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OTOTOXICITÉ PROFESSIONNELLE : UN MAL ENCORE TROP SOUVENT IGNORÉ

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IL N'Y A PAS QUE LE BRUIT QUI REND SOURD

Institut national de recherche et de sécurité
pour la prévention des accidents du travail et des maladies professionnelles

Ototoxicité: le concept

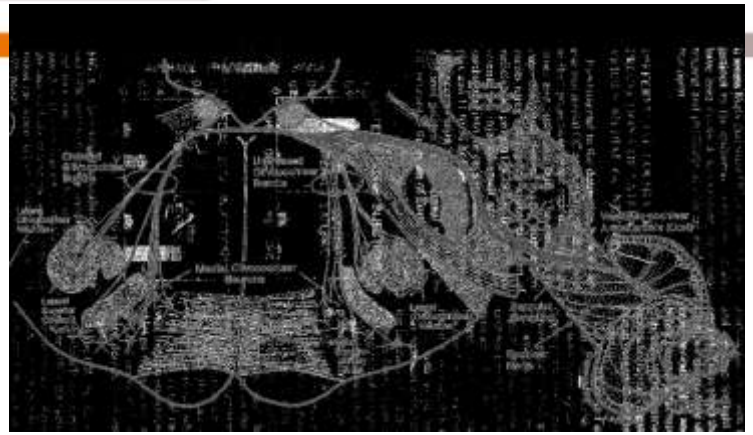
Une substance ototoxique provoque des lésions dans l'oreille interne (cochlée, vestibule) ou au niveau du nerf auditif.
L'ototoxicité peut générer des baisses d'audition, des surdités ou des acouphènes.

Origines?

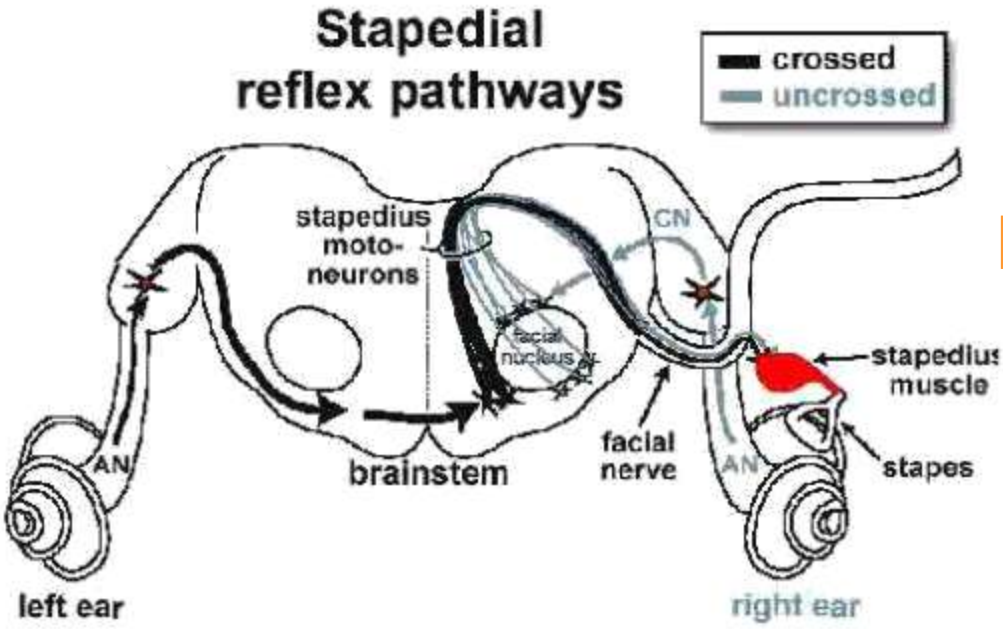
Les médicaments ototoxiques
Certains médicaments ont un effet ototoxique, comme des antipaludéens (quinine par exemple), des antibiotiques, des diurétiques, des anti-inflammatoires non stéroïdiens (comme l'aspirine) ou des anticancéreux.

Les agents chimiques ototoxiques
Certains solvants ont un effet ototoxique, comme les solvants aromatiques et chlorés.

Ces substances peuvent avoir un effet neuropharmacologique et modifier les
xes de l'oreille (olivo-cochléaire et stapédien).



Le réflexe de l'oreille interne



Le réflexe de l'oreille moyenne

Le point faible de la 2003/10/CE

Section II Article 4 6 alinea item (d)

L'employeur doit porter une attention particulière, si cela est techniquement possible, aux effets sur la santé des travailleurs d'une interaction entre bruit et substances ototoxiques provenant de l'environnement de travail.

DIRECTIVE 2003/10/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 6 February 2003

on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (noise)

(Seventeenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC)

Section II, Article 4, 6 Alinéa, item (d)

exposure limit values and the exposure action values, use the weekly noise exposure level in place of the daily noise exposure level to assess the levels of noise to which workers are exposed, on condition that:

(a) the weekly noise exposure level as shown by adequate monitoring does not exceed the exposure limit value of 87 dB(A); and

(b) appropriate measures are taken in order to reduce the risk associated with these activities to a minimum.

SECTION II

OBLIGATIONS OF EMPLOYERS

Article 4

Determination and assessment of risks

1. In carrying out the obligations laid down in Articles 6(3) and 9(1) of Directive 89/391/EEC, the employer shall assess and, if necessary, measure the levels of noise to which workers are exposed.

(1) 140 dB (C) in relation to 20 μPa.
(2) 137 dB (C) in relation to 20 μPa.
(3) 135 dB (C) in relation to 20 μPa.

exposure to impulsive noise;

(b) the exposure limit values and the exposure action values laid down in Article 3 of this Directive;

(c) any effects concerning the health and safety of workers belonging to particularly sensitive risk groups;

(d) as far as technically achievable, any effects on workers' health and safety resulting from interactions between noise and work-related ototoxic substances, and between noise and vibrations;

(e) any indirect effects on workers' health and safety resulting from interactions between noise and warning signals or other sounds that need to be observed in order to reduce the risk of accidents;

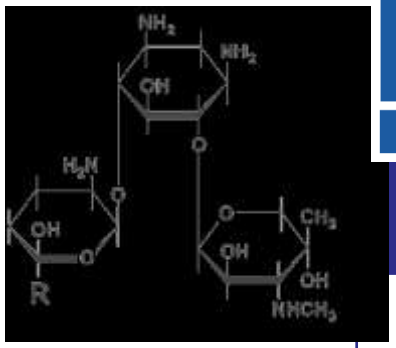
(f) information on noise emission provided by manufacturers of work equipment in accordance with the relevant Community directives;

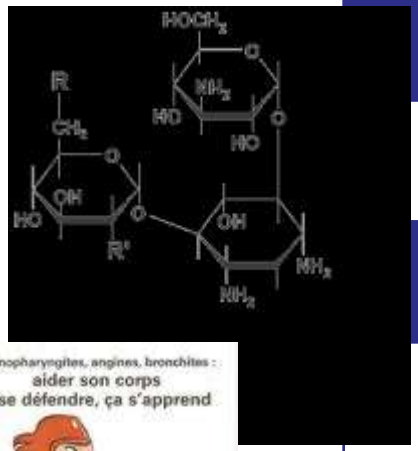
(g) the existence of alternative work equipment designed to reduce the noise emission;

(h) the extension of exposure to noise beyond normal working hours under the employer's responsibility;

Sommaire

Les antibiotiques aminoglycosidiques

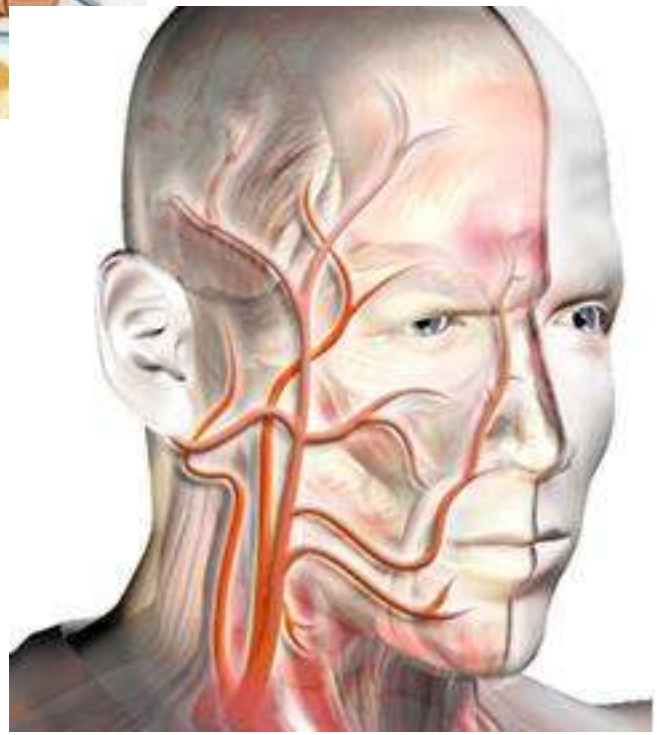




hopital

Antibiotiques	Utilisations thérapeutiques
Amikacine	infection nosocomiale
Gentamicine	pneumonie, méningite
Tobramycine	associé avec gentamicine
Kanamycine	tuberculose si résistance
Néomycine	infection de peau et muqueuse
Streptomycine	endocardite, tuberculose

Voie d’intoxication



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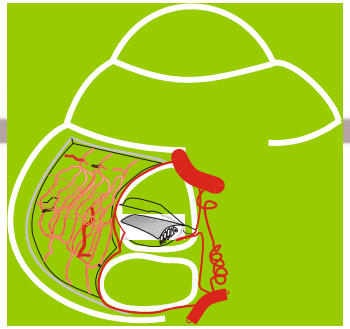

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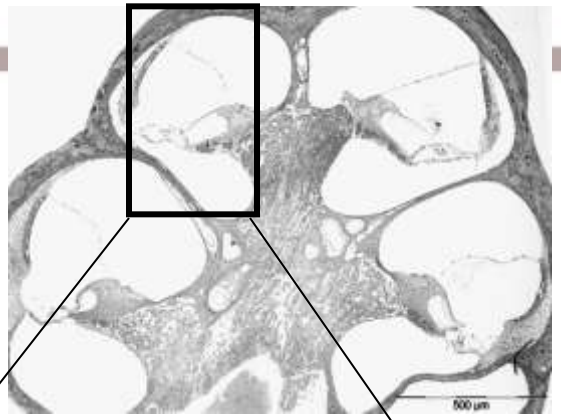
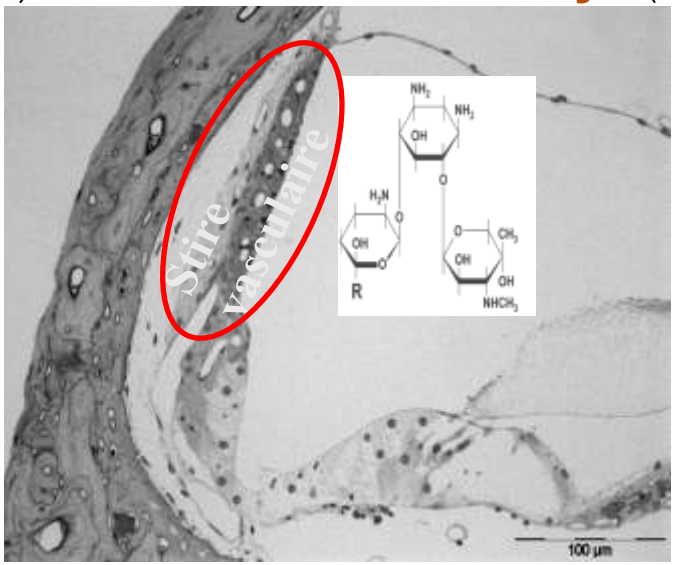


