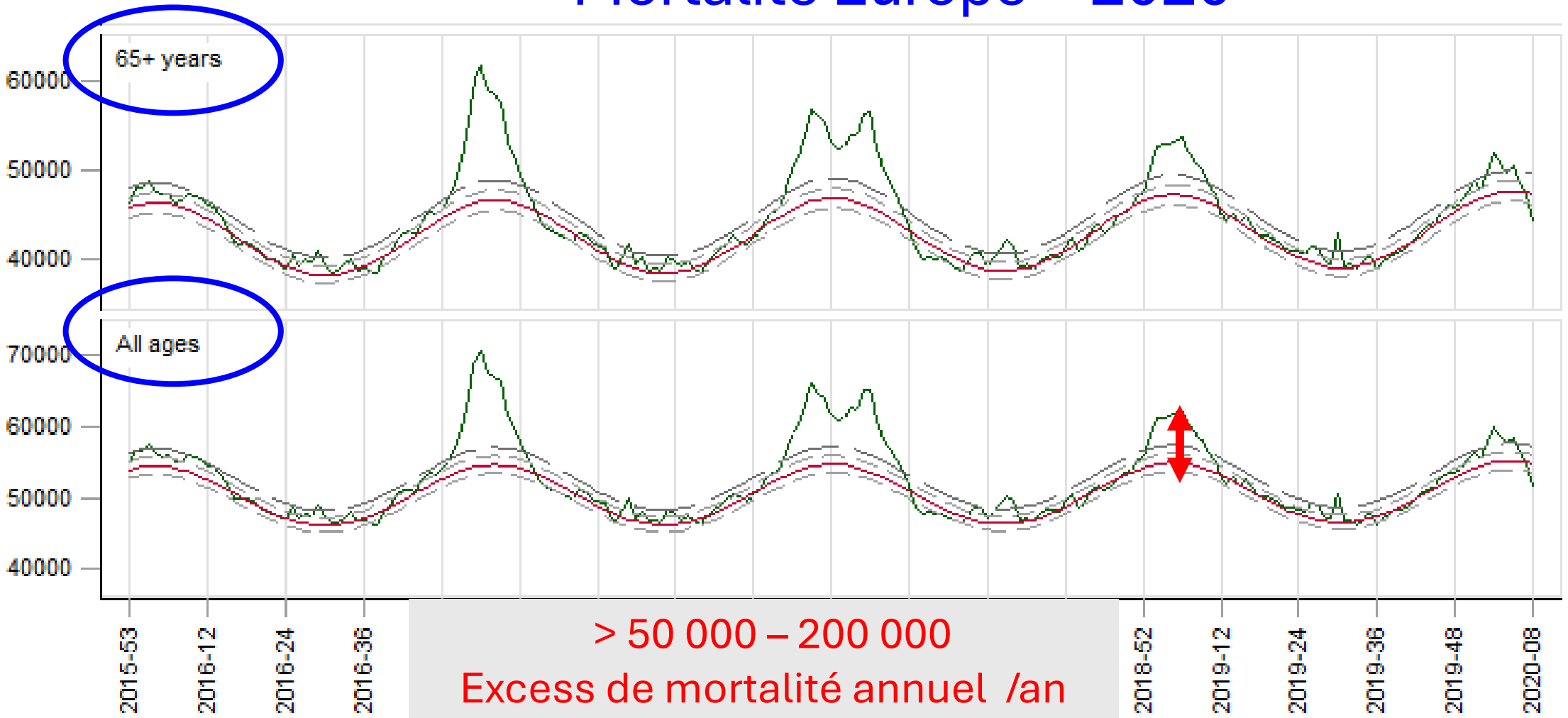
Pourquoi les infections sont

.....

plus graves

chez les personnes âgées ?

Mortalité Europe < 2020



> 50 000 – 200 000
Excess de mortalité annuel /an

http://www.euromomo.eu

Reconnaitre l’infection grave

20 ans
3 définitions qui changent

SEPSIS-1 (1992)[1]

SRIS	SEPSIS	SEVERE SEPSIS	SEPTIC SHOCK
-T >38 ou T < 36°C -FR > 20 ou pCO2 < 32mmHg -Fc > 90 bpm -GB > 12000 ou < 4000 g/dL	Infection + > 2 SIRS critères	+dysfonction d'organe ou hypotension, lactatémie, oligurie, confusion	+ hypotension réfractaire à un remplissage vasculaire adéquat

SEPSIS-2 (2001)[2]

SEPSIS	SEVERE SEPSIS	SEPTIC SHOCK
Infection + > 2 SIRS critères + signes (oligurie, hypoxémie, instabilité hémodynamique)	+dysfonction d'organe ou hypotension, lactatémie, oligurie, confusion	+ hypotension réfractaire à un remplissage vasculaire adéquat

SEPSIS-3 (2016)[3]

SEPSIS	SEPTIC SHOCK
Infection + SOFA>2	Sepsis + hypotension réfractaire au remplissage necessitant l'introduction de vasopressor >PAM 65mmHg et/ou lactate >2mmol/L

[1]Bone et al,. The ACCP/SCCM, American College of Chest Physicians/Society of Critical Care Medicine, 1992

[2]Levy et al, 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference, 2001

[3]Singer et al, The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), JAMA 2016

Definition....

