Vascularites, Cocaïne
et autres toxiques

Antoine Néel, PU-PH
Médecine Interne
CHU de Nantes

Pensées du soir

crée une image, basé sur les données de la science, qui refléterait au mieux le lien existant entre la consommation de cocaïne et les vascularites Systémiques

Sonnet 5.5 Moyen

Pensées du soir

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+ Sonnet 5.5 Moyen



La cocaïne



- La feuille de Coca



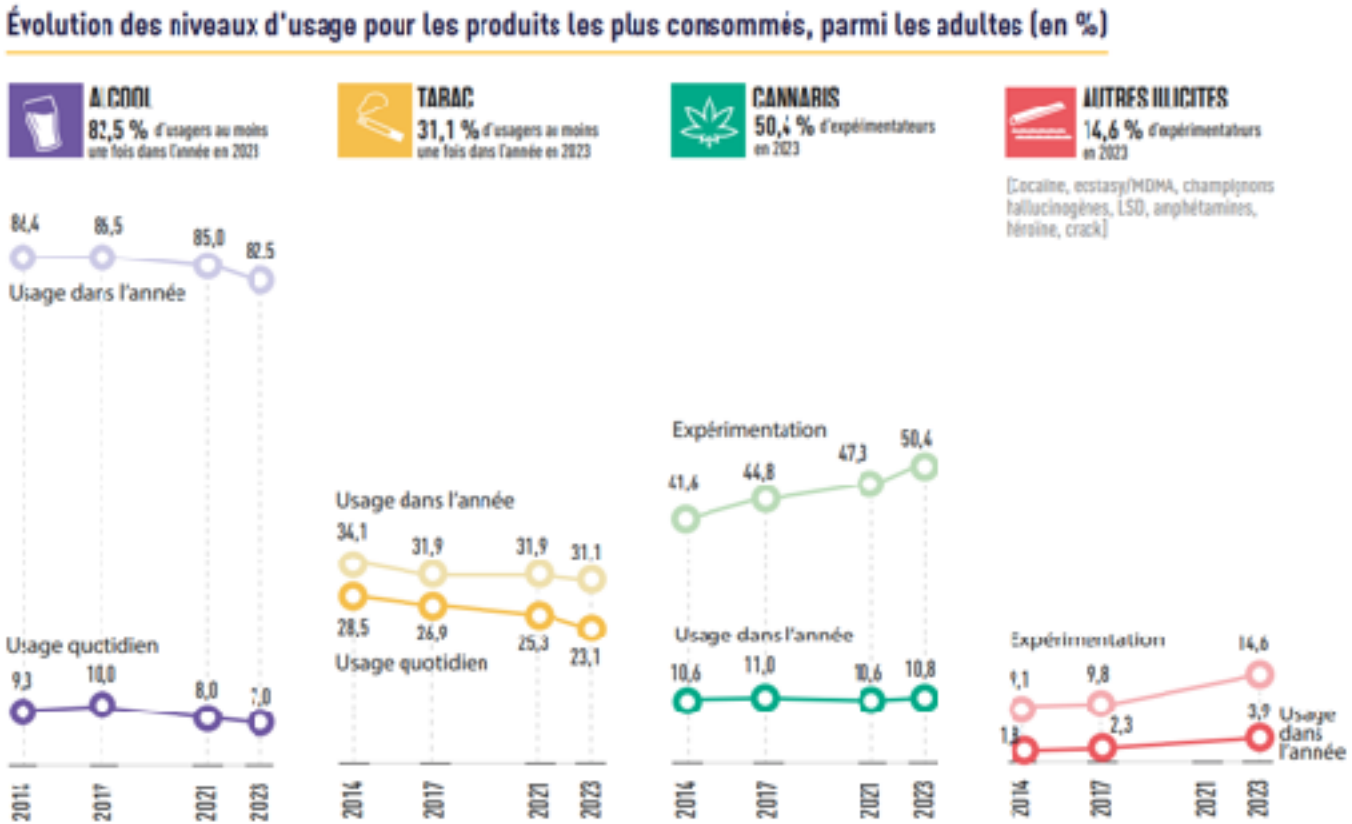
- 1855 : isolement de la substance active, « magique » (S. Freud)
- 1886 : **Coca-Cola** (John Smith Pemberton)
- 1903 : fin de la Coke dans le Cola
- 1906 : étiquetage des produits contenant de la cocaïne
- 1914 : interdiction