Les aminosides traversent la barrière hémato-labyrinthique



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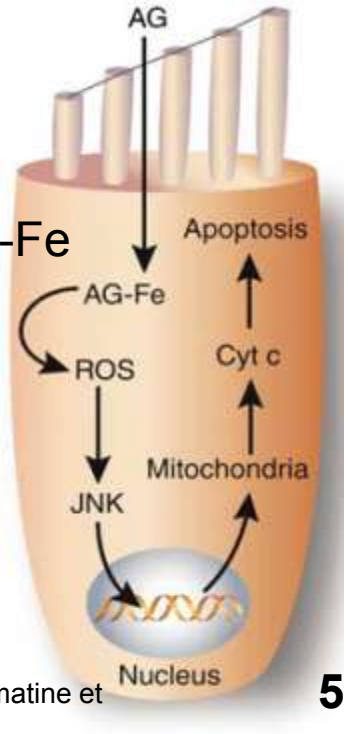
Complexe AG-Fe



5

Condensation de la chromatine et fragmentation du DNA

Caractéristiques des pertes auditives induites par les aminosides

- ✓ Pertes au niveau des fréquences élevées 8-12 kHz : problème!!!!!
- ✓ Synergie avec les effets du bruit

+

= Synergie

Sommaire

1. Effets des agents ototoxiques sur l'audition

1.1 Antibiotiques

1.2 Diurétiques

1.3 Anticancéreux

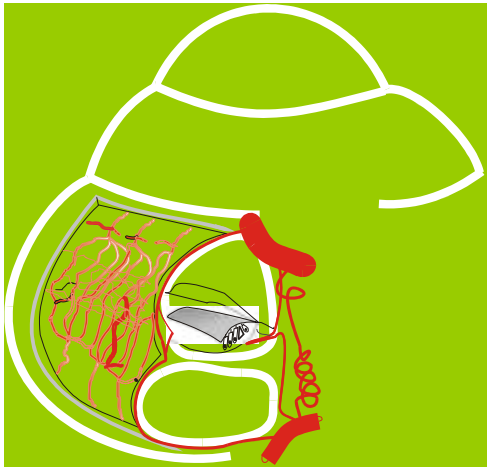
1.4 Solvants aromatiques

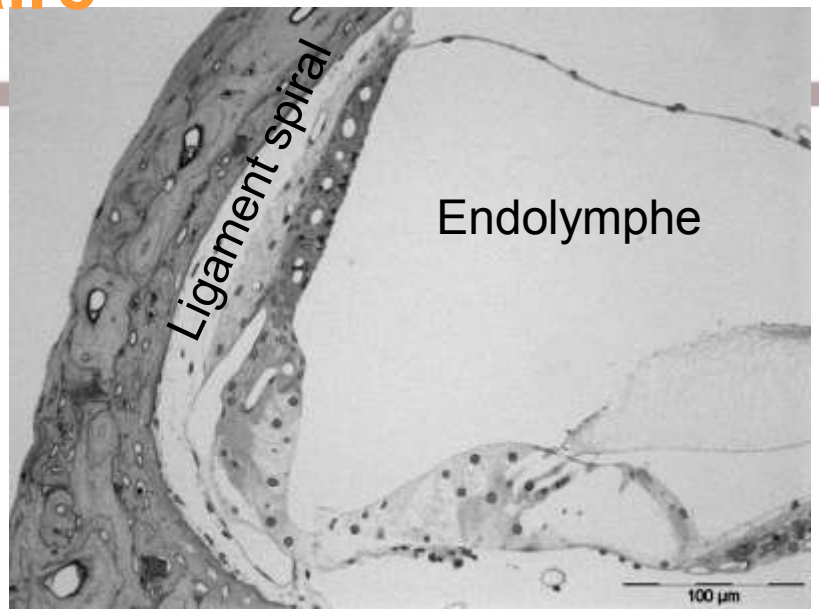
2. Effets combinés : bruit + agents chimiques

Les diurétiques de l'anse

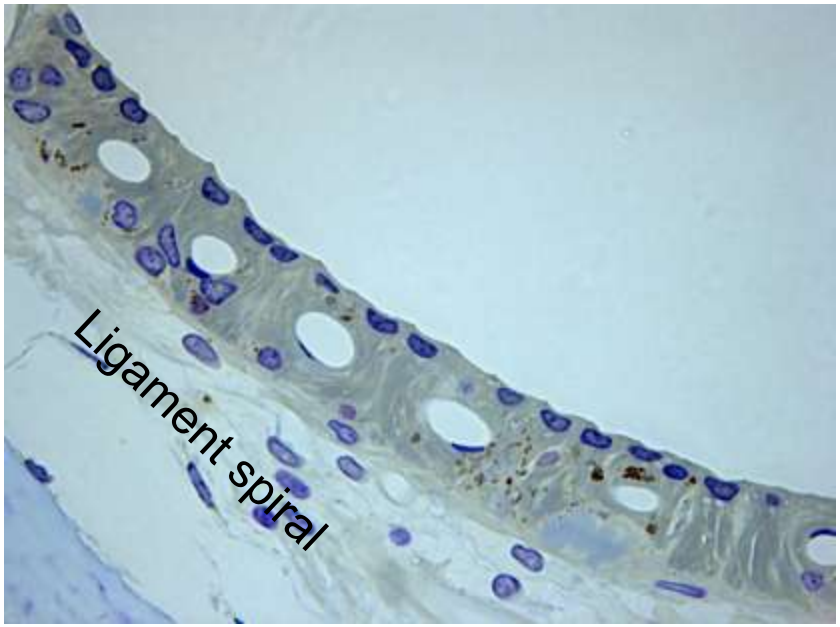
- Le furosémide (lasilix)
- L'acide éthacrynique (édécrine)
- Le bumétanide

La strie Vasculaire





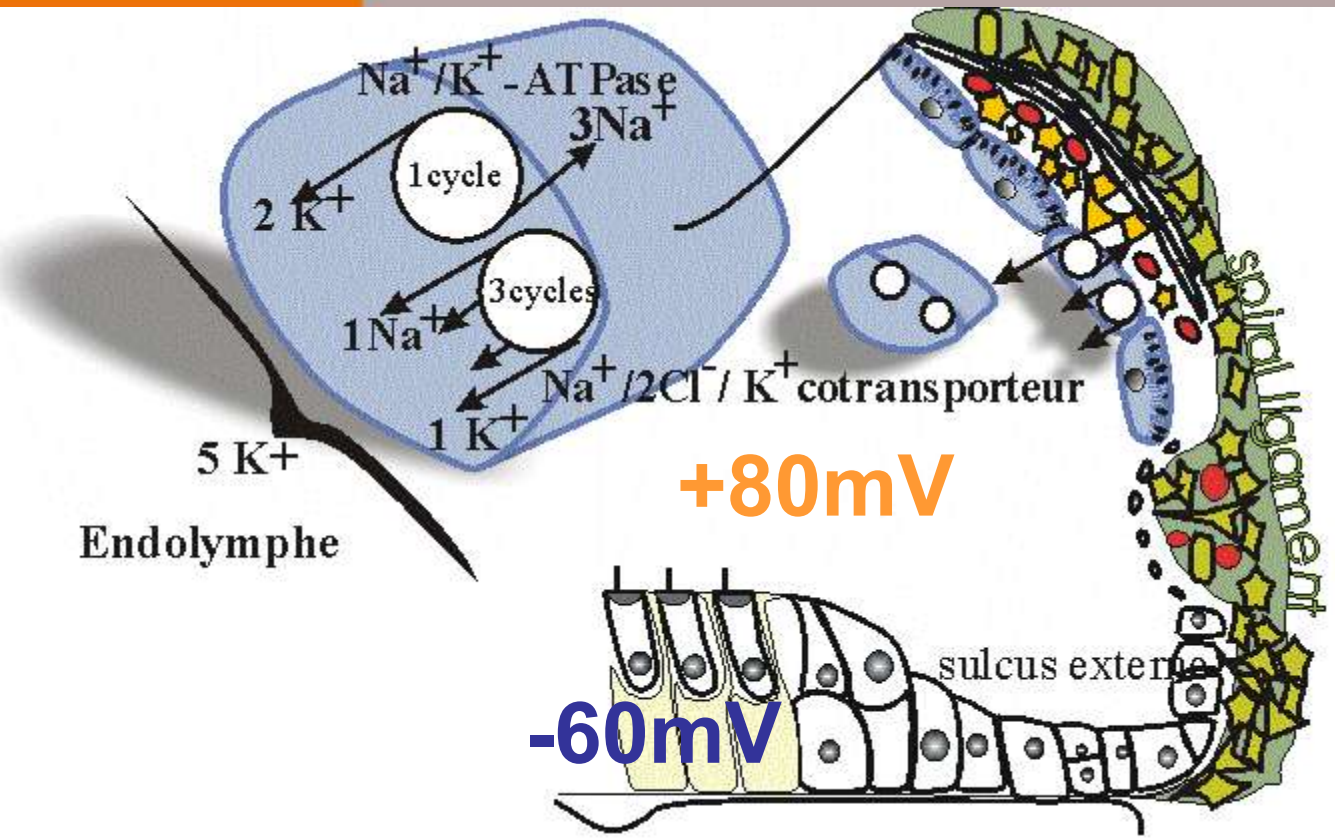
Périlymphe

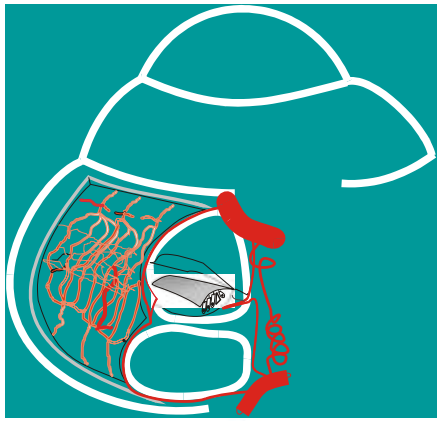


Les rôles des liquides de l'oreille interne ?

- Relaient les vibrations engendrées par la platine de l'étrier.
- Assurent la pression intra-cochléaire pour que le récepteur fonctionne.
- Procurent les nutriments et permettent d'éliminer les produits du catabolisme des cellules qui sont en contact avec le sang.
- Procurent l'environnement ionique requis pour assurer la transduction mécano-sensorielle.
- Assurent la constance du **potentiel endocochléaire**.