Sepsis
Life threatening organ dysnfunction caused by a dysregulated host response to infection

Septic shock
Sepsis + vasopressor therapy needed (i.e., cardiovascular failure)

JAMA The Journal of the American Medical Association

Singer et al., JAMA 2016

Gravité : SOFA / qSOFA

Sequential Organ Failure Assessment

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

qSOFA

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≤100 mm Hg

Soyons simples :

Hemodynamique

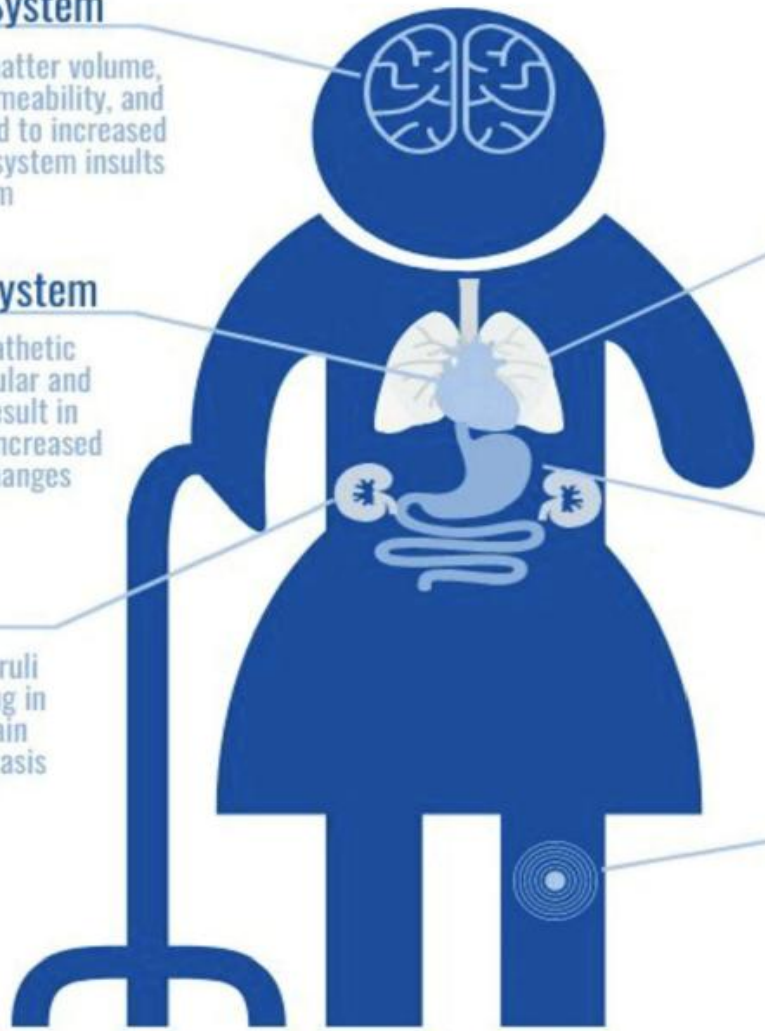
Neurologique

rRespiratoire

> 11 mortality rate = 50%

Singer et al, The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), JAMA 2016, Soo et al. Critical Care 2019, 23(186):1-15

Aging Systems and Impact on Critical Illness



Central Nervous System

increased grey-white matter volume, blood-brain-barrier permeability, and endothelial function lead to increased risk of central nervous system insults and delirium

Cardiovascular System

increased resting sympathetic tone and decreased vascular and myocardial relaxation result in preload dependence and increased sensitivity to volume changes

Renal System

decreased functional glomeruli and renal blood flow resulting in decreased ability to maintain sodium and volume homeostasis

Respiratory System

increased risk of aspiration, respiratory infections, and acute respiratory failute due to decreased mucociliary clearance and decreased cough and swallow reflex

Immune System

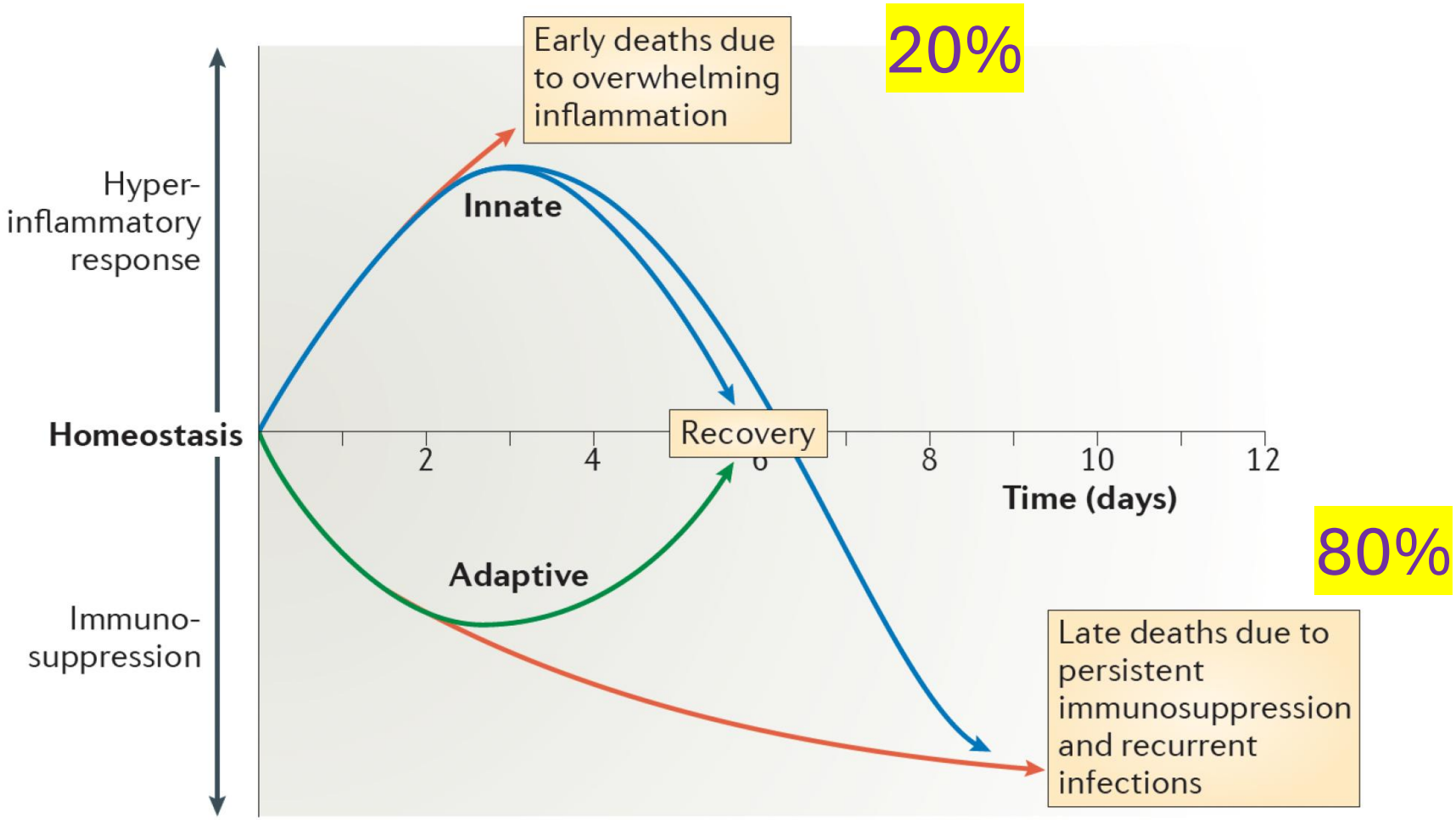
age-dependent decline in function with increased risk of dysregulated response to systemic infection