- Années 1970/1980 : le retour

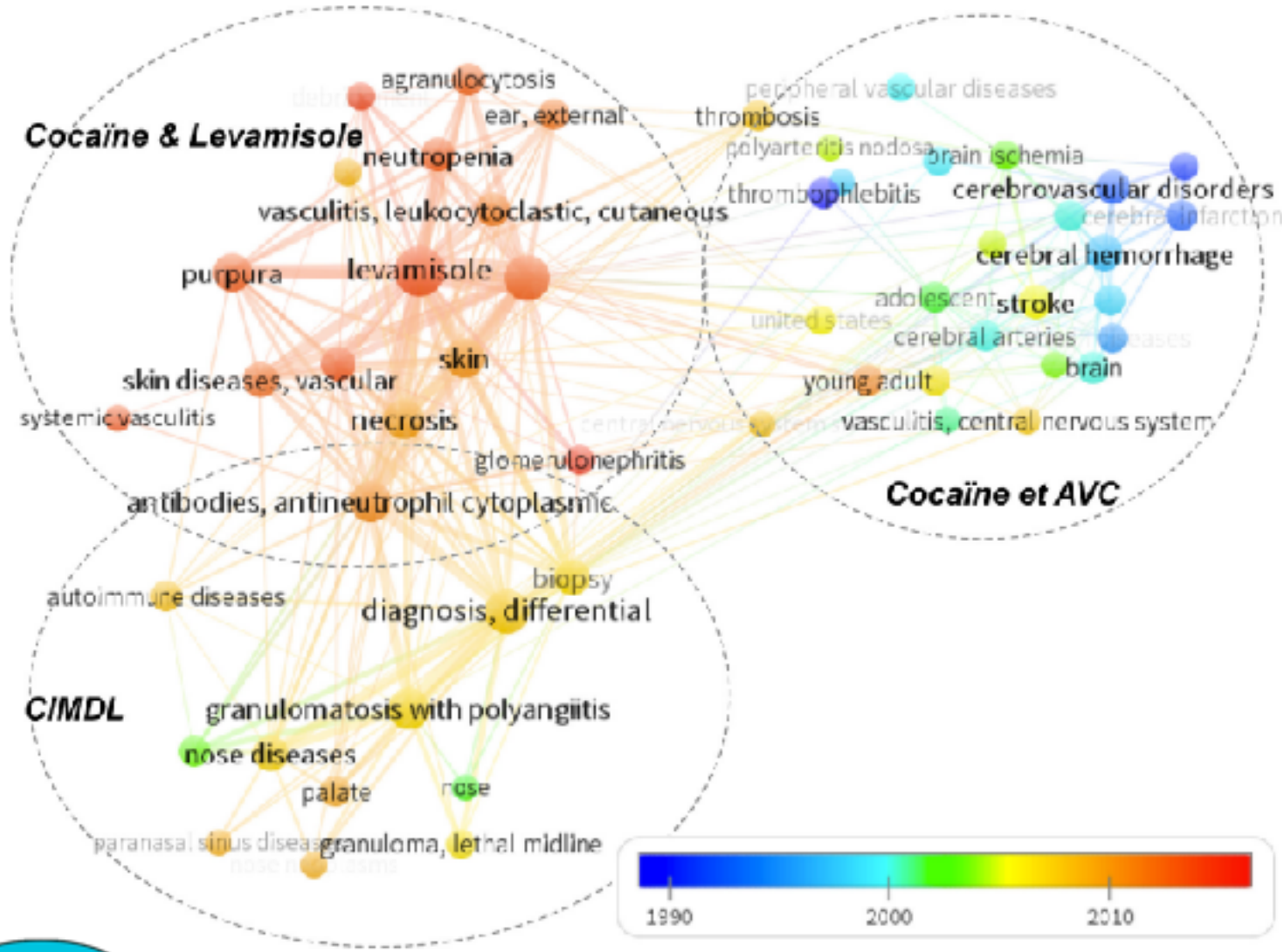
Consommation de cocaïne, France 2025

	11-75 ans	18-64 ans
• Au moins une fois dans la vie	**6,3%**	**9,4%**
• Usage au cours de l'année	**2,1%**	**2,7%**