Moteur électrique cochléaire





Ototoxicité

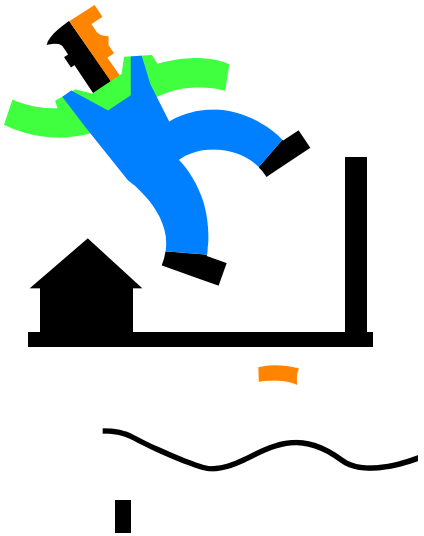
diurétiques *vs.* aminosides

1- La latence de l'accident cochléaire est brève, quelques min. seulement après ingestion

2 - La surdité est temporaire, elle disparaît en même temps que la clairance sanguine du diurétique

3 - Seule la cochlée est touchée, pas de vestibulotoxicité constatée

4 - Absence de synergie avec les effets du bruit



Synergies possibles

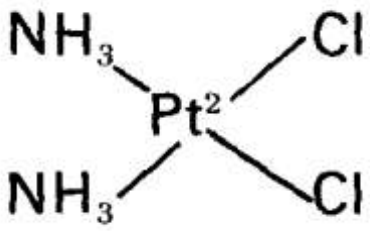
➢ Des cas cliniques ont montré qu'il existe une *S* entre les effets ototoxiques des AA et ceux des diurétiques.

➢ Étude a montré une potentialisation des effets ototoxiques de certains métaux lourds, comme le cadmium, par le furosémide.

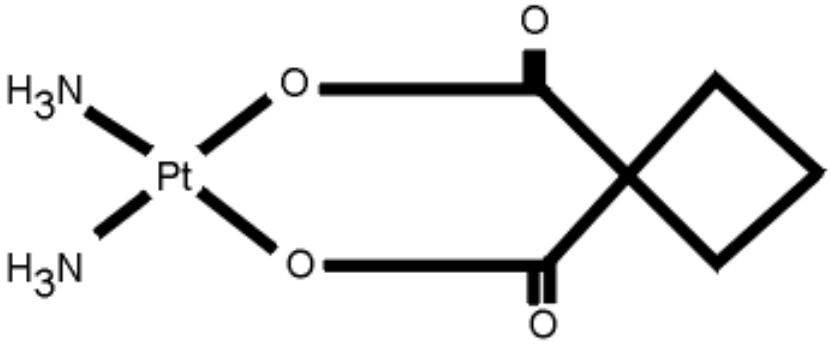
Sommaire

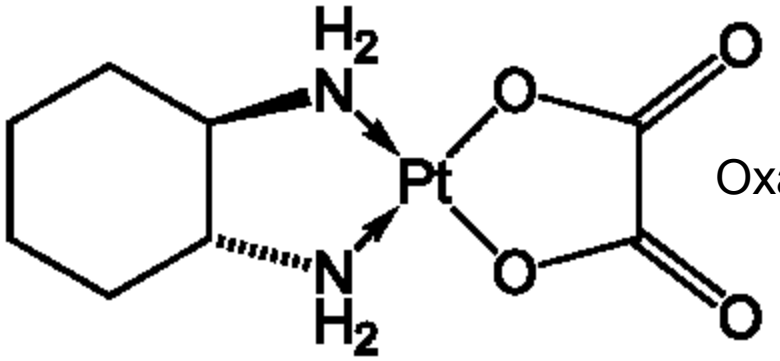
Médicaments anticancéreux (chimiothérapie)
Les dérivés du cisplatine

Cis-platine



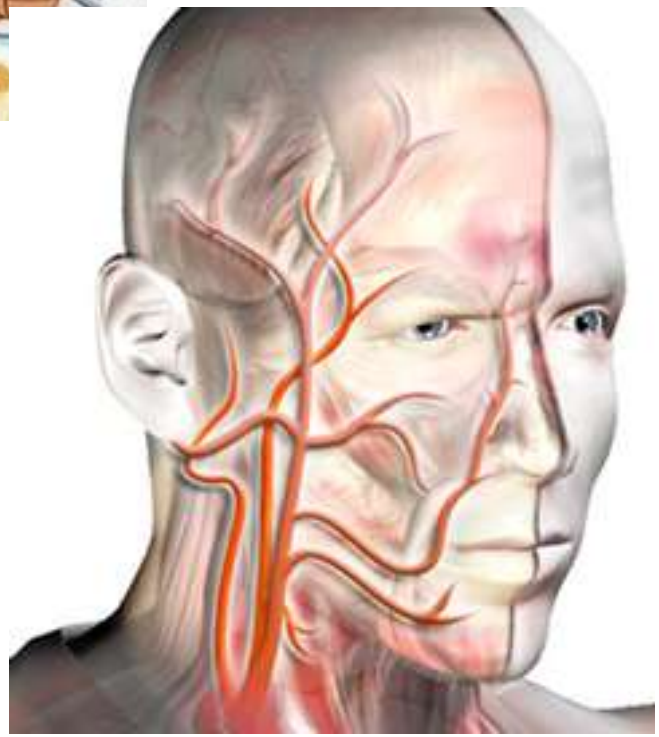
Carbo-platine



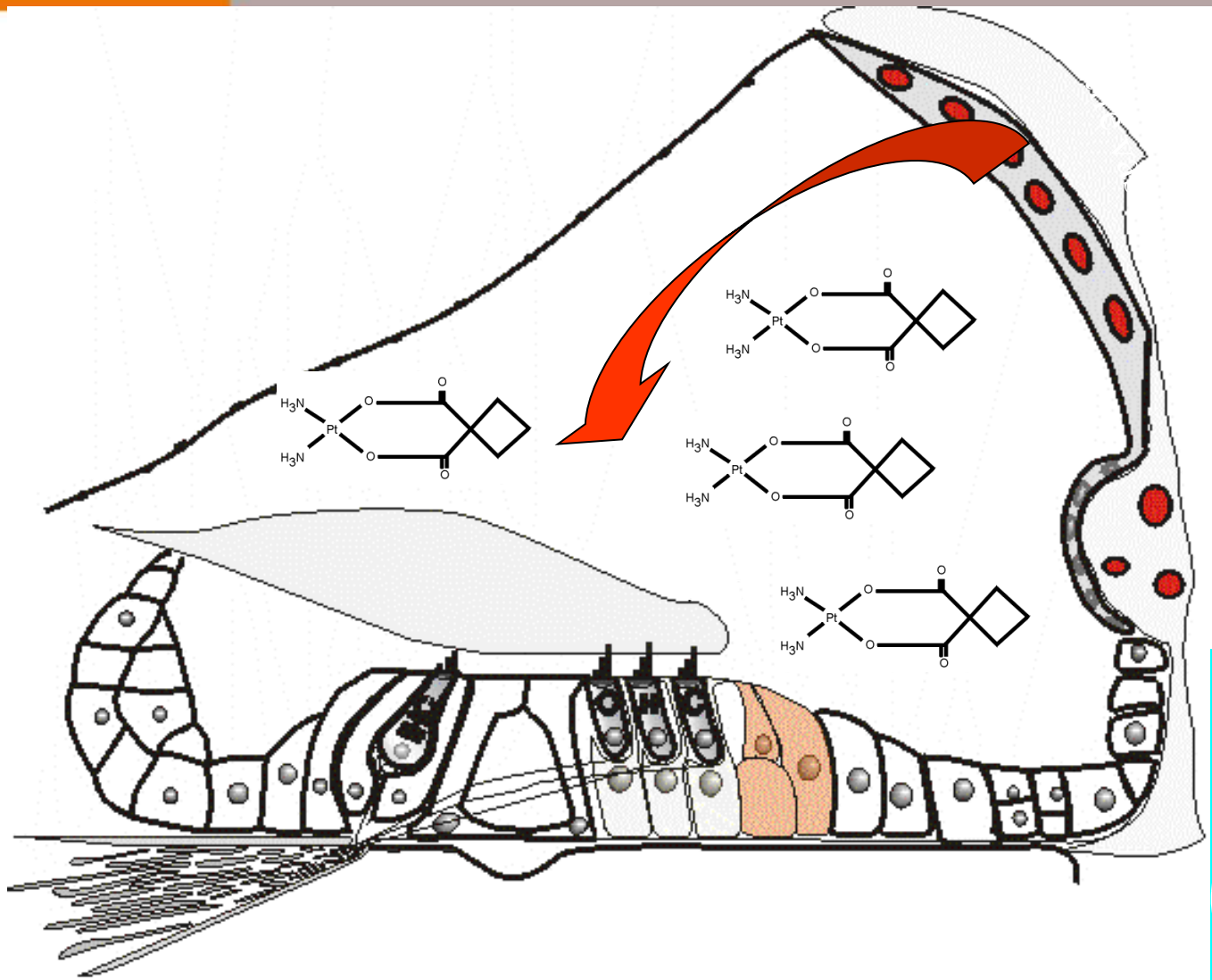


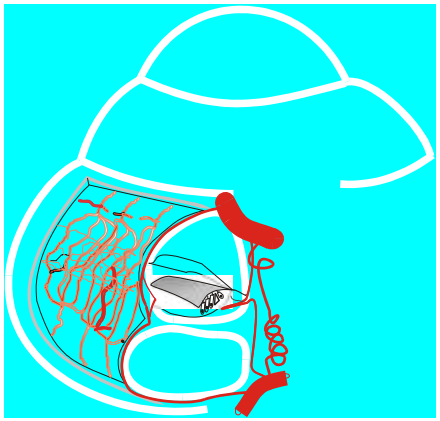
Oxaliplatine

Voie d’intoxication



Anticancéreux sont hydrophiles

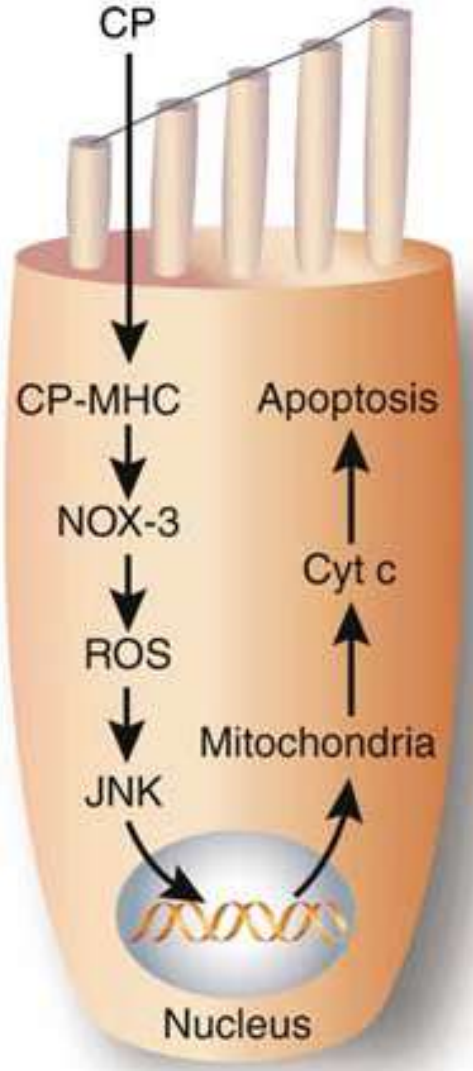




Ototoxicité du cis et carboplatine

Nicotinamide adénine dinucléotide phosphate oxidase NOX-3

Radicaux libres



Rybak L. A,d Ramkumar V. Ototoxicity. Kidney International (2007) 72, 931-935.