Musculoskeletal System

increased risk of pre-existing malnutrition and associated sarcopenia, anemia, and functional decline

Brunker LB et al Clinical Interventions in Aging 2023

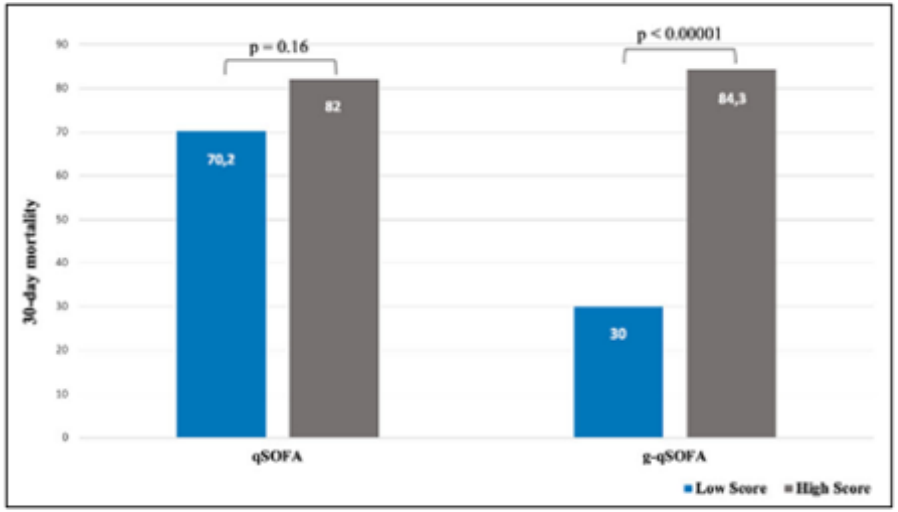
Balance PRO and ANTI Inflammatoire



Plus vous vieillissez plus c'est vrai ?

Hotchkiss, Monneret, Payen. Nature Rev Immunol 2013

Reconnaitre un sepsis : “qSOFA” or Geriatric-qSOFA



A. qSOFA and geriatric-qSOFA in relation to 30-day mortality

	qSOFA	Geriatric qSOFA
Sensitivity	73.2%	92.6%
Specificity	40.7%	50.0%
OR	1.87	12.5
Accurancy	48.8%	81.7%
PPV	29.1%	84.3%
NPV	81.9%	70.0%
Youden index	0.14	0.43

Note: OR Odds Ratio, *PPV* Positive Predictive Value, *NPV* Negative Predictive Value

B. Performance indicators of qSOFA and geriatric-qSOFA

Geriatric score use CAM definition for delirium and not Glasgow scale

Specific score is better but still enought usefull? G-q

Remelli et al. BMC Geriatrics (2021) 21:241
https://doi.org/10.1186/s12877-021-02182-1
BMC Geriatrics
RESEARCH ARTICLE Open Access
Predictive value of geriatric-quickSOFA in hospitalized older people with sepsis

Remelli et al, Predictive value of geriatric-quickSOFA in hospitalized older people with sepsis, 2021

Outcome of Septic Shock in Older Adults After Implementation of the Sepsis "Bundle"

Ali A. El Solh, MD, MPH, Morohunfolu E. Akinnusi, MD, Leith N. Alsawalha, MD, and Lilibeth A. Pineda, MD

J Am Geriat Soc 2008

-**Antibiotics** (to be administered within 4 hours)
Please consult selection guideline on reverse sheet

-**Early Goal Directed Therapy** (to be initiated within the first 6 hours)
- Insert central venous catheter and arterial line
- If CVP < 8 mmHg, infuse 0.9 NS 500 ml IV over 30 minutes. Repeat until CVP between 8-12 mmHg or between 12-15 mmHg in mechanically ventilated.
- If mean arterial pressure remains < 65 mmHg, start norepinephrine at 5 mcg/min and titrate to target MAP of 65 to 90 mmHg. Add Dopamine if necessary up to 10 mcg/min to achieve MAP of 65 to 90 mmHg.
- Measure central venous oxygen saturation every 30 minutes. If ScvO2 <70% transfuse 2 units of packed red blood cells to achieve hemoglobin < 10.0 g/dl, otherwise start dobutamine at 2.5 mcg/kg/min intravenously and titrate by 2.5 mcg/kg/min to a target ScvO2 ? 70% (maximum dose: 20 mcg/kg/min).
- If norepinephrine dose > 1.0 mcg/kg/min, initiate vasopressin at 0.04U/hr intravenously

-**Intensive Glucose Therapy**
- If serum glucose level >140 mg/dl then initiate intensive glucose therapy according to preprinted protocol

-**Assessment of Adrenal Function**
- Perform Cosyntropin Stimulation Test (CST) then begin hydrocortisone 50 mg IV every 6 hours.
- Discontinue steroids if CST is negative

-**Activated protein C (Drotrecogin alfa)**
- Review indication, inclusion, and exclusion criteria
- Complete Drotrecogin alfa physicians preprinted orders
- Obtain approval of ICU physician

Suspected infection

- Site _____
- Unknown

87/87 patients - Septic Shock – before /after study

Impact d'un In Older patients ?