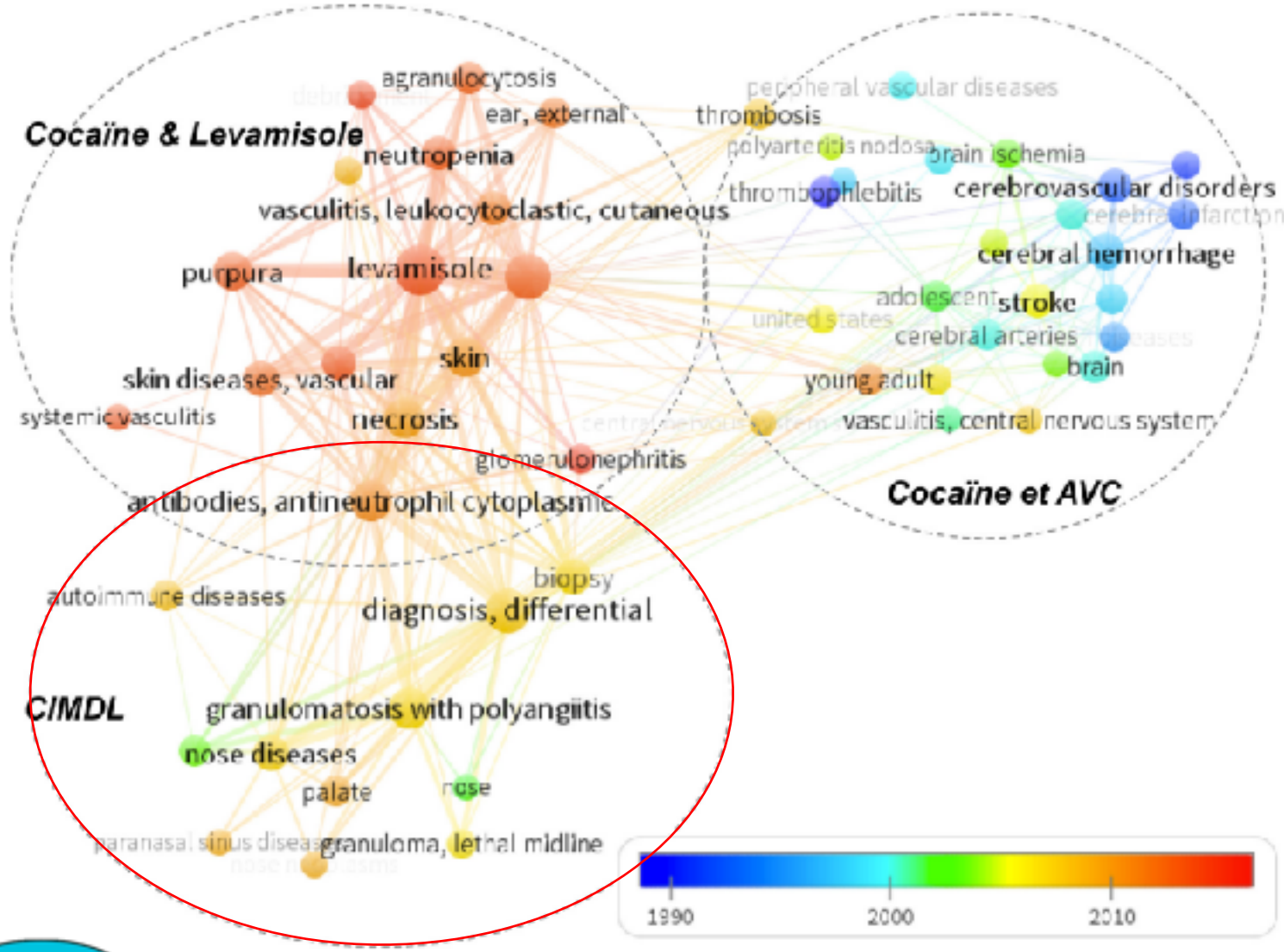
À 17 ans
1,4% a expérimenté
♂1,5%
♀1,3%

« Cocaine and vasculitis »



Néel A, et al. Joint Bone Spine 2018

Cocaine-induced Midline Destructive Lesions



Néel A, et al. Joint Bone Spine 2018

CIMDL

- **Consommateur régulier**, symptômes ORL anciens
  Obstruction nasale, épistaxis, croutes, douleurs faciales
- Lésions ulcéro-nécrotiques et croûteuses
- **Destruction** de la cloison et des cornets inférieurs
- Sinus touchés dans 50 % des cas

- Pas de signe systémique

+/- syndrome inflammatoire modéré	50%	13,6 mg/L [9,5-42]
+/- petite éosinophillie	40%	0,7 G/L [0,5-0,9]

CIMDL ≠ GPA

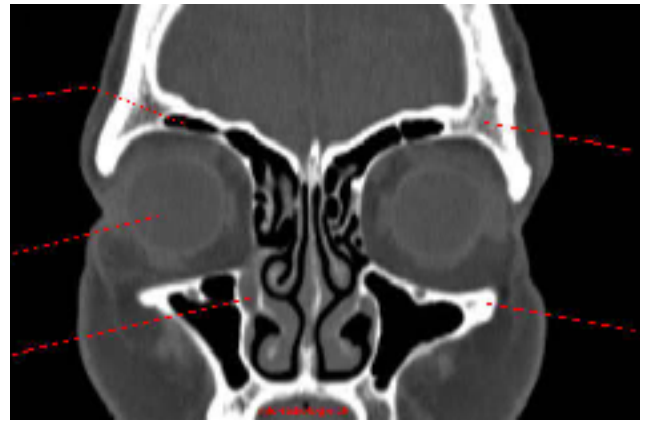