Ototoxicité des anticancéreux

1- Comme les diurétiques, les anticancéreux modifient les concentrations ioniques de l'endolymphe, mais de façon permanente

2- Comme les antibiotiques, les anticancéreux endommagent les fréquences élevées.

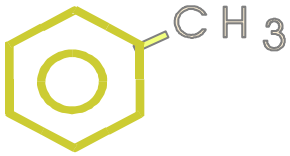
3- Comme les antibiotiques, les anticancéreux ont une clairance dans les liquides de l'oreille interne pouvant durer jusqu'à 3 mois.

4- Quant à la synergie des effets des anticancéreux avec le bruit, elle n'a pas été évaluée chez l'homme. Chez l'animal (rat et chinchilla), la synergie des effets des anticancéreux avec le bruit ne fait aucun doute.

Sommaire

Les solvants aromatiques

Toluène

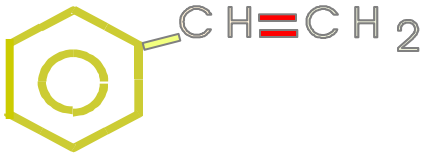


(peintures, vernis, encres, adhésifs et plastiques)

Xylènes

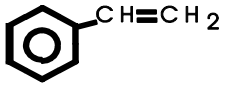
(peintures, vernis, encres, insecticides, caoutchouc et produits pharmaceutiques)

Styrène



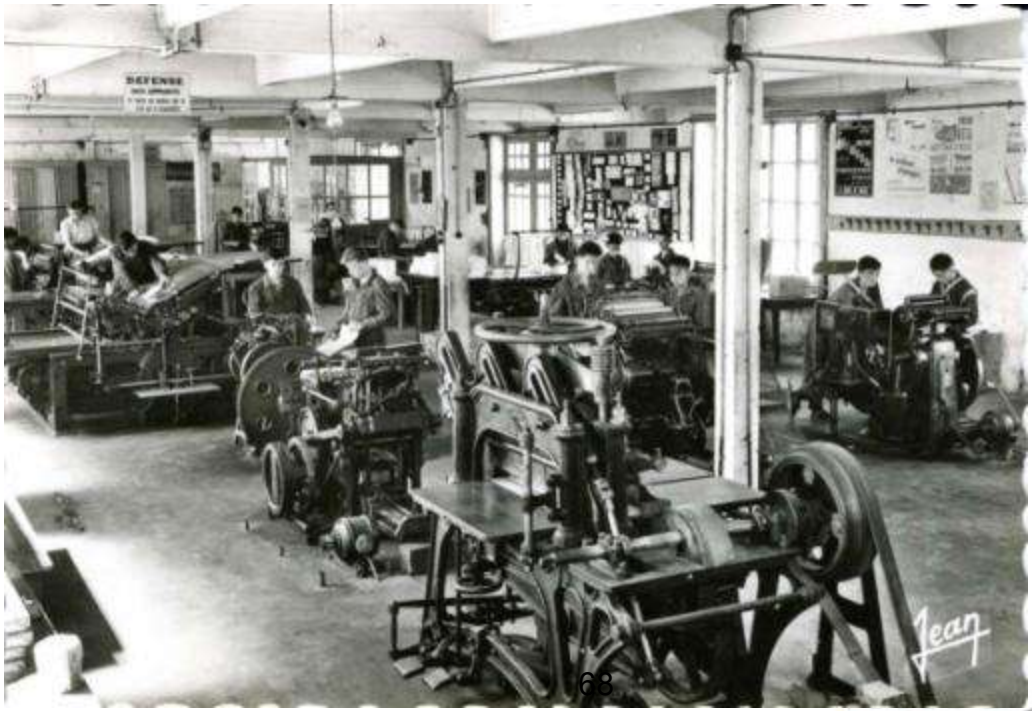
(résine de polystyrène renforcée à la fibre de verre)

Où les trouve-t-on?

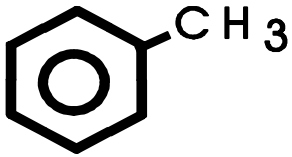


un mélange détonnant...

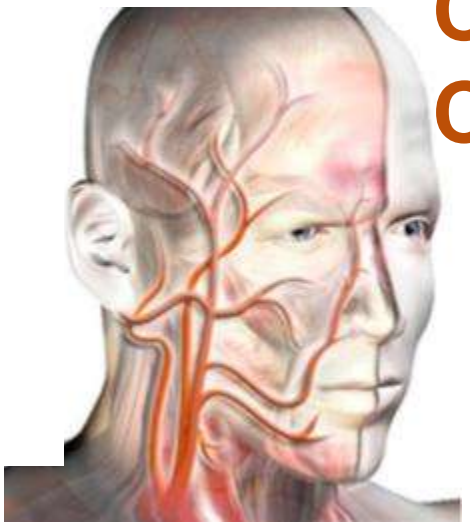
(résine de polystyrène renforcée à la fibre de verre)



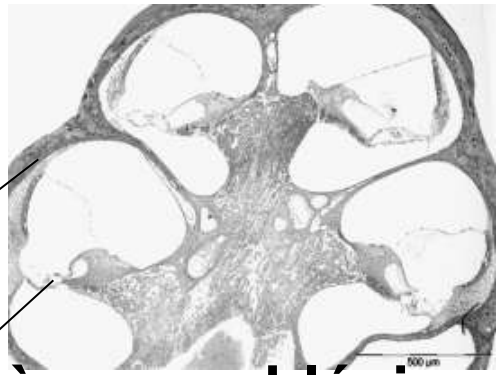
peintures, vernis, encres, adhésifs, plastiques



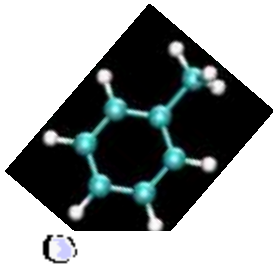
La voie d'intoxication

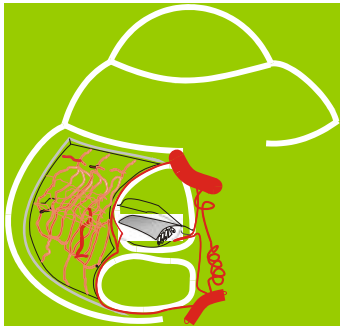


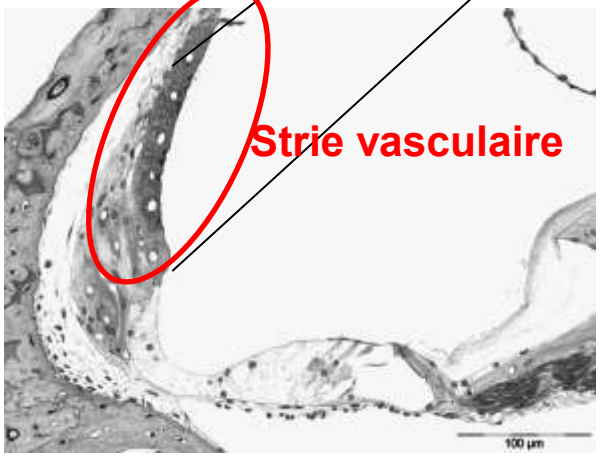
Charge sanguine : C_{art} TOL



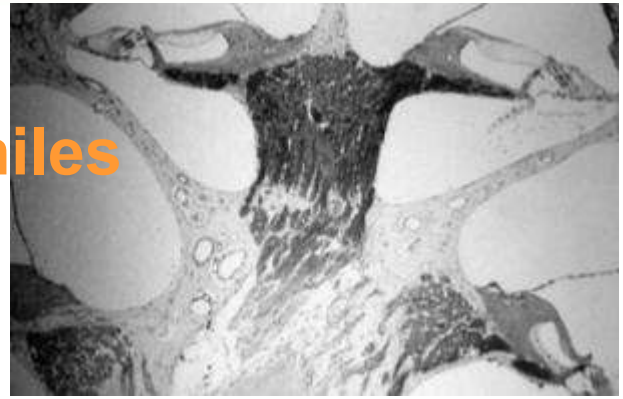
Artères cochléaires







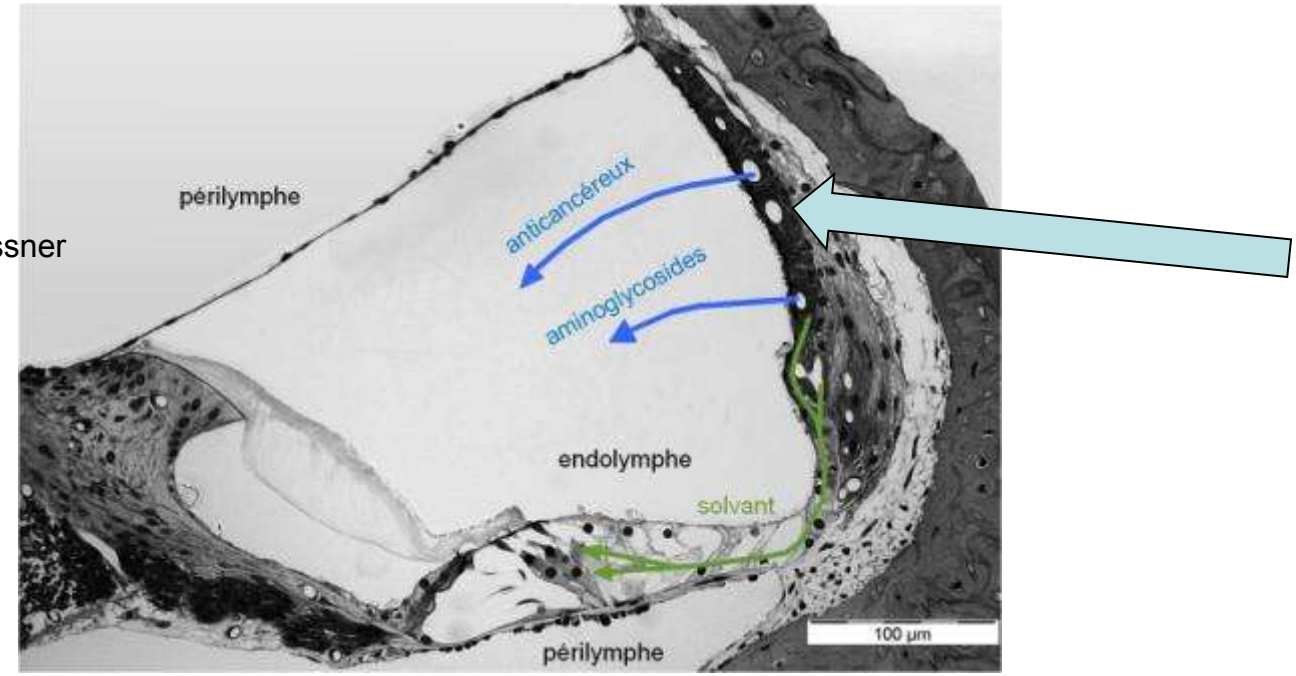
Les AA et les AC sont hydrophiles tandis que le Solvants sont lipophiles