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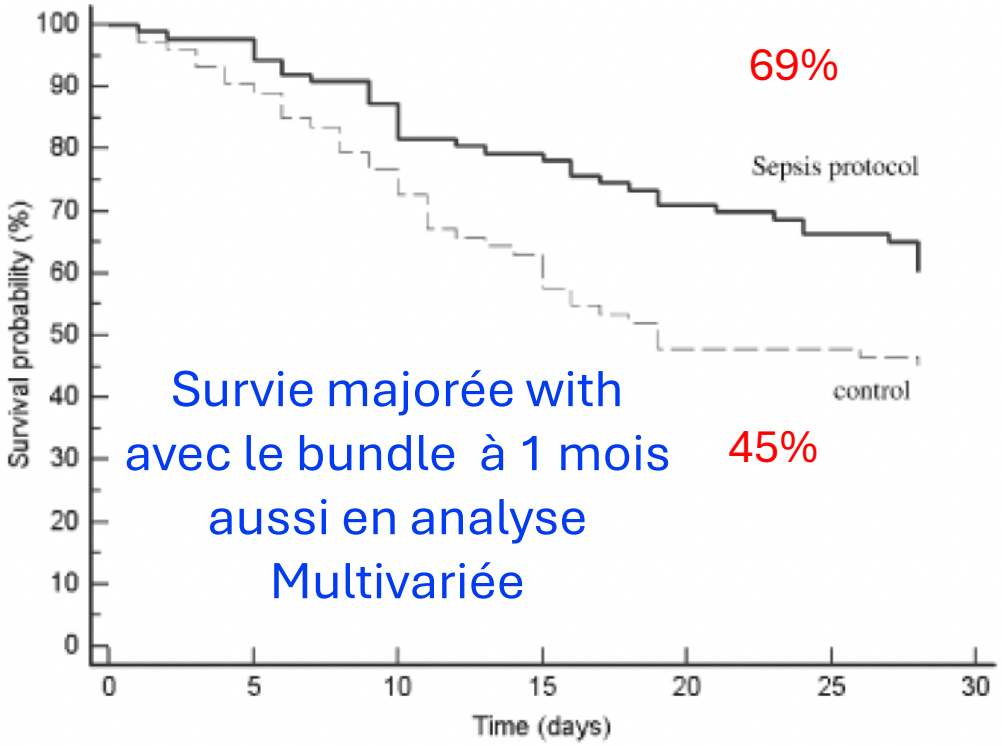


69%

45%

Survie majorée with avec le bundle à 1 mois aussi en analyse Multivariée

choc septique : quand on traite correctement c'est mieux !!

Table 2. Clinical Characteristics of the Study Population

Characteristic	Treatment (n = 87)	Control (n = 87)	*P*-Value
Baseline values, mean ± SD			
White blood cells, 10^9/L	15.6 ± 8.8	17.6 ± 7.7	.11
Platelet, 10^9/L	248 ± 134	218 ± 121	.23
Blood glucose, mg/dL	180 ± 119	195 ± 135	.48
Creatinine, mg/dL	1.7 ± 1.1	1.6 ± 0.9	.79
Lactate, mmol/L	7.8 ± 2.7	7.1 ± 2.3	.38
Acute Physiology and Chronic Health Evaluation* II score	42 ± 18	40 ± 16	.46
Therapeutic intervention			
Intravenous fluid in the first 6 hours, mL, mean ± SD	3,960 ± 1,990	2,490 ± 1,020	<.001
Administration of antibiotics within 4 hours of presentation, n (%)	83 (95)	79 (91)	.37
Adequate initial antibiotics, n (%)	84 (97)	73 (84)	.01
Packed red blood cell transfusion, n (%)	12 (14)	11 (13)	.98
Mechanical ventilation, n (%)	67 (77)	59 (68)	.24
Hydrocortisone, n (%)	83 (95)	14 (16)	<.001
Vasopressin, n (%)	53 (61)	9 (10)	<.001
Drotrecogin alfa, n (%)	11 (13)	2 (2)	.02

Infection
https://doi.org/10.1007/s15010-022-01927-3

RESEARCH

Infectious encephalitis in elderly patients: a prospective multicentre observational study in France 2016–2019

Caractéristiques cliniques

	<65 years (n=236)	65–79 years (n=184)	≥80 years (n=74)	P
Male gender	153/236 (65)	109/184 (59)	41/73 (56)	0.304
Diabetes	19/233 (8)	33/184 (18)	15/74 (20)	0.003
Cancer	3/236 (1)	21/183 (11)	15/73 (21)	<0.001
Haematological malignancies	3/235 (1)	19/183 (10)	5/73 (7)	<0.001
Immunodeficiency	9/236 (4)	39/184 (21)	11/74 (15)	<0.001
Autoimmune diseases	3/233 (1)	14/183 (8)	6/71 (8)	<0.001
Neurological diseases	8/236 (3)	14/184 (8)	7/74 (9)	0.054
International travel within the last 6 months	54/225 (24)	22/173 (13)	5/69 (7)	<0.001
Coma	18 (8)	9 (5)	11 (15)	0.025
Impaired consciousness	84 (36)	74 (41)	39 (53)	0.032
Confusion	127 (54)	126 (69)	53 (72)	0.002
Fever	146 (62)	73 (40)	14 (19)	<0.001
Skin rash	16 (7)	18 (10)	17 (23)	<0.001
Headache	146 (62)	73 (40)	14 (19)	<0.0001
CSF white cells count/mm^3	114 [34–302]	61 [13–220]	62 [17–180]	0.010
Varicella-zona virus	16 (7)	27 (15)	22 (30)	<0.001
Mycobacterium tuberculosis	10 (4)	1 (0.5)	0 (0.0)	0.023
Listeria monocytogenes	3 (1)	13 (7)	7 (9)	<0.001

France : ENCEIF Centres
2016 -2019
494 patients
age Moyen : 57

Encephalite

Pourquoi les infections sont

.....

plus graves

chez les personnes âgées ?

Long terme mortalité et….

