Oxygénothérapie hyperbare et infections ostéo articulaires

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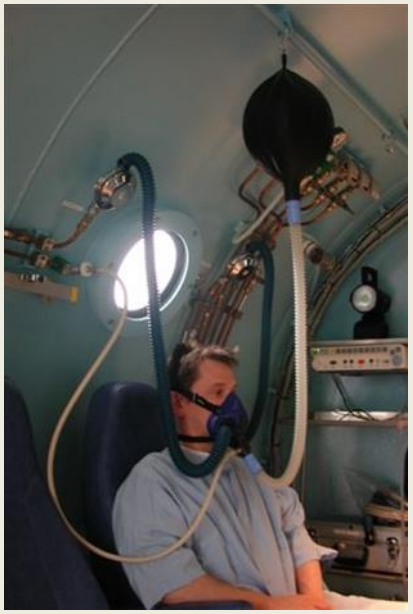
OHB: définition

- Méthode thérapeutique
  - qui consiste à faire inhaler de l'O_2
  - au sein d'une enceinte étanche
  - dont la pression intérieure est supérieure à la pression atmosphérique

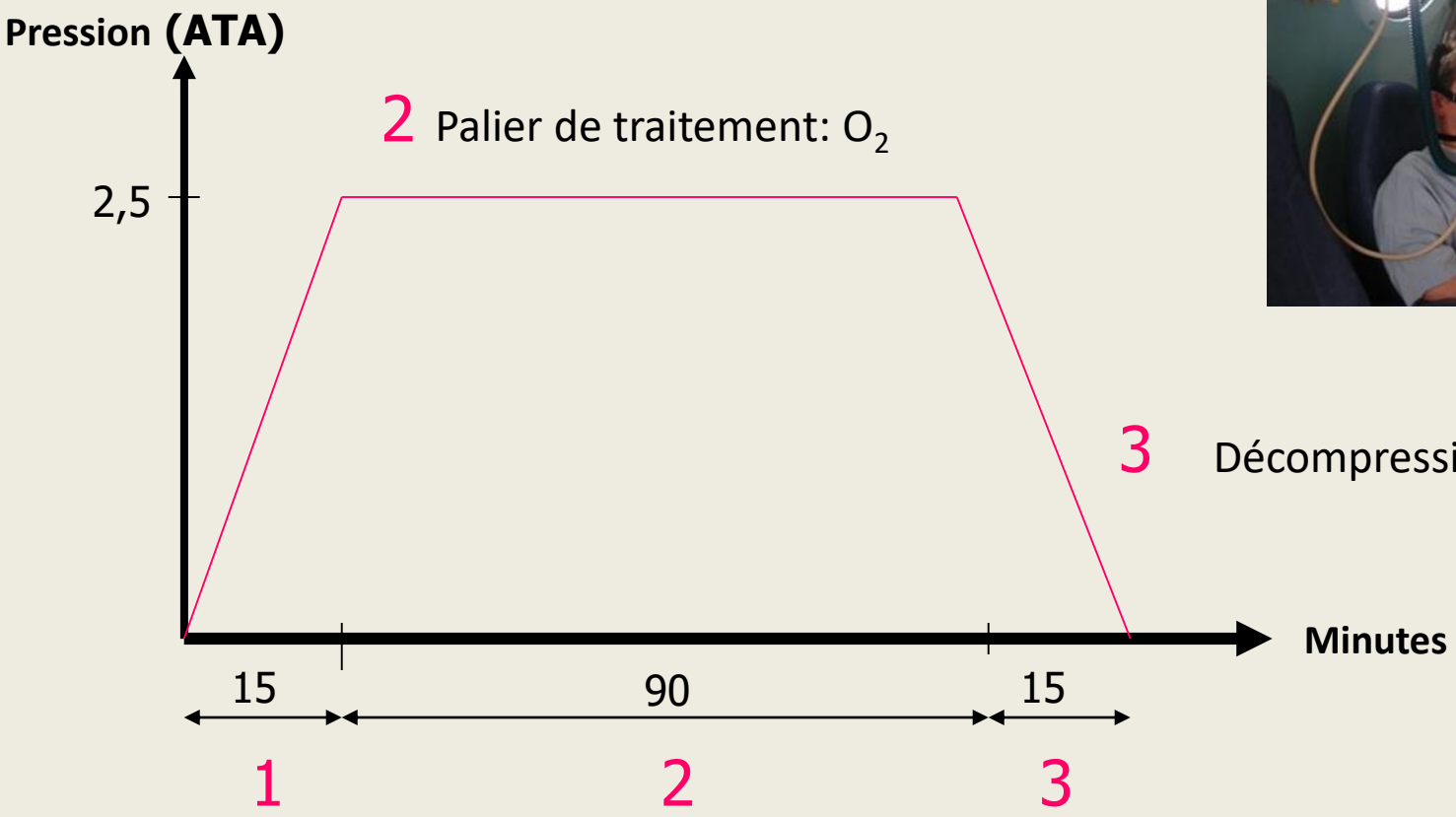
OHB: fonctionnement

OHB: modalités d'administration

- Les séances: de 90 min à plusieurs heures
  1 à plusieurs 10^{aines} de séances