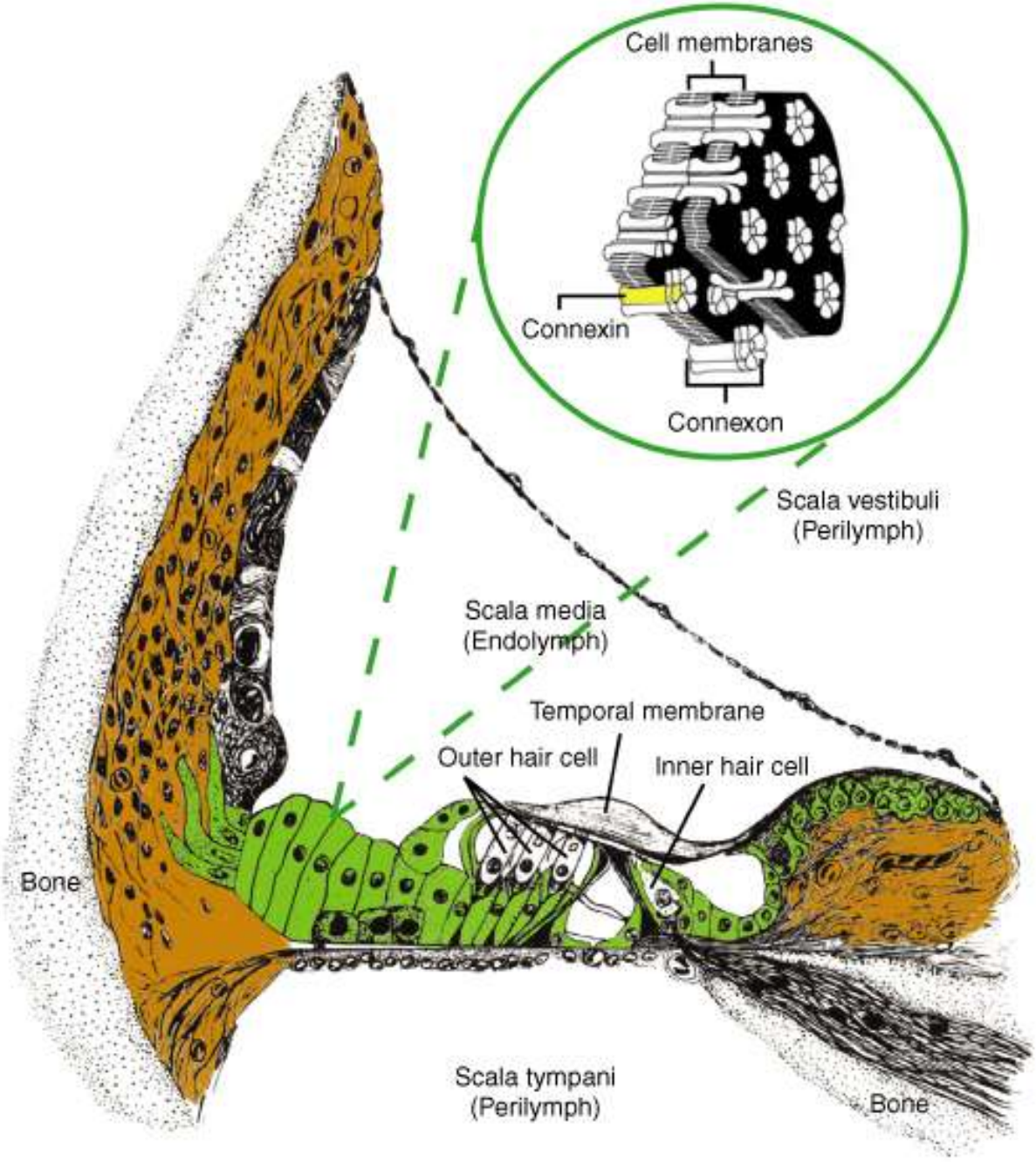


strie vasculaire

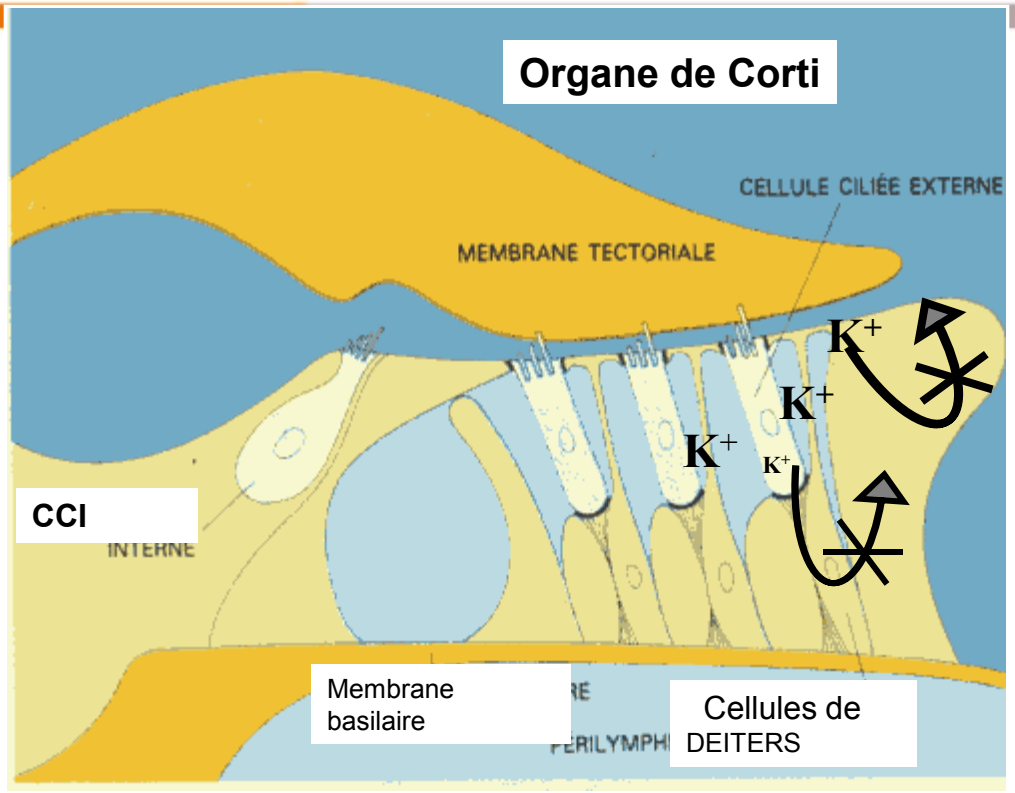
membrane de Reissner

organe de Corti




Cell membranes
Connexin
Connexon
Scala vestibuli
(Perilymph)
Scala media
(Endolymph)
Temporal membrane
Outer hair cell
Inner hair cell
Bone
Scala tympani
(Perilymph)
Bone

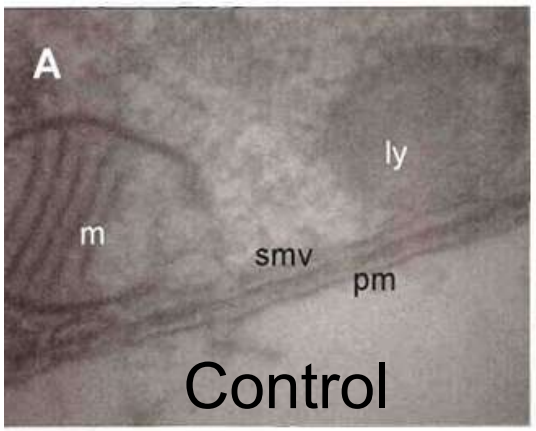
empoisonnement

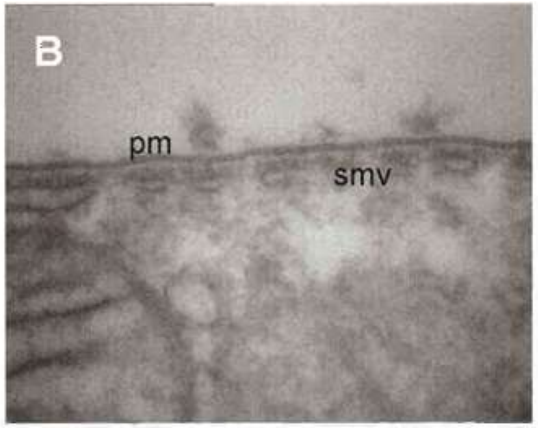


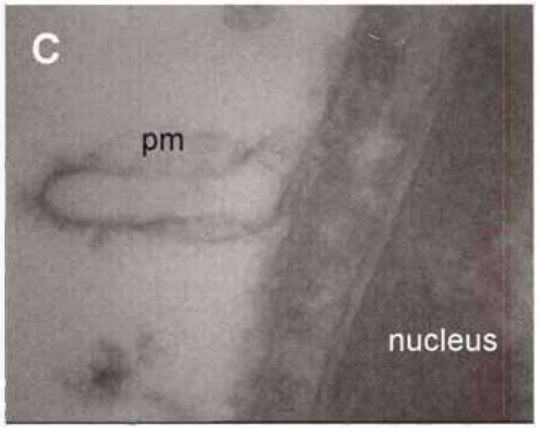
réabsorption

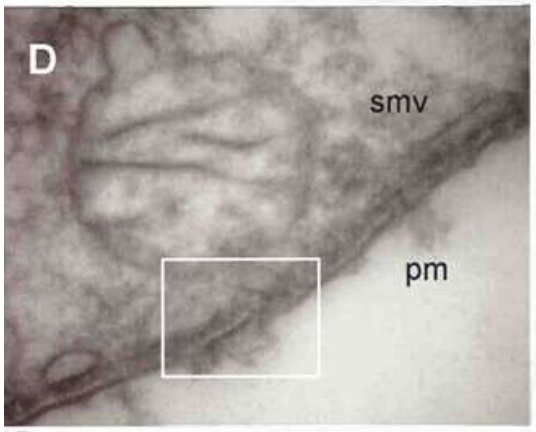
L'altération des cellules de Hensen et des Deiters perturbe l'environnement ionique autour des CCE et modifier la réabsorption du K+