Infection
https://doi.org/10.1007/s15010-022-01927-3

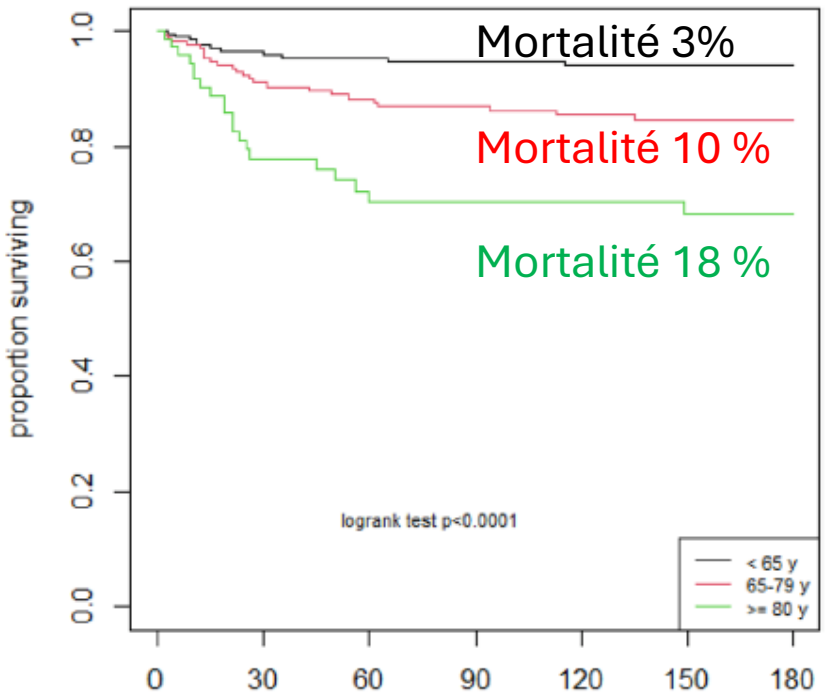
RESEARCH

Infectious encephalitis in elderly patients: a prospective multicentre observational study in France 2016–2019

Paul Petitgas[1,2] · Pierre Tattevin[1] · Alexandra Mailles[3] · Pierre Fillâtre[4] · Jean-Paul Stahl[5] on behalf of the ENCEIF scientific committee, Investigators group

France : ENCEIF Centres 2016 -2019 494 patients

Survie : 6 mois : L'âge peut être un Facteur pronostic fort

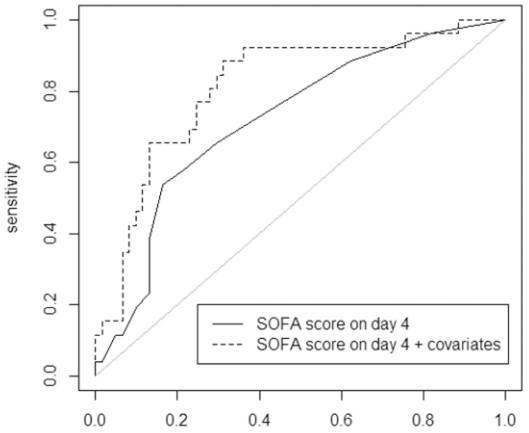


	Univariate analysis			Multivariate analysis[a]		
	HR	CI 95%	*P*	HR	CI 95%	*P*
Age (ref < 65 years)						
65–79 years	2.6	[1.3–5.3]	0.0084	1.9	[0.9–4.1]	0.1124
≥ 80 years	6.1	[2.9–12.7]	<0.0001	5.2	[2.3–11.7]	<0.0001
Immunodeficiency	3.1	[1.7–5.5]	<0.0001	–	–	–
Coma on admission	3.8	[1.9–7.3]	<0.0001	3.4	[1.6–6.9]	0.0011
Fever on admission	0.7	[0.4–1.2]	0.1873	0.8	[0.4–1.6]	0.5931
Headache on admission	0.3	[0.2–0.6]	0.0006	0.8	[0.4–1.7]	0.5827
Infratentorial neurological signs on admission	0.4	[0.2–1.0]	0.051	0.7	[0.3–1.8]	0.4377
CSF Protein ≥ 0.8 g/L	1.9	[1.1–3.4]	0.0313	2.6	[1.4–5.0]	0.0028
CSF white cells > 80/mm^3	0.6	[0.3–0.9]	0.0467	0.6	[0.3–1.1]	0.0926
Viral encephalitis	1.7	[0.9–3.0]	0.0690	1.9	[1.0–3.7]	0.0418

plus grave ? : impact court et long terme

Dynamic SOFA score assessments to predict outcomes after acute admission of octogenarians to the intensive care unit

Emmanuelle Loyrion[1], Lydiane Agier[2], Thibaut Trouve-Buisson[1], Gaetan Gavazzi[3], Carole Schwebel[4], Jean-Luc Bosson[2], Jean-François Payen[1]*



court terme : SOFA dynamique

La fragilité pré admission (Le CFS)

=

Meilleur predicteur de la dependance fonctionnelle post rea

Table 4. Logistic regression model of loss of autonomy for patients who were still alive on day 90 including SOFA scores adjusted for independent covariates (primary analysis with 49 patients). The loss of autonomy (change in [Δ] ADL) was calculated as ADL score at 90 days–ADL score on day 1, and was defined as ΔADL <0. The change in the SOFA score (ΔSOFA) was calculated as SOFA score on day 1 –SOFA score on day 4.

Variables	Odds ratio	95% CI lower bound	95% CI upper bound	P value
Age	0.08	-0.19	0.35	0.541
Preadmission frailty	2.49	0.06	4.92	0.045
Preadmission CIRS-g	0.14	-0.11	0.38	0.274
Preadmission medications	0.30	-0.13	0.73	0.168
Preadmission anticoagulant	-0.85	-3.68	1.99	0.559
ADL score on admission	-0.70	-3.02	1.63	0.556
Neurological failure on admission	-0.39	-2.33	1.55	0.694
Respiratory support on admission	-0.90	-3.28	1.48	0.458
SOFA on day 4	-0.21	-0.59	0.18	0.302
ΔSOFA	0.21	-0.25	0.67	0.369

SOFA, sequential organ failure assessment; CI, confidence interval; CIRS-g, Cumulative Illness Rating Scale for Geriatrics; ADL, Activities of Daily Living.