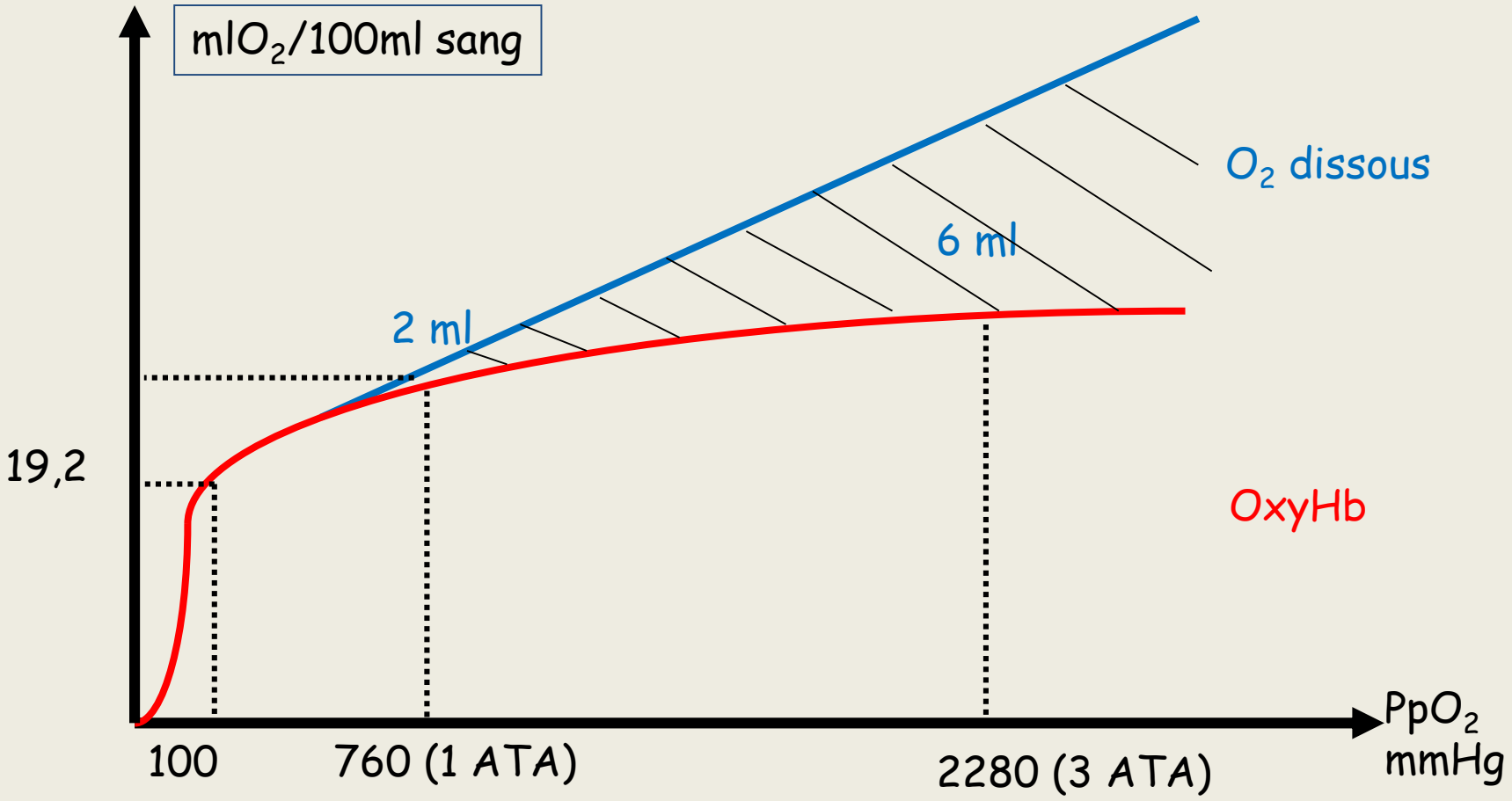


1 Compression



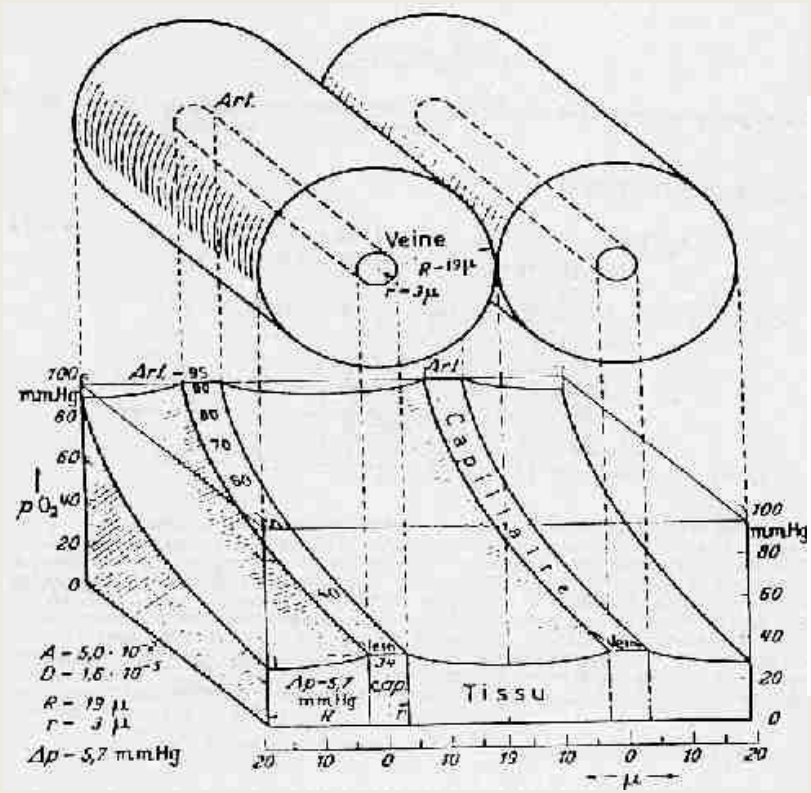
OHB et réoxygénation

- Transport de l'O_2
  - $CaO_2 = 1{,}34 \times Hb \times \% + 0{,}0031 \times PaO_2$

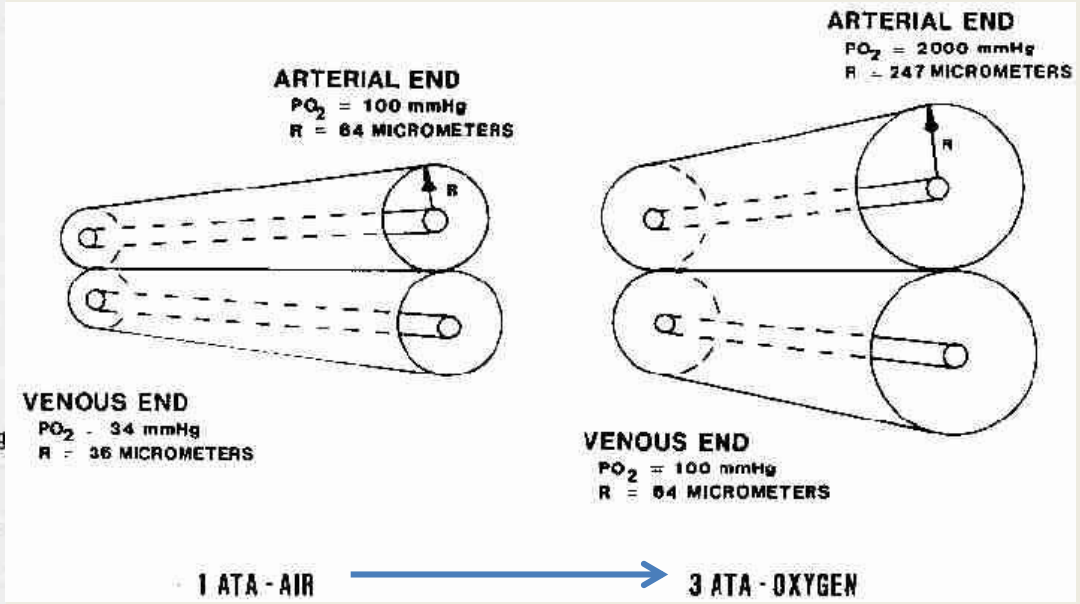


OHB et réoxygénation

- Délivrance tissulaire de l'O_2



Normobarie



En hyperbarie

Réoxygénation

- Délivrance de l'O_2: et dans les tissus infectés?