- **Extension centrifuge** :

  Cornets moyens et supérieurs, parois latérales,

  Palais dur et mou

  Ni atteinte otologique, ni pseudotumeur orbitaire

  ! cellulite infectieuse possible



- **Histologie** :
  - inflammation non spécifique, ± vascularite leucocytoclasique, micro-abcès
  - Pas de granulome, de cellule géante ni de nécrose profonde


A
B

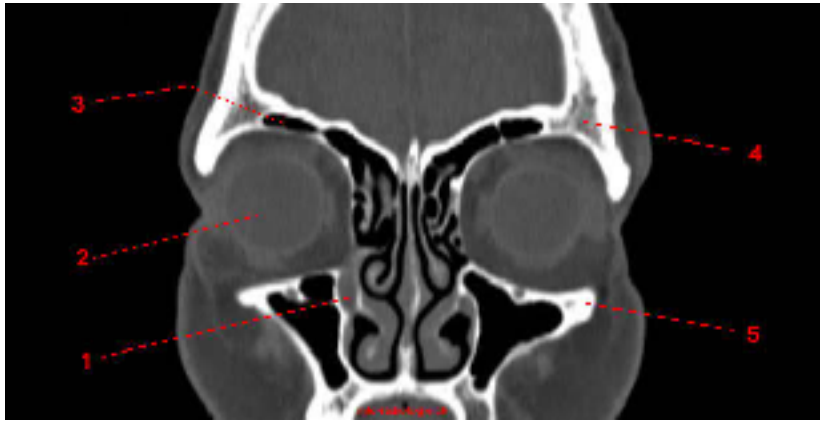

A
B




C

CIMDL : scanner

TDM ORL, N=32	n	%
Perforation septum	30	**94**
Epaisissement muqueux	17	53
Érosion inféro-latérale	13	**41**
Fistule palais	6	**19**
Sinusite	5	16
Erosion cornet supérieur	3	9
Erosion lame papyracée	3	9
Orbite	2	6