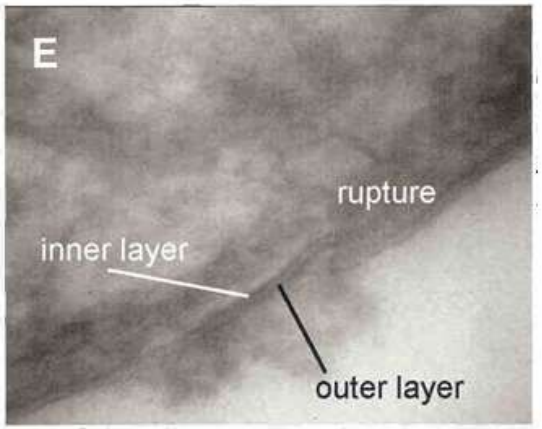
Péroxidation des lipides











Membrane des cellules ciliées

Une signature histopathologique différente

BRUIT

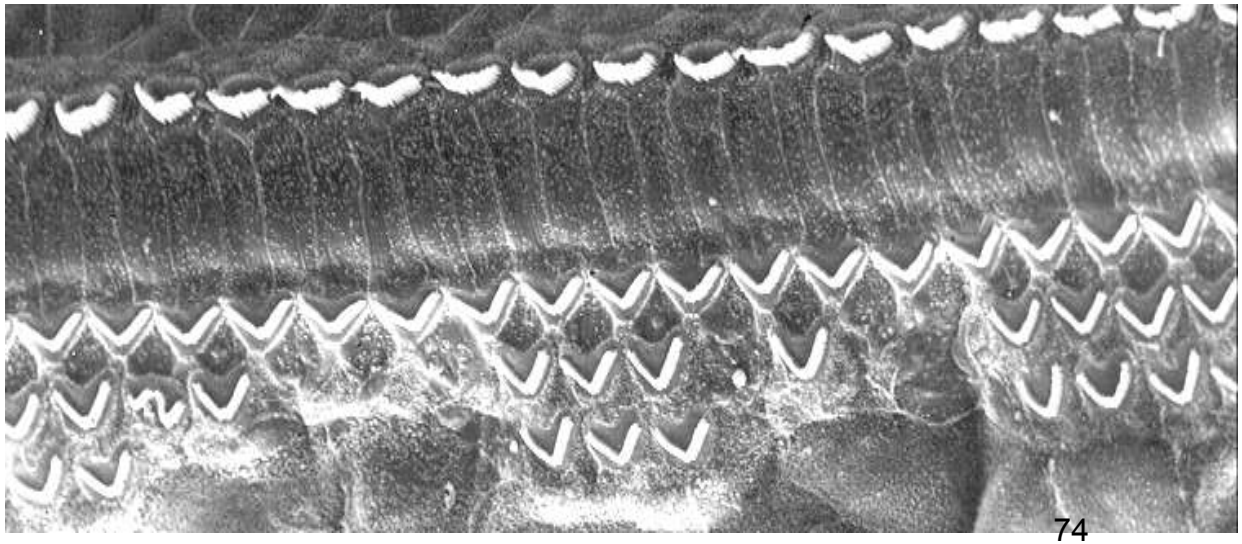
CCI

CCE1

CCE2

CCE3

SOLVANT



CCI

CCE1

CCE2

CCE3

Sommaire

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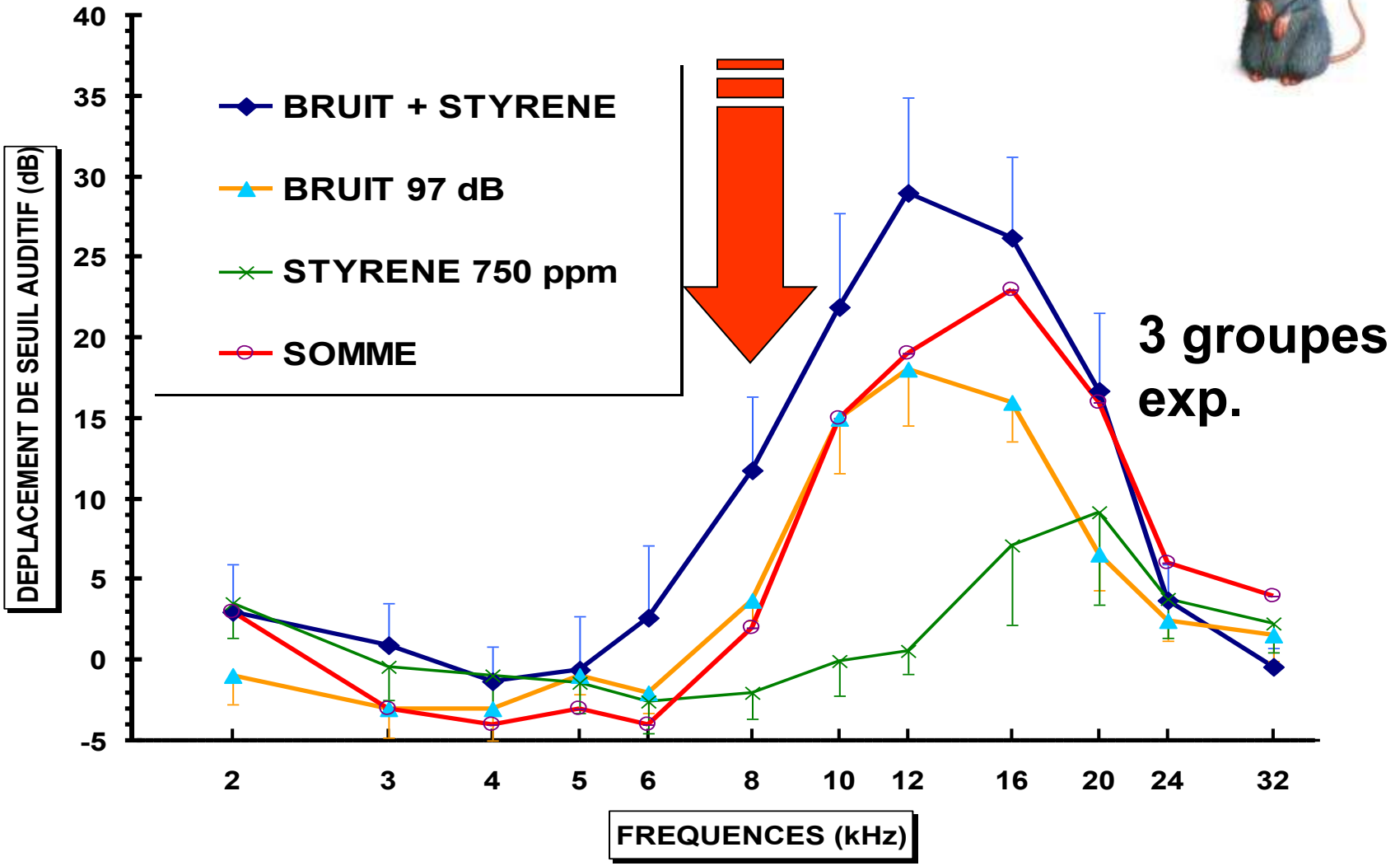
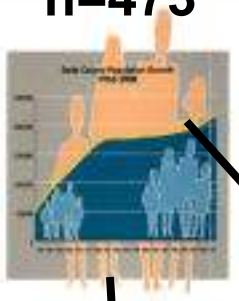
Synergie


BRUIT + STYRENE
BRUIT 97 dB
STYRENE 750 ppm
SOMME
3 groupes exp.
DEPLACEMENT DE SEUIL AUDITIF (dB)
40
35
30
25
20
15
10
5
0
-5
2
3
4
5
6
8
10
12
16
20
24
32
FREQUENCES (kHz)

Population

n=473



référence

n=157 (o ppm+73 dB)

89,2dB(A)

n=66

59,9 ppm

n=194

87dB(A) + 34 ppm

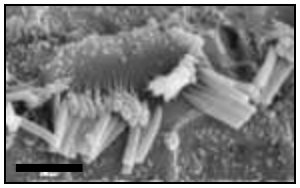
n=56

Odd ratio (styrène) = 4 fois plus grand que groupe référence

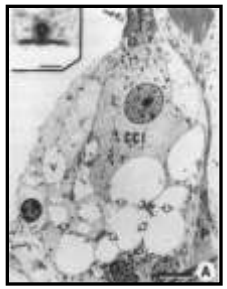
Odd ratio (bruit) = 3,3 fois plus grand / référence