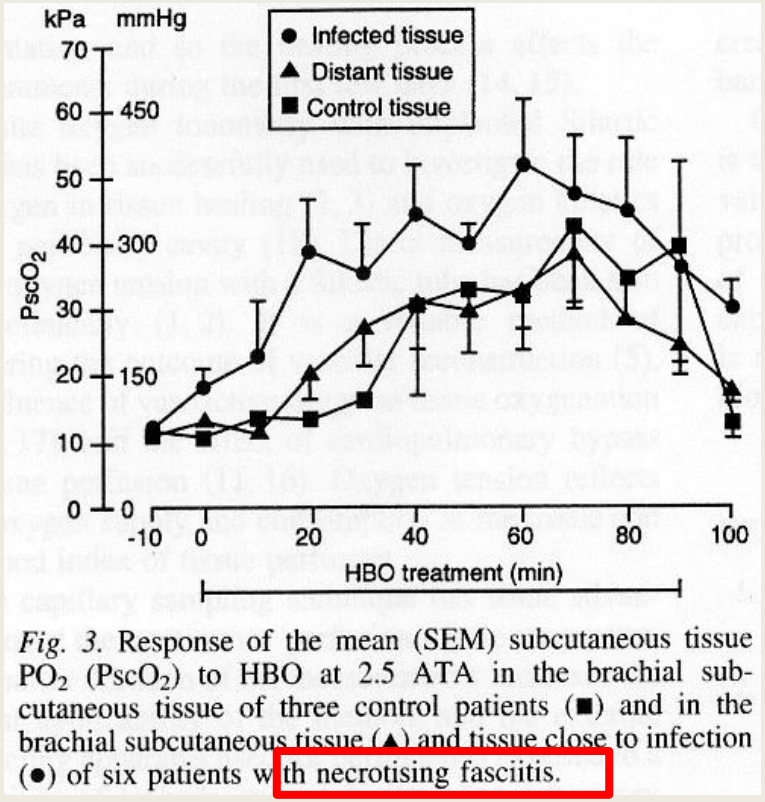
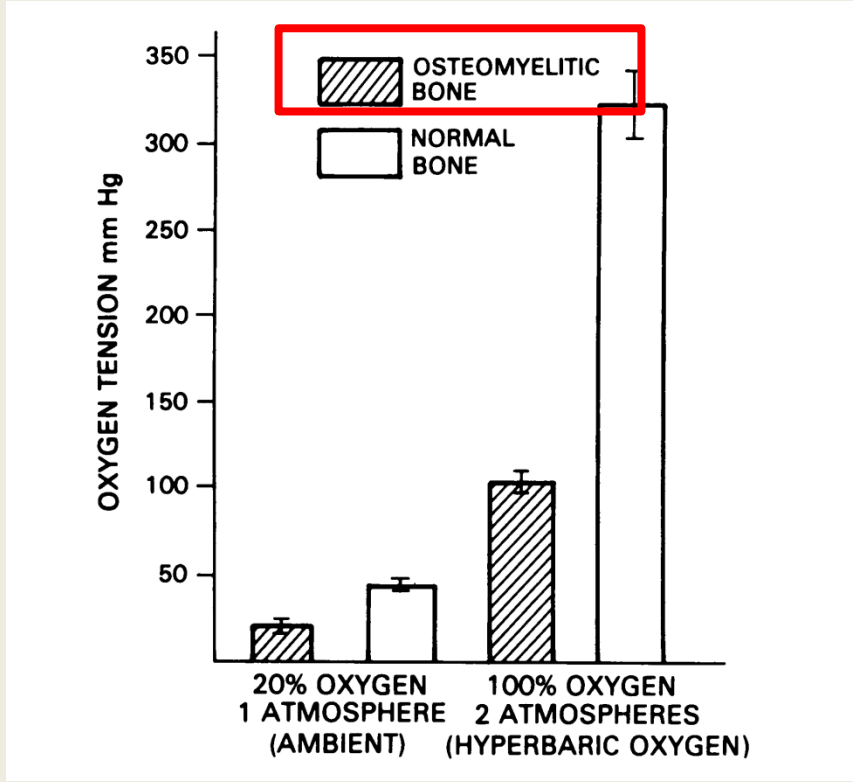


Fig. 3. Response of the mean (SEM) subcutaneous tissue PO_2 ($PscO_2$) to HBO at 2.5 ATA in the brachial subcutaneous tissue of three control patients (■) and in the brachial subcutaneous tissue (▲) and tissue close to infection (●) of six patients with necrotising fasciitis.

Korhonen K. Tissue gas tension in patients with necrotising fasciitis and healthy controls during treatment with hyperbaric oxygen: a clinical study. Eur J Surg 2000; 166: 530-4.



Mader JT et al. A Mechanism for the amelioration by hyperbaric oxygen of experimetal Staphylococcal osteomyelitis in rabbits. J Inf Dis 1980;142:915-22.

Esterhai Jr JL et al. Effect of hyperbaric oxygen exposure on oxygen tension within the medullary canal in the rabbit tibial osteomyelitis model. J Orthop Res 1986;4:330-6.

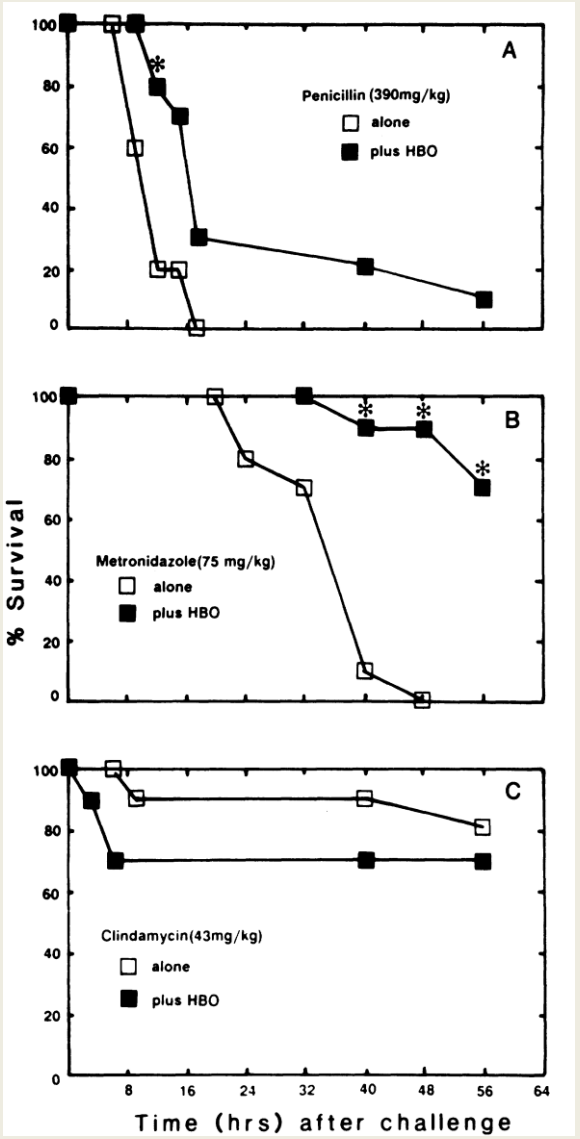
Action anti infectieuse directe

- Les germes anaérobies

Table 2. Efficacy of HBO in experimental clostridial gas gangrene.

Animal [reference]	Conditions of treatment	*C. perfringens* challenge inoculum	Survival (%) HBO	Survival (%) No HBO
Mouse [19]	3 ATA* for 50 min every 8–16 h for 3–5 d	$0.5–1.0 \times 10^8$ cfu, washed	85	50
		Plus sterile dirt	84	83
		Plus $CaCl_2$	44	40
		Plus crushed limb	64	55
Mouse [20]	3 ATA for 30 min every 12 h for 1–4 d	24-h culture plus sterile dirt and crushed limb	96	9
Mouse [21]	3 ATA for 90 min every 6 h on day 1, every 12 h on days 2 and 3	$1–5 \times 10^5$ cfu		
		Plus adrenaline	100	9
		Plus $CaCl_2$	60	45
Dog [22]	3 ATA for 2 h, then every 12 h on days 1 and 2, then once on day 3	Spores plus adrenaline	0	0
		Plus antibiotics	55	55
		Plus surgery	0	0
		Plus surgery and antibiotics	95	70

* ATA = atmospheres absolute (pressure).



Stevens DL. Evaluation of therapy with hyperbaric oxygen for experimental infection with *clostridium perfringens.* Clin Infect Dis 1993; 17: 231-7.

OHB et action anti infectieuse indirecte

- Les germes aérobies: l'OHB est elle un AB?

Table 2. Effect of various treatments on chronic experimental osteomyelitis due to *Staphylococcus aureus* in rabbits.

	Treatment group				
Effect	Died before treatment began	Control (no treatment)	Hyperbaric oxygen	Hyperbaric oxygen plus cephalothin	Cephalothin
Positive bone culture*	9/9 (100)	10/11 (91)	5/14 (36)	6/15 (40)	8/17 (47)
Mortality*	9/9 (100)	2/11 (18)	1/14 (7)	2/15 (13)	2/17 (12)
Weight change during infection (kg)†	−0.36 ± 0.15	0.48 ± 0.14	0.97 ± 0.2	0.61 ± 0.2	0.52 ± 0.13
Severity of infection†					
Gross	2.1 ± 0.3	2.2 ± 0.4	1.6 ± 0.3	1.7 ± 0.2	1.6 ± 0.3
Radiologic	1.6 ± 0.2	2.9 ± 0.3	2.3 ± 0.3	2.2 ± 0.3	2.2 ± 0.2
Animals with sequestrum*	2/9 (22)	10/11 (91)	11/14 (79)	11/15 (73)	13/17 (76)

*Data are number of animals with effect/number in treatment group (percentage).
†Data are mean ±SE.