Loyrion E et al Plos One 2021

Clinical Frailty Scale*

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 Managing Well – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 Vulnerable – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 Terminally Ill - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

interactions Complexes mais
gravité du sepsis / age

Frailty scale predict The long term (6-month) mortalité
in older (>80y) ICU admitted patients

Table 2. Multivariate analysis, factors affecting 6-month mortality of very old critically ill patients with SOFA ≥ 2 acutely admitted to the ICU

Variables	HR (95% CI)	*P*-value
Sepsis versus other acutely admitted & SOFA ≥2	0.89 (95% CI 0.77–1.02)	0.09
Age (5 years increase)	1.16 (95% CI 1.09–1.25)	<0.0001
SOFA (one-point increase)	1.16 (95% CI 1.14–1.17)	<0.0001
Frailty: vulnerable (CFS 4) versus fit (CFS < 4)	1.15 (95% CI 0.99–1.33)	0.07
Frailty: frail (CFS > 4)	1.34 (95% CI 1.18–1.51)	<0.0001
Own home versus other	0.90 (95% CI 0.80–1.01)	0.06
Female versus male	0.96 (95% CI 0.87–1.07)	0.49
CPS 10–15 versus CPS 0–9	0.94 (95% CI 0.83–1.05)	0.27
CPS >15 versus CPS 0–9	1.02 (95% CI 0.89–1.18)	0.75

ADL Or CFS to long term predict survival

results from an observational study in 241 European ICUs

Lenneke E.M. Haas[1], Ariane Boumendil[2], Hans Flaatten[3], Bertrand Guidet[4], Mercedes Ibarz[5], Christian Jung[6], Rui Moreno[7], Alessandro Morandi[8], Finn H. Andersen[9], Tilemachos Zafeiridis[10], Sten Walther[11], Sandra Oeyen[12], Susannah Leaver[13], Ximena Watson[14], Carole Boulanger[15], Wojciech Szczeklik[16], Joerg C. Schefold[17], Maurizio Cecconi[18], Brian Marsh[19], Michael Joannidis[20], Yuriy Nalapko[21], Muhammed Elhadi[22], Jesper Fjølner[23], Antonio Artigas[24], Dylan W. de Lange [25], VIP2 study group**

Grippe et événements cardiovasculaires

insuffisance cardiaque et infarctus

1932

Excès de DÉCÈS pour causes cardiorespiratoires 14 % EN 1918

Collins et al. *Public Health Rep*. 1932; 47: 2159-79.

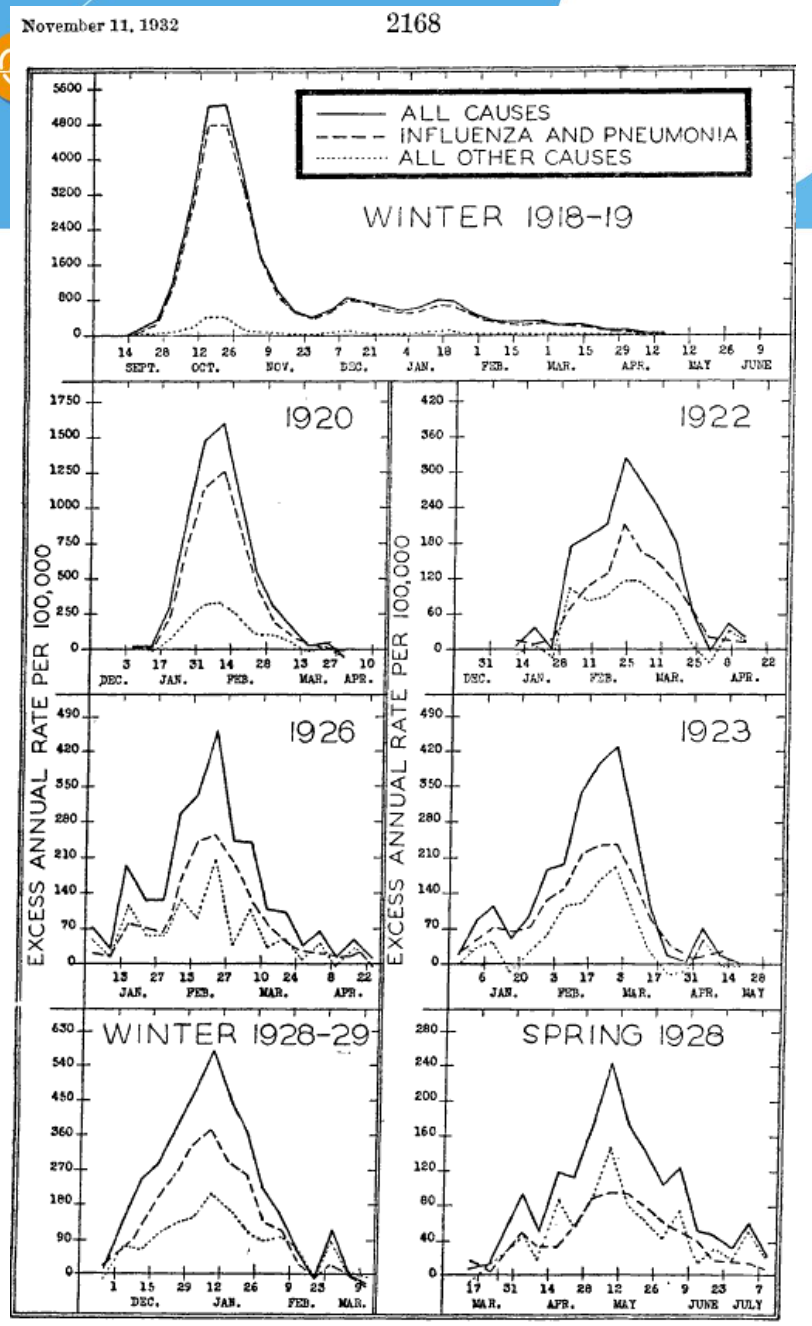


FIGURE 4.—Weekly excess mortality rates (annual basis) from all causes, from influenza and pneumonia, and from all other causes during 7 epidemics in a group of 35 large cities in the United States, 1918–1929. (Excess over expected or normal rates for corresponding weeks based on 7-year medians. For details of computations see footnotes to Tables 3 and 4.)