Odd ratio (styrène+bruit) = 11 fois plus grand / référence

Fragilité du récepteur

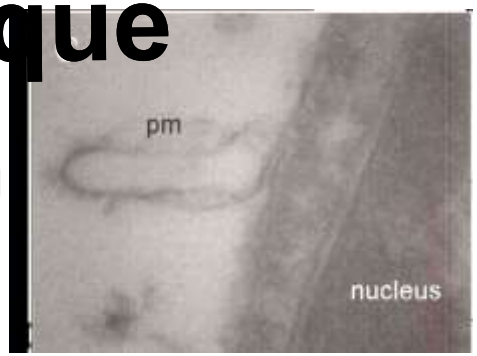


Effet mécanique



Excitotoxicité

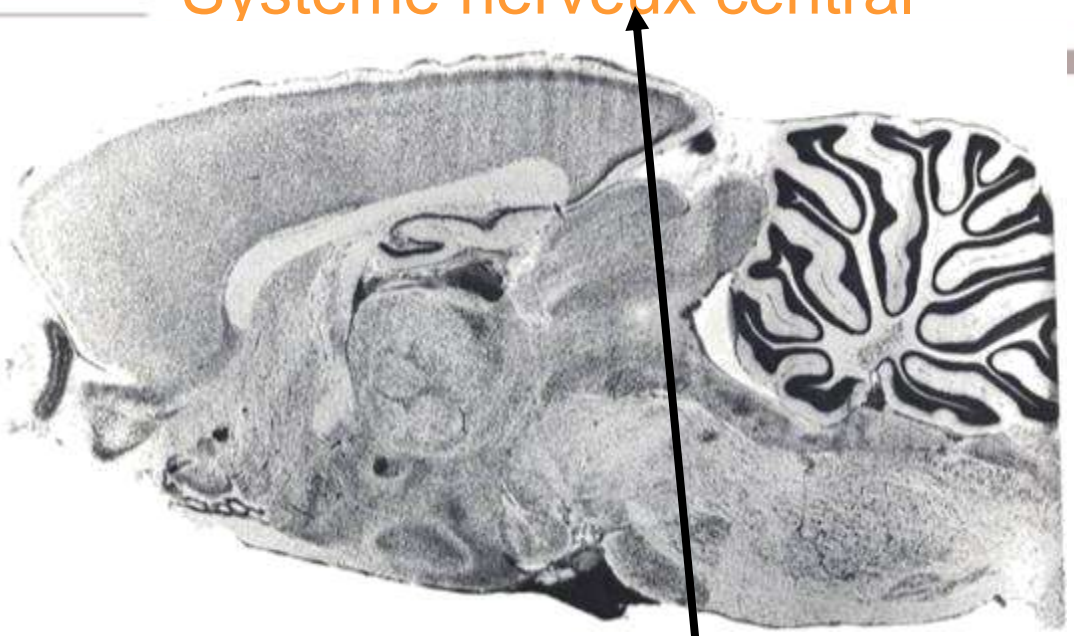
+

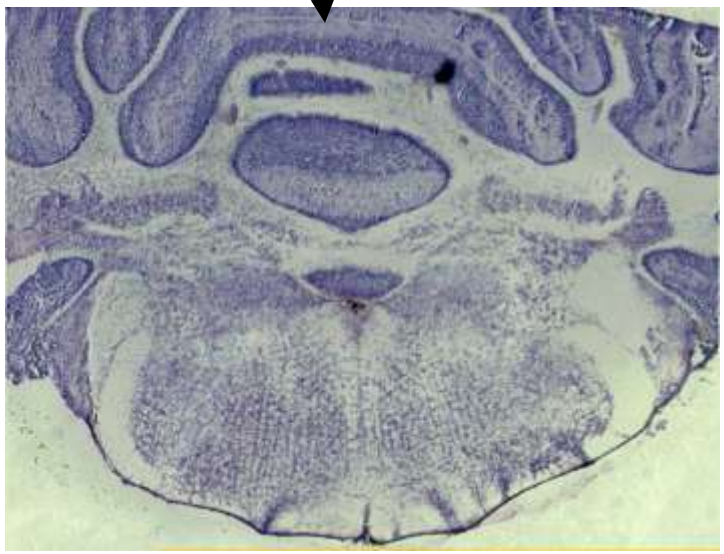


ROS

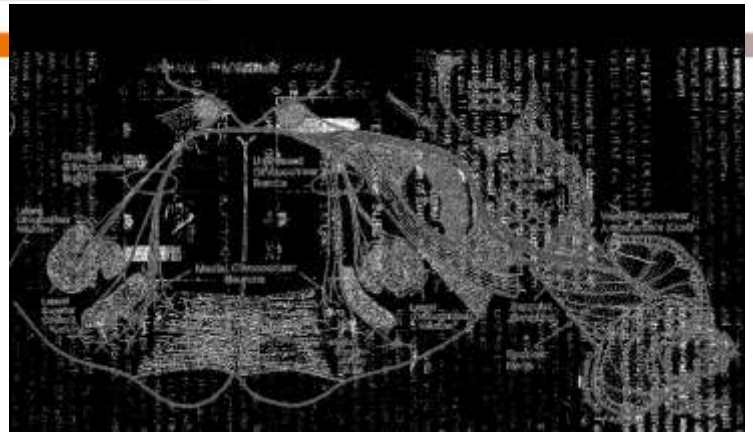
? = Synergie

Système nerveux central

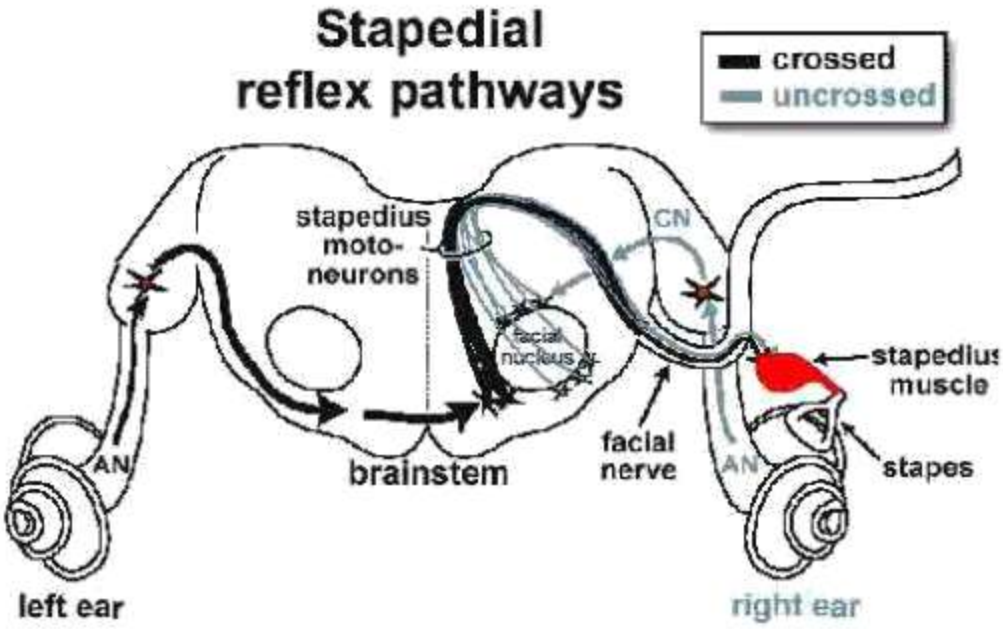


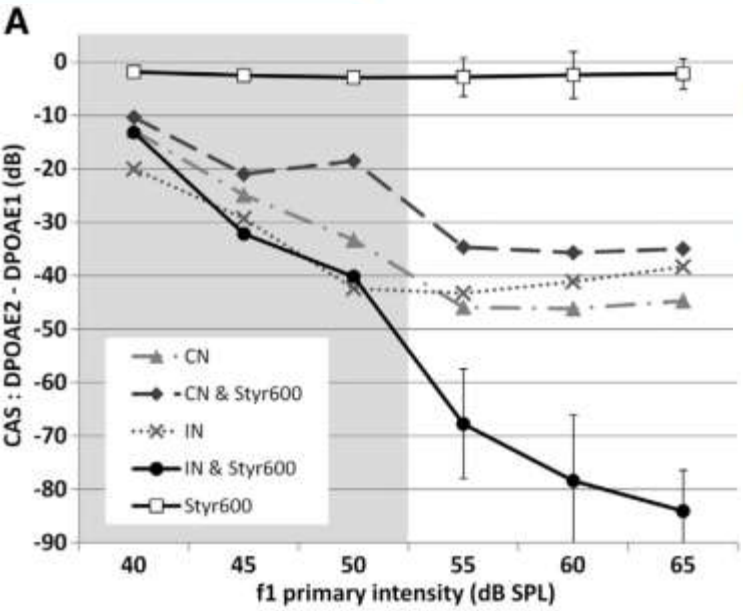


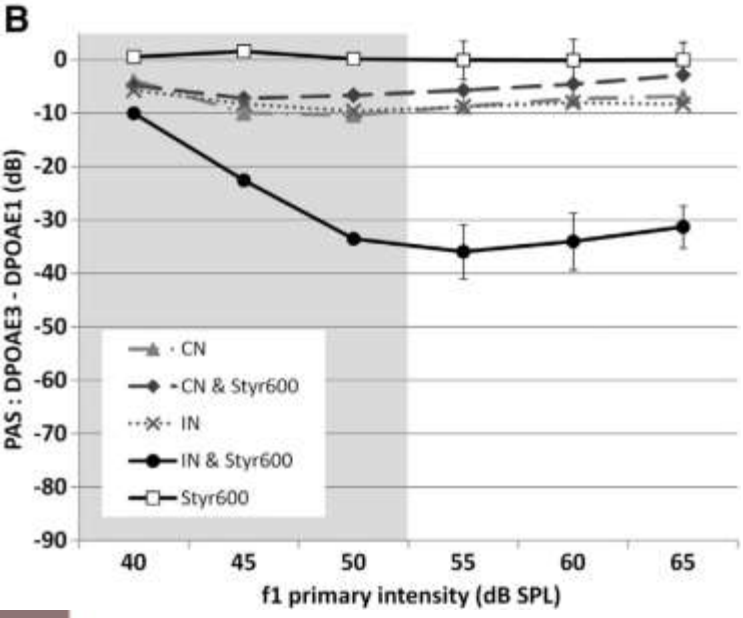
Le réflexe de l'oreille interne



Le réflexe de l'oreille moyenne







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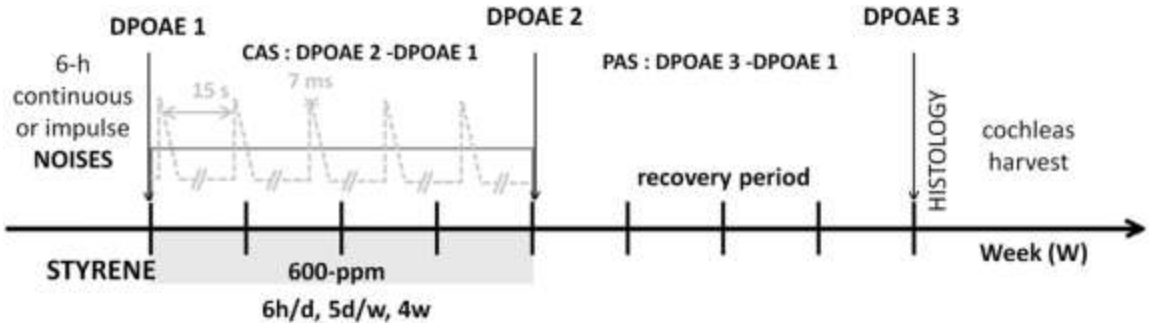
The tonotopicity of styrene-induced hearing loss depends on the associated noise spectrum

Thomas Venet [1], Pierre Campo *, Aurélie Thomas [1], Chantal Cour [1], Benoît Rieger [1], Frédéric Cosnier [1]

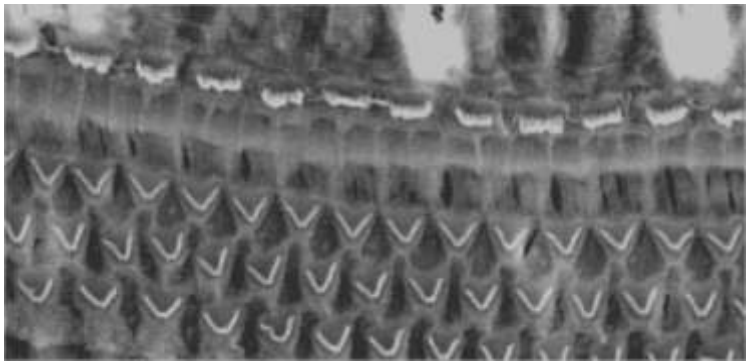
Institut National de Recherche et de Sécurité, Rue du Morvan, CS 60027, F-54519 Vandoeuvre Cedex, France

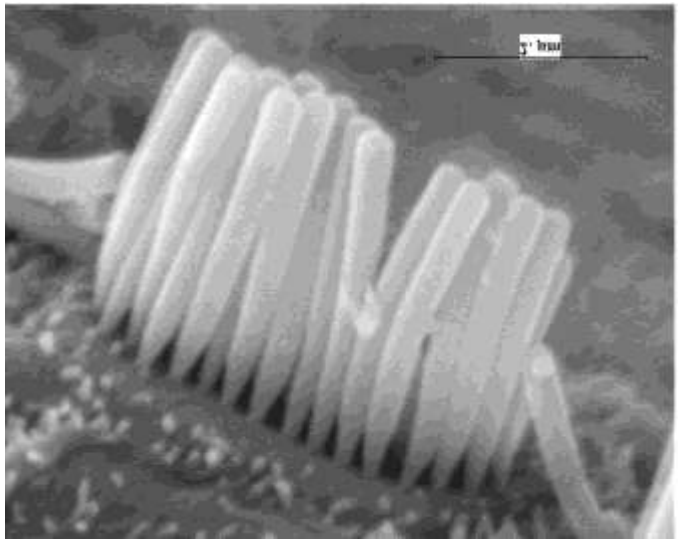


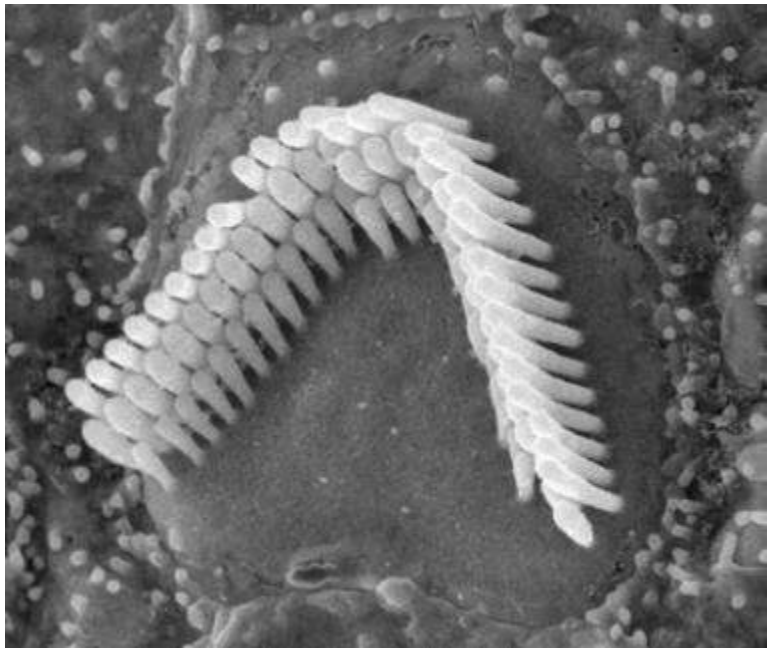
Merci pour votre attention

Nancy France

Les stéréocils







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Acceleration of Age-Related Hearing Loss by Early Noise Exposure: Evidence of a Misspent Youth