Mader JT et al. Therapy with hyperbaric oxygen for experimental osteomyelitis due to *Staphylococcus Aureus* in rabbits. J Inf Dis 1978;138(3):312-8.

OHB et action anti infectieuse indirecte

- Les germes aérobies: phagocytose restaurée

Ostéomyélite à *SA*: Perfusion tissulaire

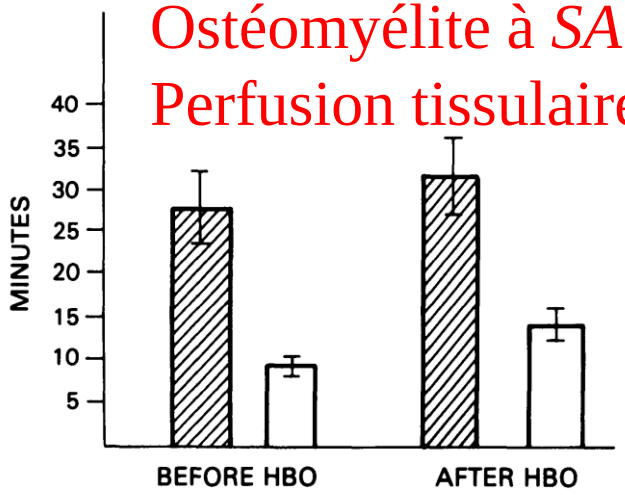
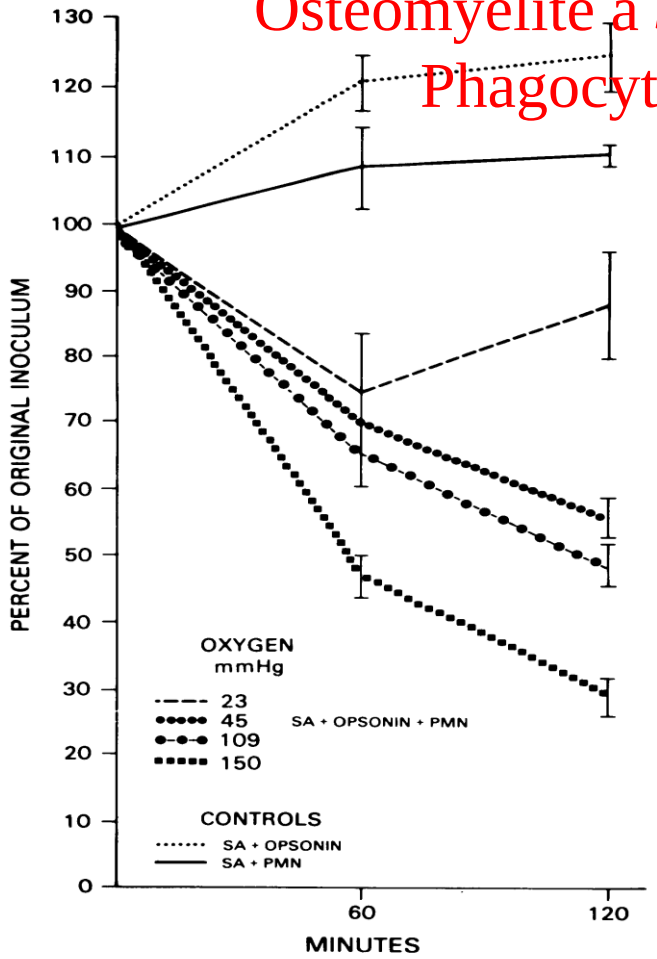


Figure 1. Argon washout in normal (□) and osteomyelitic (▨) bone in rabbits. The data are mean (± SE [brackets]) time (min) required for the partial pressure of Ar to be reduced by 50%, before and after exposure to hyperbaric oxygen (HBO). The partial pressures were measured by a mass spectrometer.

Mader JT et al. A Mechanism for the amelioration by hyperbaric oxygen of experimetal Staphylococcal osteomyelitis in rabbits. J Inf Dis 1980;142:915-22.

Ostéomyélite à *SA*: Phagocytose



OHB et action anti infectieuse indirecte

- OHB et antibiotiques: effet post antibiotique

TABLE 2. Effect of hyperoxia or hyperbaric oxygen on growth recovery of *P. aeruginosa* ATCC 27853

Oxygen exposure (n^a)	Time interval for growth recovery (h)[b]	
	Control	Tobramycin-treated
Normoxia (9)	2.20 ± 0.13	2.89 ± 0.13[c]
Hyperoxia (9)	2.03 ± 0.12	3.45 ± 0.19[d,e]
Hyperbaric oxygen (4)	2.67 ± 0.09[f,g]	4.42 ± 0.18[c,h,i]

[a] *n*, Number of experiments.
[b] Bacteria were exposed to tobramycin and one of three oxygen tensions for 1 h. Tobramycin was removed by filtration. Numbers are means ± standard errors of the mean and represent the time needed for bacteria to increase 1.0 $\log_{10}$ CFU/ml under normoxic conditions after the removal of tobramycin.
[c] Significantly different ($P < 0.02$) from respective controls without tobramycin.
[d] Significantly different ($P < 0.002$) from respective controls without tobramycin.
[e] Significantly different ($P < 0.02$) from the normoxia and tobramycin-treated group.
[f] Significantly different ($P < 0.05$) from normoxia.
[g] Significantly different ($P < 0.01$) from hyperoxia.
[h] Significantly different ($P < 0.001$) from the normoxia and tobramycin-treated group.
[i] Significantly different ($P = 0.01$) from the hyperoxia and tobramycin-treated group.

TABLE 3. Effect of hyperoxia or hyperbaric oxygen on protein synthesis in *P. aeruginosa* ATCC 27853

Oxygen exposure	L-[^{35}S]methionine incorporation (dpm/$\log_{10}$ CFU [*n*])[a]		
	0 h		1 h, Tobramycin
	Control	Tobramycin	
Normoxia	415 ± 185 (9)	16.7 ± 6.5[b] (9)	18.5 ± 7.3[b] (6)
Hyperoxia	514 ± 237 (9)	7.4 ± 4.3[b] (9)	13.8 ± 6.3[b] (6)
Hyperbaric oxygen	202 ± 52 (9)	−7.2 ± 11.6[b,c] (9)	6.4 ± 12.1[b] (3)

[a] Bacteria were exposed to tobramycin and one of three oxygen tensions for 1 h. Tobramycin was removed by filtration and bacteria were pulsed for 5 min (35°C) under normoxic conditions with 0.5 μCi of L-[^{35}S]methionine. Bacteria were then chased for 5 min with 1 mM unlabeled methionine. Data are means ± standard errors of the mean. *n*, Number of experiments. The value 0 h refers to protein synthesis measured immediately after removal of tobramycin; the value 1 h refers to protein synthesis measured 1 h after removal of tobramycin.
[b] Significantly different ($P = 0.0001$) from controls at 0 h.
[c] Value approximating background.

Park MK et al. Hyperoxia prolongs the aminoglycoside-induced postantibiotic effect in *pseudomonas aeruginosa*. Antimicrob Agents Chemother 1991;35(4):691-5.