TABLE 2 Age- and season-adjusted incidence ratio (IR) for first myocardial infarction and first stroke in periods after *Streptococcus pneumoniae* and respiratory viruses (combined) compared with baseline time

Time period after sample days	IR for *S. pneumoniae* (95% CI)	p-value	IR for respiratory viruses (95% CI)	p-value
Outcome: myocardial infarction#				
1–3	5.98 (2.47–14.4)	<0.001	5.59 (1.77–17.6)	0.003
4–7	3.79 (1.41–10.1)	0.008	3.00 (0.74–12.1)	0.12
8–14	1.65 (0.53–5.15)	0.38	1.00 (0.14–7.15)	0.99
15–28	2.04 (0.96–4.31)	0.06	2.12 (0.79–5.70)	0.13
Baseline	1.00		1.00	
Outcome: stroke¶				
1–3	12.3 (5.48–27.7)	<0.001	6.79 (1.67–27.5)	0.007
4–7	8.23 (3.39–19.9)	<0.001	5.43 (1.34–21.9)	<0.001
8–14	4.90 (2.02–11.8)	<0.001	5.01 (1.59–15.7)	<0.001
15–28	4.09 (2.02–8.27)	<0.001	4.02 (1.62–9.95)	<0.001
Baseline	1.00		1.00	

#: n=1227; ¶: n=762.

Warren-Gash, et al. Eur Respir J 2018

Pneumonies communautaire et EHPAD : Déclin fonctionnel

	CAP		NHAP		
n	99	79			1780
Functional decline	23%	29%	59%	28,8	31.1%
Date of Evaluation (d)	15	180	90 -1.5 ADL	30_90	180
Risk Factors	PSI	no	PSI/CURB	Multiples	Multiples
	Torres JAGS 2003	Sharma Infec Dis clin Pract	Arduin M 2023 submitted	Binder J Gerontol 2003	Bula JAGS 2005

2006

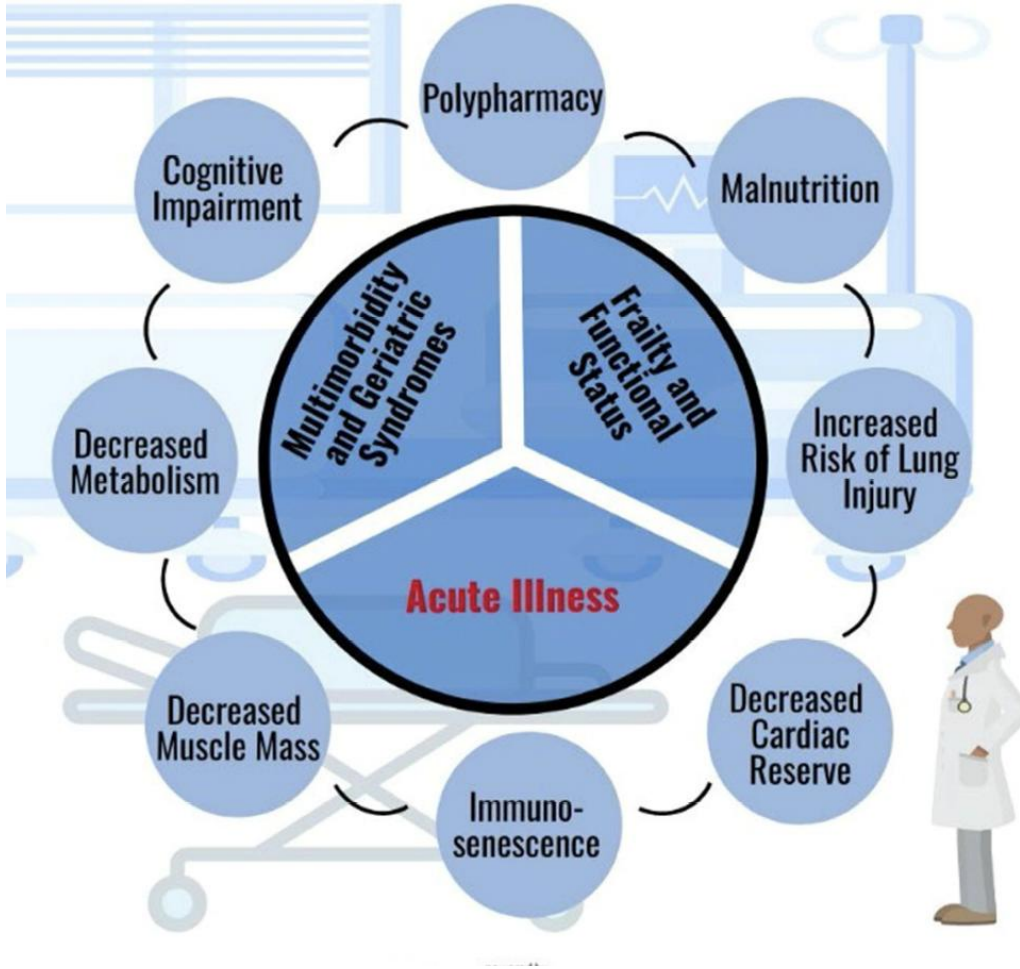
Sepsis plus grave : impact a long terme

Goals of care

Recommendations
74. For adults with sepsis or septic shock, we **recommend** discussing goals of care and prognosis with patients and families over no such discussion *Best Practice Statement*
75. For adults with sepsis or septic shock, we **suggest** addressing goals of care early (within 72 h) over late [72] *Weak recommendation, low-quality evidence*
76. There is **insufficient evidence to make a recommendation** for any specific standardised criterion to trigger goals of care discussion

Post-discharge follow-up

Recommendations
91. For adult survivors of sepsis or septic shock, we **recommend** assessment and follow-up for physical, cognitive, and emotional problems after hospital discharge Best Practice Statement
92. For adult survivors of sepsis or septic shock, we **suggest** referral to a post-critical illness follow-up programme if available *Weak recommendation, very low-quality evidence*
93. For adult survivors of sepsis or septic shock receiving mechanical ventilation for > 48 h or an ICU stay of > 72 h, we **suggest** referral to a post-hospital rehabilitation programme *Weak recommendation, very low-quality evidence*



B Evans L et al Intensive Care Med (2021 runker LB et al Clinical Interventions in Aging 2023. Vallet et al. Annals of Intensive Care 2023

Et la génétique .....