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Abstract

Age-related and noise-induced hearing losses in human
and potential interactions among, numerous variables
retrospective clinical study suggests an age-noise inter
loss in previously noise-damaged ears (Gates et al., 20
model by comparing noise-induced and age-related he
CaJ mice exposed identically (8-16 kHz noise band at
different ages (4-124 weeks) and held with unexposed
weeks). When evaluated 2 weeks after exposure, maxi
animals (4-8 weeks) were 40-50 dB; older-exposed ani
at the same postexposure time. However, when held f
previous exposure demonstrated AHL and histopathol
animals or old-exposed animals held for 2 weeks only.
deterioration of cochlear neural responses, without ad

2006

Contents lists available at ScienceDirect
Hearing Research
journal homepage: www.elsevier.com/locate/heares

Research paper

Impact of noise or styrene exposure on the kinetics of presbycusis

Pierre Campo[a,*], Thomas Venet[a], Cécile Rumeau[a], Aurélie Thomas[a], Benoît Rieger[a], Chantal Cour[a], Frédéric Cosnier[a], Cécile Parietti-Winkler[b,c]

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ABSTRACT

Presbycusis, or age-related hearing loss is a growing problem as the general population ages. In this longitudinal study, the influence of noise or styrene exposure on presbycusis was investigated in Brown Norway rats. Animals were exposed at 6 months of age, either to a band noise centered at 8 kHz at a $Lex,8h = 85$ dB (86.2 dB SPL for 6 h), or to 300 ppm of styrene for 6 h per day, five days per week, for four weeks. Cubic distortion product otoacoustic emissions (2f1-f2 DPOAEs) were used to test the capacity of the auditory receptor over the lifespan of the animals. 2f1-f2DPOAE measurements are easy to implement and efficiently track the age-related deterioration of mid- and high-frequencies. They are good indicators of temporary auditory threshold shift, especially with a level of primaries close to 60 dB SPL. Post-exposure hearing defects are best identified using moderate, rather than high, levels of primaries. Like many aging humans, aging rats lose sensitivity to high-frequencies faster than to medium-frequencies. Although the results obtained with the styrene exposure were not entirely conclusive, histopathological data showed the presbycusis process to be enhanced. Noise-exposed rats exhibit a loss of spiral ganglion cells from 12 months and a 7 dB drop in 2f1-f2DPOAEs at 24 months, indicating that even moderate-intensity noise can accelerate the presbycusis process. Even though the results obtained with the styrene exposure are less conclusive, the histopathological data show an enhancement of the presbycusis process.

2011

La synergie des effets ototoxiques avec ceux du bruit devrait renforcer la notion d'ototoxicité.

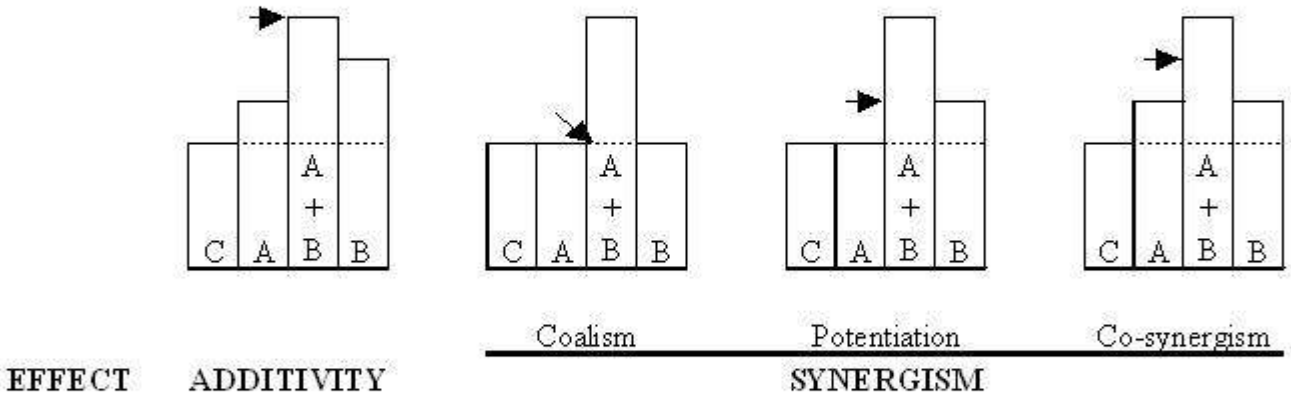
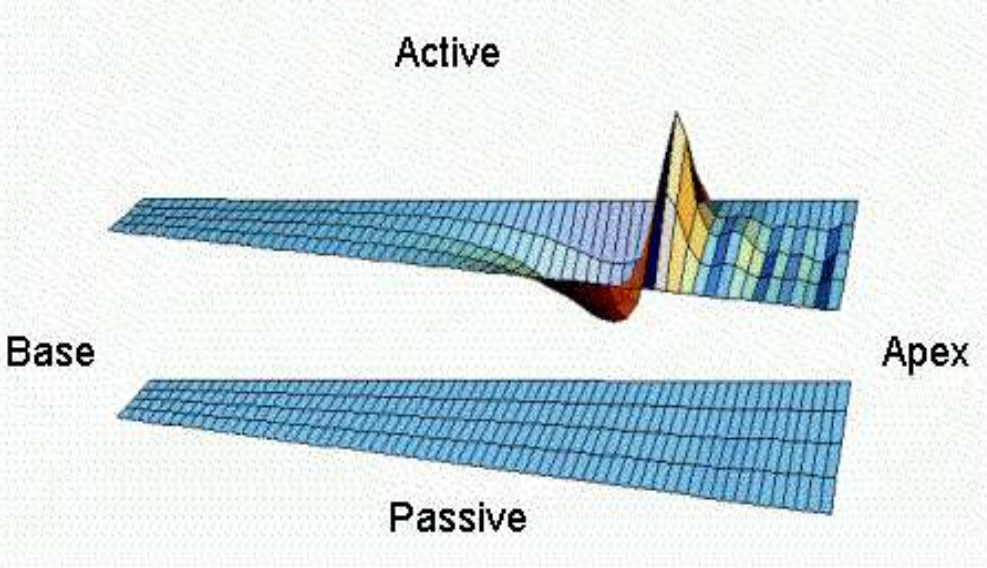


Fig. 6: Graphic illustration of different outcomes after exposure to agents A and B. C=control (unexposed) group. Arrow indicates predicted effect. Dotted line indicates control value (extract from Nylén, 1994).

Rôles des cellules ciliées externes

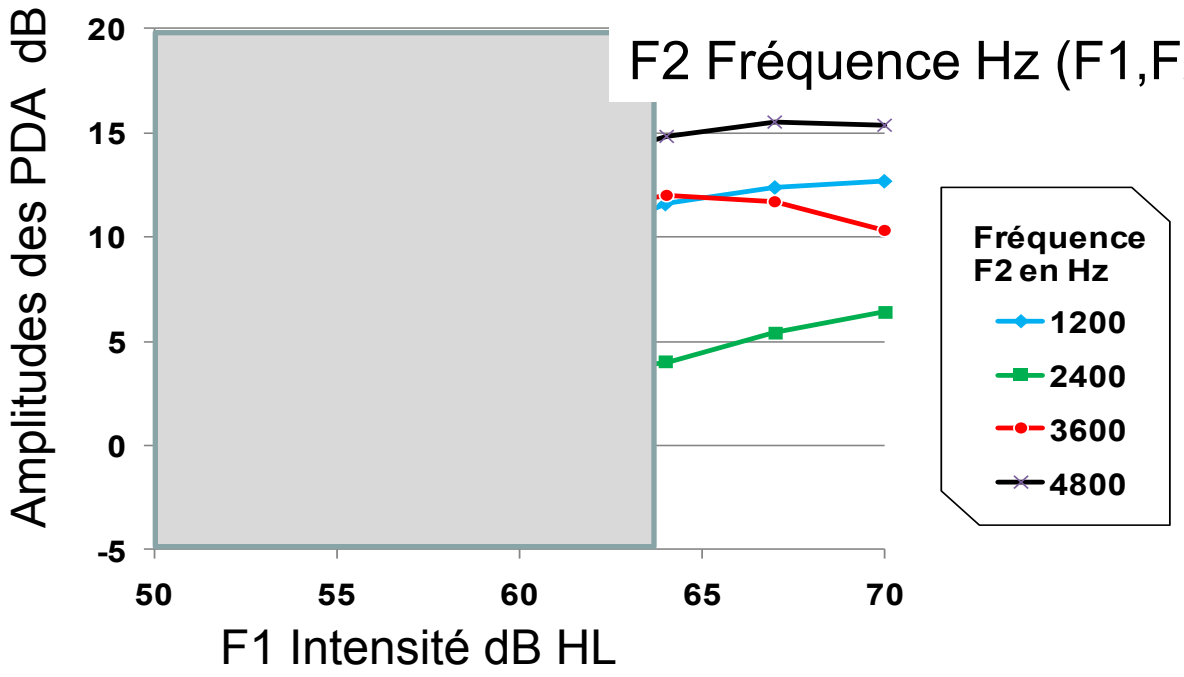


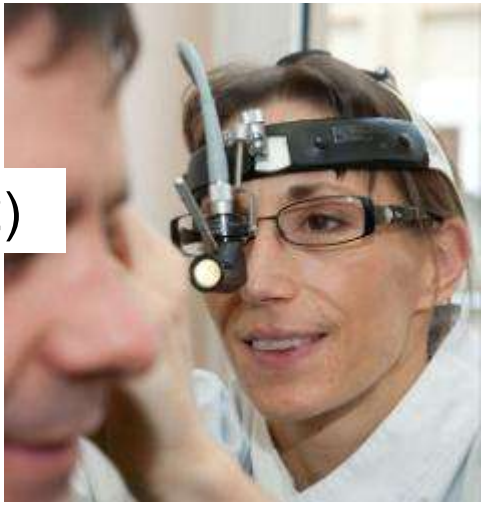
✓Amplification et sélectivité du signal mécanique :
phénomène actif *rapide*

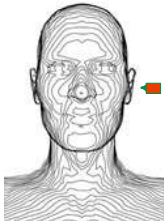
✓Adaptation de la compliance via les 95 % de fibres efférentes :
phénomène actif *lent*

✓**Conditionne l'excitation des cellules ciliées internes**

Approche de type “Input-Output”







VENET et al. (2011) Neuronal circuits involved in the middle-ear acoustic reflex. Toxicol. Sci. 2011, 119 (1), 146-155