OHB et ostéomyélite

- OHB et antibiotiques: potentialisation
  - Débridement +/- AB local +/- OHB
    - Ostéomyélite à *Staph A*, à 3 semaines d'évolution

Table 3: Quantitative Evaluation of Osteomyelitis, Experimental and Control Groups

Group Assignment	CFU * g^{-1} tibial bone, mean value ± SD
A. Control Group	
1. 3 weeks after infection, n = 12	$4.9 \times 10^6 \pm 0.37$
2. therapy with 0.9 percent NaCl after 2 weeks, n = 12	$2.0 \times 10^6 \pm 0.17$
3. therapy with 0.9 percent NaCl after 4 weeks, n = 11	$3.7 \times 10^6 \pm 0.42$
B. Therapy with HBO_{22} (1h 3 ATA, 2×/j)	
1. after 2 weeks, n = 11	$6.2 \times 10^5 + 0.06$
2. after 4 weeks, n = 12	$1.7 \times 10^5 \pm 0.03$
C. Therapy with gentamicin-collagen sponge	
1. after 2 weeks, n = 12	$9.8 \times 10^2 \pm 0.024$
2. after 4 weeks, n = 12	$1.4 \times 10^2 \pm 0.002$
D. Therapy with HBO_2 + gentamicin-collagen sponge	
1. after 2 weeks, n = 12	$1.0 \times 10^2 \pm 0{,}002$
2. after 4 weeks, n = 11	0*

* Organisms in the bone suspension were no longer detectable after 4 weeks in 9 of 11 animals. Only in animal No. 4 and No. 9 infection was observed ($0{,}43 \times 10^1$ and $0{,}28 \times 10^1$ CFU of tibial bone)

Mendel V et al. Synergy of HBO_2 and a local antibiotic carrier for experimental osteomyelitis due to *Staphylococcus Aureus* in rats. Undersea Hyperb Med 2004;31(4):407-16.

OHB et ostéomyélite

- OHB et antibiotiques: potentialisation
  - Ostéomyélite à *SA*: +/- OHB +/- Cefazolin
  - Médiastinite à *SARM* (rat), sans chirurgie +/- AB +/- OHB

Outcome Treatment of Experimental Mediastinitis

Group	Therapy (7j)	Number of culture negative/total	Bacterial count*
Group 1	No therapy	6/6	0.0
Group 2[§]	No therapy	0/6	5.94 ± 0.52
Group 3[§,‖]	HBO[†]	0/6	4.20 ± 0.81
Group 4[§,‖]	Linezolid[‡]	0/6	4.21 ± 0.41
Group 5[§,‖]	Vancomycin[‡]	0/6	3.62 ± 0.49
Group 6[§,‖]	Teicoplanin[‡]	0/6	3.59 ± 0.54
Group 7[§,‖,¶,#]	Linezolid[c] + HBO[†]	0/6	2.49 ± 0.85
Group 8[§,‖,¶,#,$,¥]	Vancomycin[‡] + HBO[†]	2/6	1.76 ± 1.47
Group 9[§,‖,¶,#,$,¥]	Teicoplanin[‡] + HBO[†]	2/6	1.75 ± 1.49

*Mean ± SD $\log_{10}$ CFU/g.
†Administered once daily.
‡Administered intraperitoneal twice daily.
§$P < 0.05$ compared with group 1.
‖$P < 0.05$ compared with group 2.
¶$P < 0.05$ compared with group 3.
#$P < 0.05$ compared with group 4.
$$P < 0.05$ compared with group 5.
¥$P < 0.05$ compared with group 6.

Mendel V et al. Therapy with hyperbaric oxygen and cefazolin for experimental osteomyelitis due to *Staphylococcal Aureus* in rats. Undersea Hyperb Med 1999;26(3):169-74.
Turhan V. HBO as adjunctive therapy in experimental mediastinitis. J Surg Res 2009; 155: 111-5.

Cicatrisation des tissus hypoxiques

- Multiplication des fibroblastes
- Synthèse de collagène
- Néoangiogénèse
- Réépithélisation

TABLE I
Microangiographic Vascular Density Equivalents (VDE)*

	Normobaric Air (n = 7)	Normobaric Oxygen (n = 14)	Hyperbaric Oxygen (n = 14)
Maximum VDE	18	19	99
Minimum VDE	6	6	78
Mean VDE	13 S.D. 3.1	13 S.D. 3.7	93 S.D. 4.4

p ≤0.89 for normobaric air versus normobaric oxygen, p ≤0.001 for normobaric versus hyperbaric oxygen, and p ≤0.001 for normobaric air versus hyperbaric oxygen.

TABLE II
Histologic Vascular Density Equivalents (VDE)

	Normobaric Air (n = 7)	Normobaric Oxygen (n = 14)	Hyperbaric Oxygen (n = 14)
Level I VDE	5 S.D. ± 1.7	4 S.D. ± 1.4	21 S.D. ± 3.3
Level II VDE	3 S.D ± 1.0	3 S.D. ± 1.0	13 S.D. ± 2.8
Level III VDE	5 S.D. ± 1.3	6 S.D. ± 1.7	13 S.D. ± 2.1

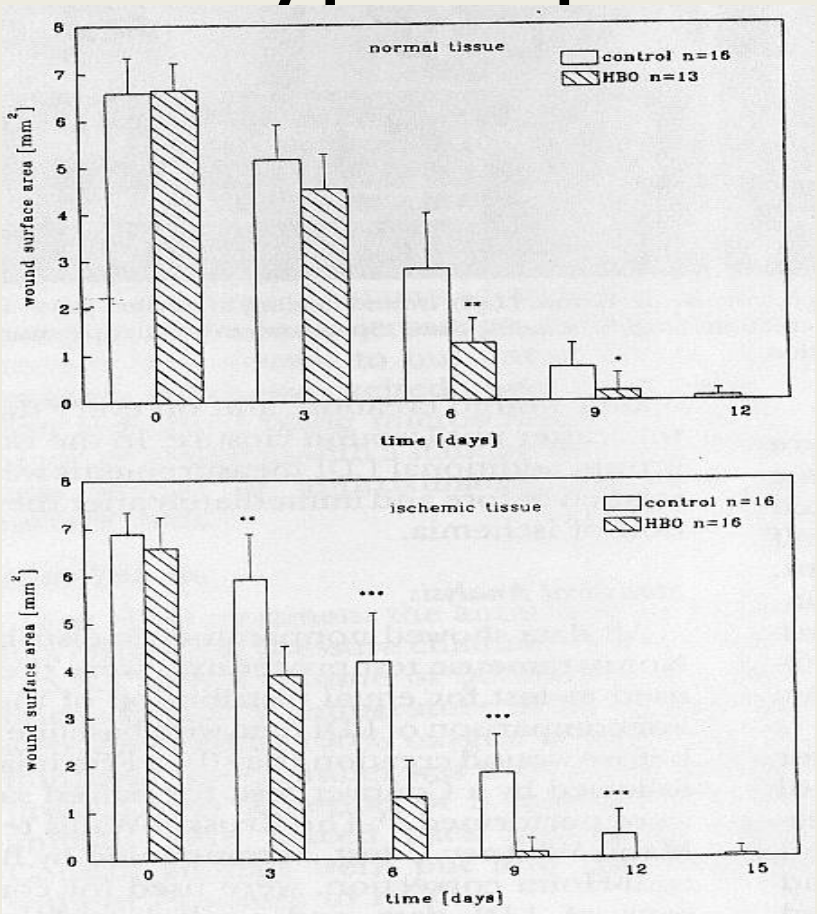


FIG. 2. Wound surface area (mm²) in normal (*above*) and ischemic (*below*) tissue plotted against time (days) after wound creation. Mean ± SD, $*p \leq 0.05$, $**p \leq 0.01$, $***p < 0.001$. Mann-Whitney U test with Bonferroni-Holm correction for comparison between treated and control group.

Marx RE et al. Relationship of oxygen dose to angiogenesis induction in irradiated tissue. *Am J Surg* 1990;160:519-24

Uhl E et al. Hyperbaric oxygen improves wound healing in normal and ischemic skin tissue. *Plas Reconst Surg* 1994;93:835-41.