Article

The major genetic risk factor for severe COVID-19 is inherited from Neanderthals

https://doi.org/10.1038/s41586-020-2818-3 Hugo Zeberg[1,2]✉ & Svante Pääbo[1,3]✉

Essort de la paléogénomique met en évidence :

Les différences et les similitudes génétiques entre Homo sapiens et Néanderthal (Croatie)
(disparu il y a 30 000 ans)
3% de materiel genetique commun...
Un nouvel Hominidé....(Denisova (Siberie)

Prix nobel Médecine 2022

https://www.lemonde.fr/international/article/2022/10/03/le-prix-nobel-de-medecine-2022-attribue-au-suedois-svante-paabo-qui-a-sequence-le-genome-de-l-homme-de-neandertal_6144178_3210.html

Article

The major genetic risk factor for severe COVID-19 is inherited from Neanderthals

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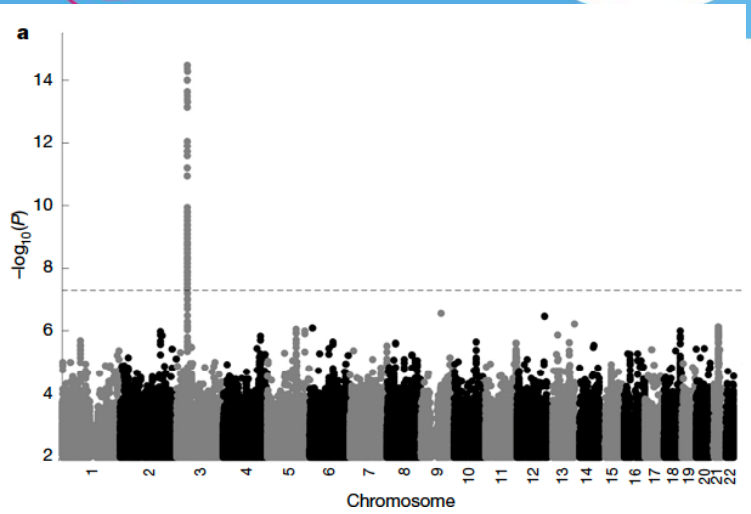
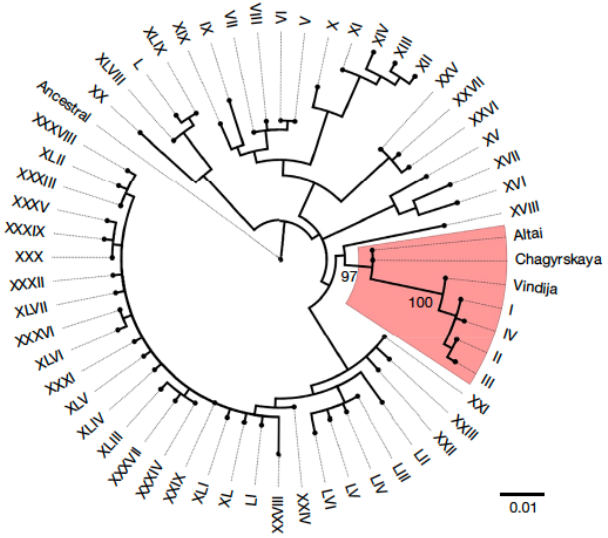
Association génétique (pls Haplotypes) et gravité COVID 19

chromosome 3 / 6 gènes

chromosome 19 : groupe ABO



« 1000 genome project « comparant les haplotypes actuels aux Genomes « de Neanderthal »...253 haplotypes



Distribution geographique des Haplotypes à risque

Take Home Messages

ce qu'on sait … dans le titre…

Plus fréquent et plus grave

à court et long terme

Les infections contribuent a des evenements non infectieux graves

Des Facteurs de risque spécifiques dont l'âge

la vitesse d'intervention (Dc et Therap) est majeure pour la gravité

Take Home Messages

ce qu'on peut penser :

l'accumulation des FDR majore le risque mais jusqu'ou ?

Le rôles des premières barrières sans doute +++
Mais trop peu d'étude s' y interessent alors que…

La gravité immédiate dépend
de la gravité de l'évènement aigue,
de la localisation de l'infection
des réserves d'organes (Fragilité et dépendance)
(Risque et pronostique)

Take Home Messages

ce qu'on ne sait pas …

l'immunosenescence rend compte de la susceptibilité aux infections

L'immunosenescence = fragilité systémique

avoir un marqueur rendant compte de notre capacité à répondre correctement à des agents différents

Si on n'a pas récupérer trop de gènes trop mauvais de nos anciens congénères

Merci de votre attention

"Ce qui est naturel, c'est le microbe.
Le reste, la santé, l'intégrité, la pureté,
si vous voulez, c'est un effet de la volonté et
d'une volonté qui ne doit jamais s'arrêter"

Albert Camus, La Peste (1947)

15ème CONGRÈS de la Société de Gérontologie de Bordeaux et du Sud-Ouest

“ ÇA CHAUFFE EN GÉRIATRIE !

9 et 10 oct. 2025 | LE CONNECTEUR BIARRITZ

SGBSO SOCIÉTÉ DE GÉRONTOLOGIE DE BORDEAUX ET DU SUD-OUEST

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Journée nationale
Save the date
11 décembre,Paris
Ginger

savoir danser
et
...raconter....

par mail : c.cheneau@infectiologie.com

UGA Université Grenoble Alpes

TIMC Techniques de l'Ingénierie Médicale et de la Complexité — Informatique, Mathématiques et Applications, Grenoble

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