Action anti oedémateuse

- Vasoconstriction hyperoxique et métabolisme

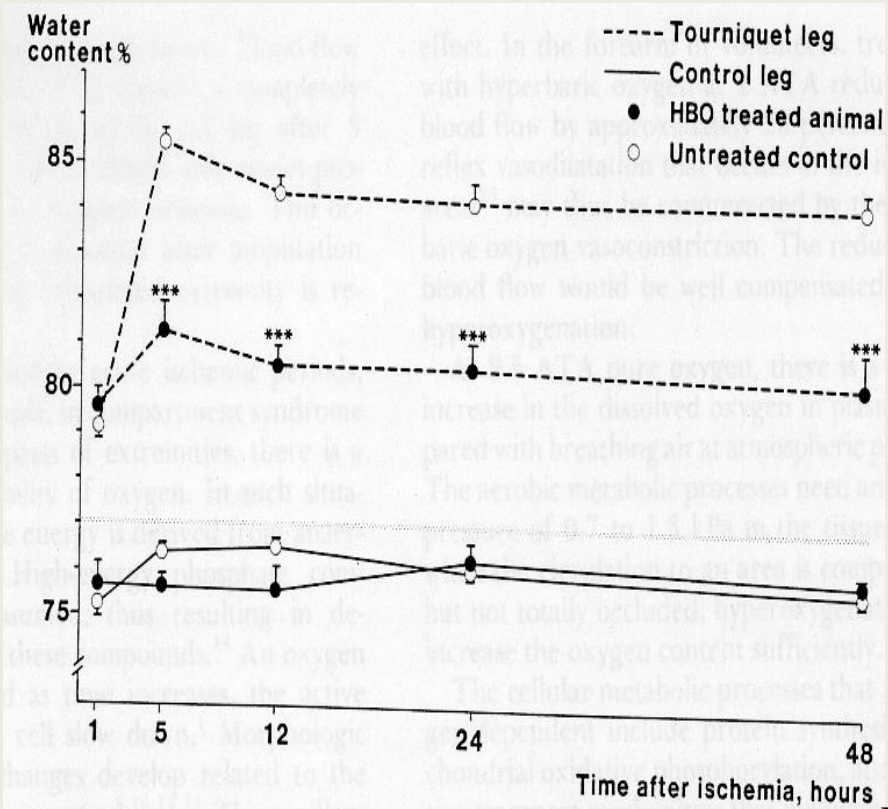


FIG. 2. Water content, mean values plus or minus SEM of tourniquet and control leg in ischemic hyperbaric oxygen-treated (*IH*) and ischemic control animals (*IC*). Stars denote statistically significant difference between tourniquet legs of IH and IC animals. ***: $p < 0.001$; shaded area: normal controls (*NC*); mean values ± SEM.

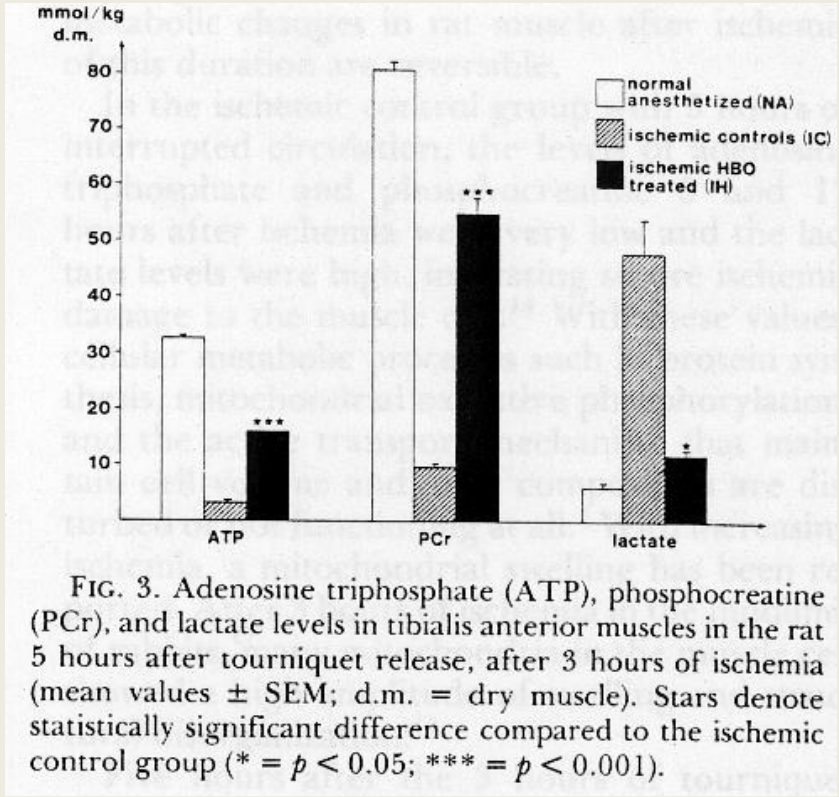


FIG. 3. Adenosine triphosphate (ATP), phosphocreatine (PCr), and lactate levels in tibialis anterior muscles in the rat 5 hours after tourniquet release, after 3 hours of ischemia (mean values ± SEM; d.m. = dry muscle). Stars denote statistically significant difference compared to the ischemic control group (* = $p < 0.05$; *** = $p < 0.001$).

Nylander G et al. Reduction of post-ischemic edema with hyperbaric O_2. *Plast Recontr Surg 1985; 76: 596-601.*

Nylander G et al. Metabolic effects of hyperbaric oxygen in post-ischemic muscle. *Plast Reconst surg* 1987; 79: 91-6.

OHB et infections osseuses en pratique

- Esterhai Jr. JL et al. Adjunctive hyperbaric oxygen therapy in the treatment of chronic refractory osteomyelitis. J Trauma 1987;27(7):763-8.
  - Prospectif non randomisé: 14 OHB vs 14 sans OHB
    - Inefficacité…
- Kawashima M et al. Hyperbaric Oxygen Therapy in orthopedics conditions. Undersea Hyperb Med 2004;31(1):155-62.
  - Rétrospectif non randomisé
    - 689 ostéomyélites (433 OHB vs 256 sans OHB)
    - P<0,01 mais « bon » (?), comparabilité des groupes
- Onen MR et al. Efficacity of hyperbaric oxygen therapy in iatrogenic spinal infections. Spine 2015; 40(22):1743-8.
  - Série 19 infections du rachis post op (dont des ostéomyélites…)
- Coulson A et al. Femoral vein cannulation in the treatment of osteomyelitis. Wounds 2016;28(6):194-9.
  - Série 8 pieds diabétiques avec ostéomyélites réfractaires

Hart BB. Hyperbaric oxygen for refractory osteomyelitis. Undersea Hyperb Med 2021;48(3):297-321.

OHB et infections osseuses en pratique

- Barili F et al. Role of Hyperbaric oxygen therapy in the treatment of post operative organ/space sternal surgical site infections. World J Surg 2007;31(8): 1702-6.
  - Prospectif non randomisé: 14 OHB vs 18 refus d'OHB

Table 3 Details of organ/space sternal SSI

Parameter	Group 1 (HBO)	Group 2 (non-HBO)	*p*
Organ/space sternal SSI pathogens			0.973
Staphylococcus aureus	5 (35.7%)	7 (38.9%)	
Staphylococcus epidermidis	6 (42.9%)	7 (38.9%)	
Staphylococcus coagulase(-)	3 (21.4%)	4 (22.2%)	
Time from surgery to recognized infection (days)	14.9 ± 6.8	9.9 ± 7.1	0.130

SSI: surgical site infection

Table 4 Clinical outcomes

Parameter	Group 1 (HBO)	Group 2 (non-HBO)	*p*
Duration of infection until sterilization (days)	31.8 ± 7.6	29.3 ± 5.8	0.357
Duration of infection until wound closure (days)	34.7 ± 7.7	31.1 ± 6.0	0.199
Infection relapse rate	0	6 (33.3%)	0.024
Interval between first and second infections (days)	—	7.67 ± 1.4	—
Duration of intravenous antibiotic use (days)	47.8 ± 7.4	67.6 ± 25.1	0.036
Total hospital length of stay (days)	52.6 ± 9.1	73.6 ± 24.5	0.026

OHB et infections osseuses en pratique

- Petites séries hétérogènes
  - Définition / classifications…
  - Localisations…
  - Terrains sous jacents…
  - Traitements…
  - Sélections…

Hart BB. Hyperbaric oxygen for refractory osteomyelitis. Undersea Hyperb Med 2021;48(3):297-321.

OHB et infections osseuses en pratique

- OHB préventif
  - Roje Z et al. Influence of adjuvant HBOT on short-term complications during surgical reconstruction of upper and lower extremity war injuries: retrospective cohort study. *Croat Med J 2008;49:224-32.*
    - Série rétrospective

Table 4. Short-term complications of extremity war wounds with respect to adjuvant hyperbaric oxygen (HBO) therapy in 388 patients treated at Split University Hospital between 1991 and 1995, with adjustment for North Atlantic Treaty Organization (NATO) strategy of emergency war surgery

	No. (%) of patients in the group			OR (95% CI)*	
Complications	without HBO therapy (n = 289)	with HBO therapy (n = 99)	*P*	raw	adjusted for NATO
Deep soft tissue infection	196 (68)	35 (35)	<0.001†	3.8 (2.3-6.1)	3.9 (2.4-6.2)
Osteomyelitis	214 (74)	62 (63)	0.030†	1.7 (1.1-2.8)	1.5 (1.0-2.4)
Skin graft lyses	151 (52)	23 (23)	<0.001†	3.6 (2.1-6.1)	3.8 (2.2-6.4)
Flap necrosis	147 (51)	15 (15)	<0.001†	5.8 (3.2-10.5)	6.2 (3.4-11.2)
Time to granulation formation (days; median, range)	12 (1-12)	9 (5-57)	<0.001‡	–	–

*Odds ratio (OR) with 95% confidence intervals (95% CI) for short term complications of war wounds when HBO therapy was not applied and when it was applied. The adjustment for use of NATO surgical strategy was performed by multiple logistic regression, with HBO therapy and NATO surgical strategy as the binary independent variables.
†χ^2 test.
‡Mann-Whitney test.

OHB et recommandations

Type 1 indications	Level of evidence		
	A	B	C
Anaerobic or mixed bacterial infections			X
CO poisoning		X	
Decompression illness			X
Gas embolism			X
Open fractures with crush injury		X	
Osteoradionecrosis (mandible)		X	
Prevention of osteoradionecrosis after dental extraction		X	
Soft tissue radionecrosis (cystitis, proctitis)		X	
Sudden deafness		X	

Pas dans les infections ostéo articulaires…

Mathieu D et al. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for acceped and non-accepted clinical indications and practice of HBOT. Diving Hyperb Med 2017; 47: 24-32.

European Committee for Hyperbaric Medicine

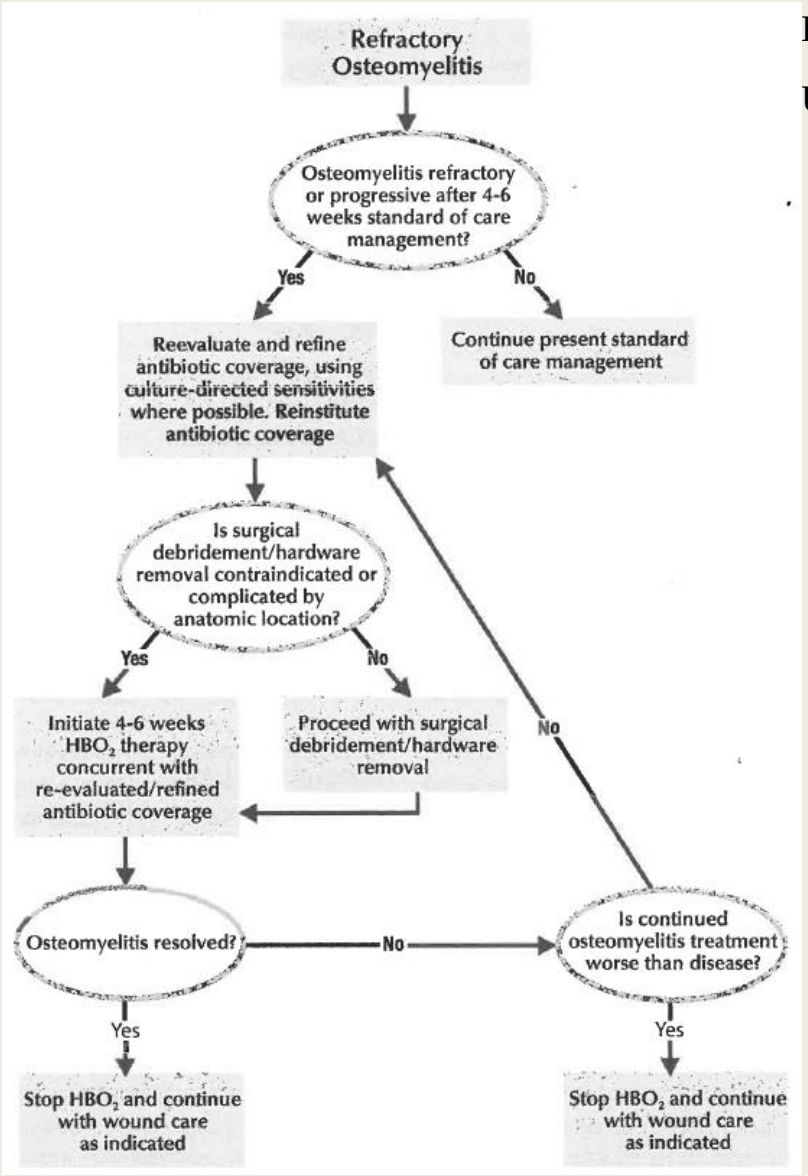
OHB et recommandations

Type 2 indications		
Burns, 2nd degree more than 20% BSA		X
Central retinal artery occlusion (CRAO)		X
Compromised skin grafts and musculocutaneous flaps		X
Crush injury without fracture		X
Diabetic foot lesions	X	
Femoral head necrosis	X	
Ischemic ulcers		X
Neuroblastoma, stage IV		X
Osteoradionecrosis (bones other than mandible)		X
Pneumatosis cystoides intestinalis		X
Radio-induced lesions of soft tissues (other than cystitis and proctitis)		X
Refractory chronic osteomyelitis		X
Surgery and implant in irradiated tissue (preventive treatment)		X

- Adjuvant à chirurgie et antibiothérapie

Mathieu D et al. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for acceped and non-accepted clinical indications and practice of HBOT. Diving Hyperb Med 2017; 47: 24-32.

OHB et recommandations ostéomyélites



Hart BB. Hyperbaric oxygen for refractory osteomyelitis.

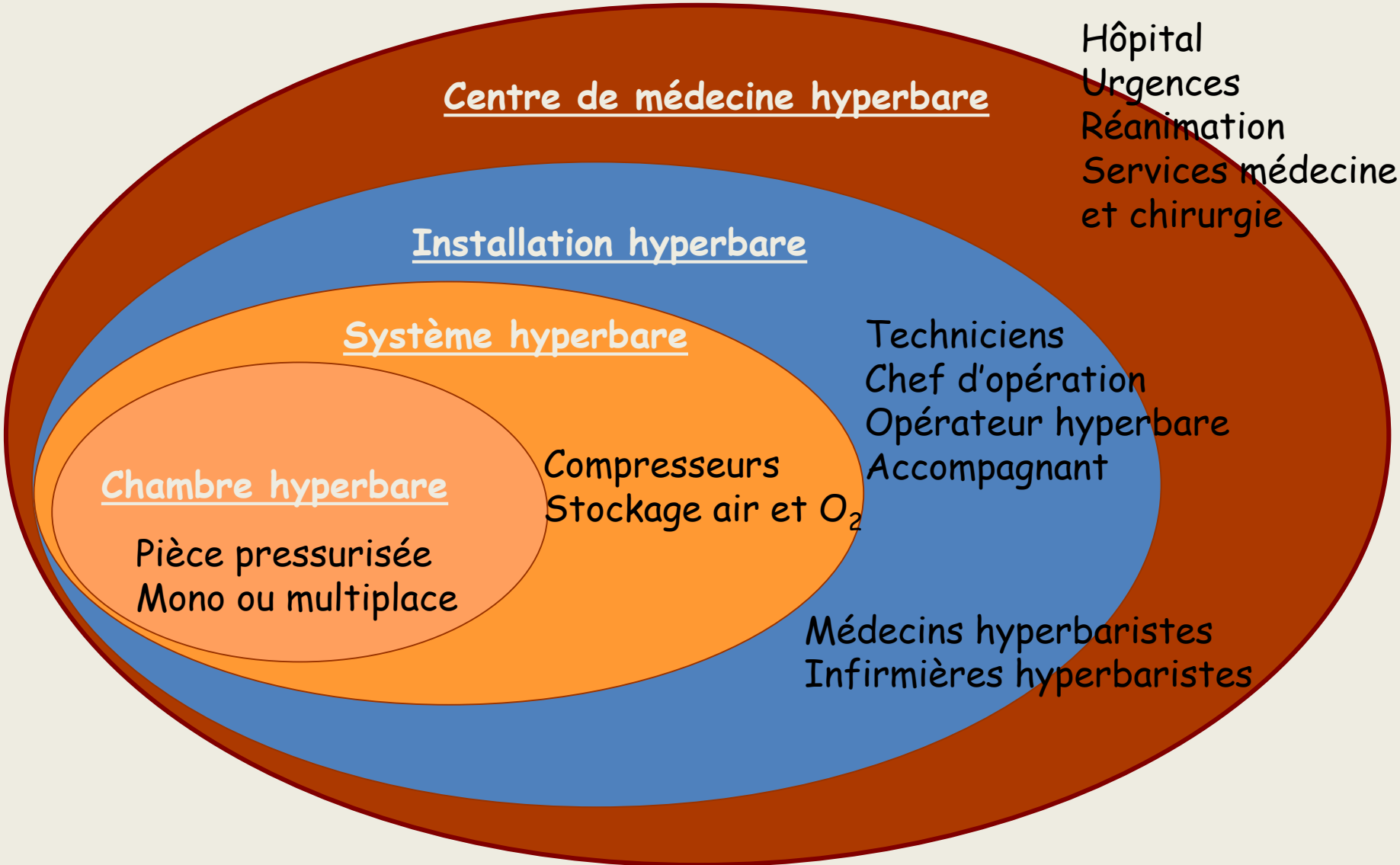
Undersea Hyperb Med 2021;48(3):297-321.

Refractory chronic osteomyelitis

- We suggest HBOT be used in the treatment in chronic refractory osteomyelitis (Type 2 recommendation, Level C evidence).
- We suggest compromised hosts be identified as, in particular, they may benefit from HBOT (Type 2 recommendation, Level C evidence).
- We suggest HBOT protocol be individualized based on the condition and compliance of the patient (Type 2 recommendation, Level C evidence).
- We recommend the effects of HBOT be evaluated repeatedly during and after treatment using the same diagnostic methods as used pre HBOT. HBOT treatment should last at least 11–12 weeks, approx. 60 sessions, before any significant clinical effect should be expected. (Type 1 recommendation, Level C evidence).

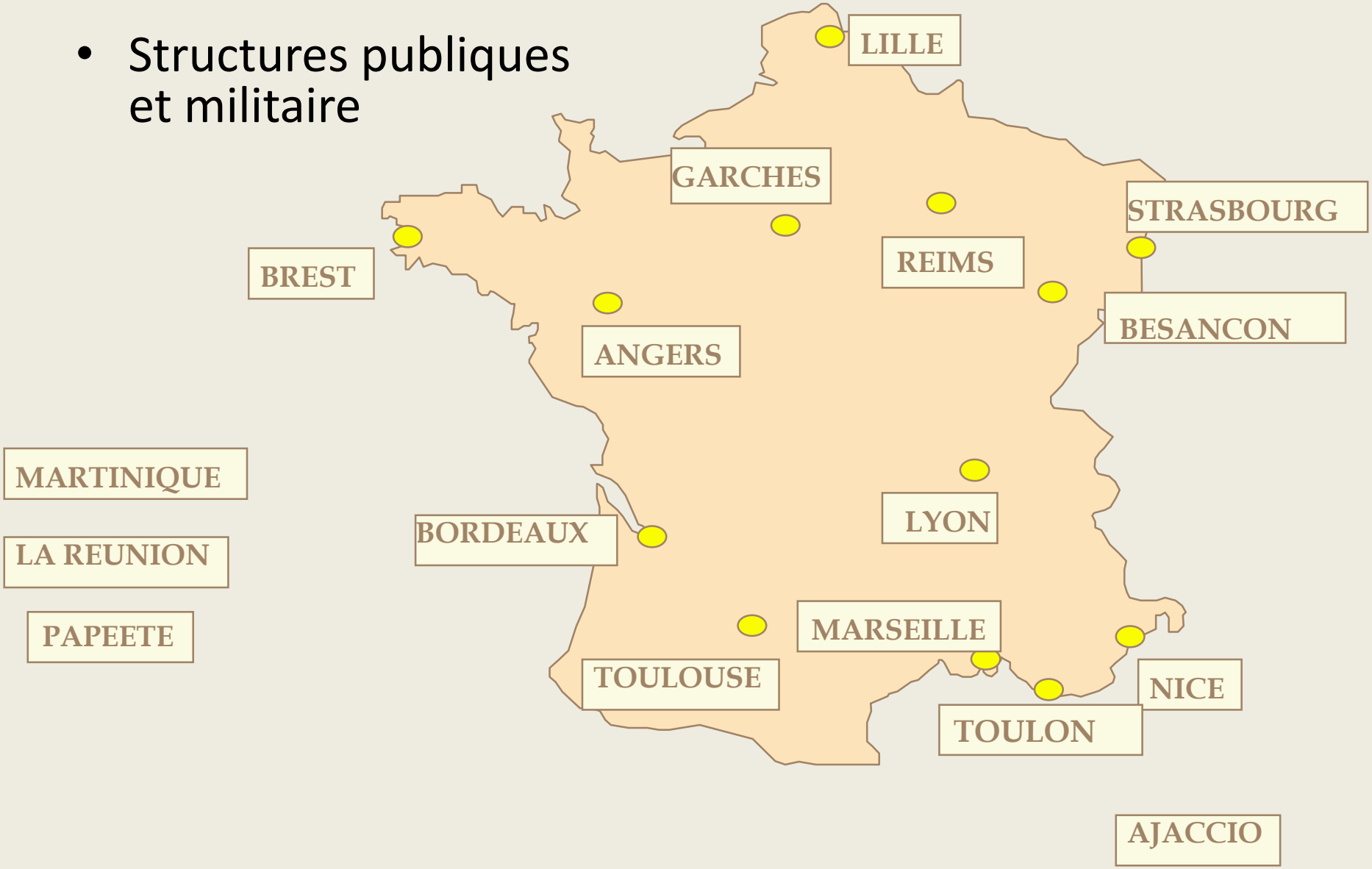
Mathieu D et al. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for acceped and non-accepted clinical indications and practice of HBOT. Diving Hyperb Med 2017; 47: 24-32.

OHB: structure d'un centre hyperbare



OHB en France

- Structures publiques et militaire



Happy New-Year !

Zalig Kerstfeest - Frohe Weih

Christmas - Zalig Kerstfeest -

Joyeux Noël - Merry Christmas - Z

Before HBO

After HBO

Hyperbaric Oxygen is also effective as a cure for many diseases !!