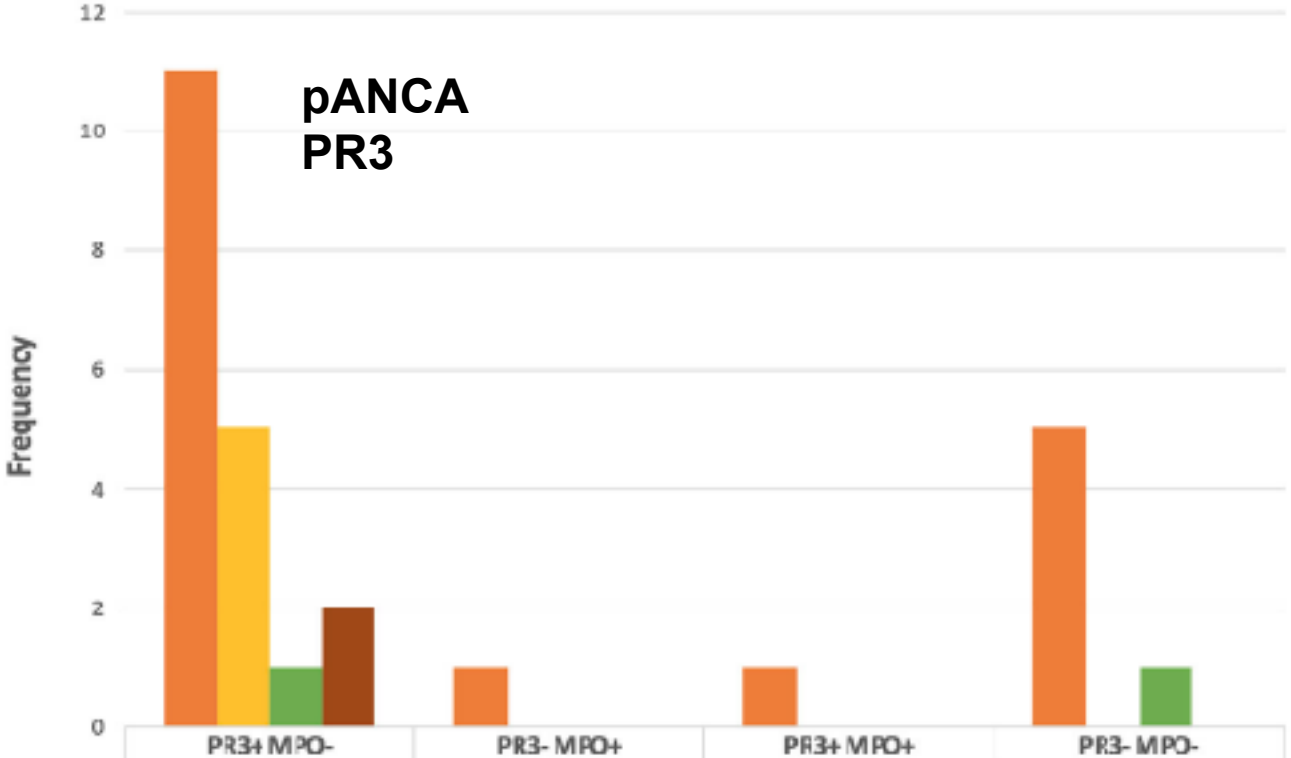


Pendolino AL, et al. Laryngoscope 2024

CIMDL et ANCA

- IFI : (~70%) positive, majoritairement **p-ANCA**
- Spécificité Ag : **PR3**
- Anti-HNE : 28-84%

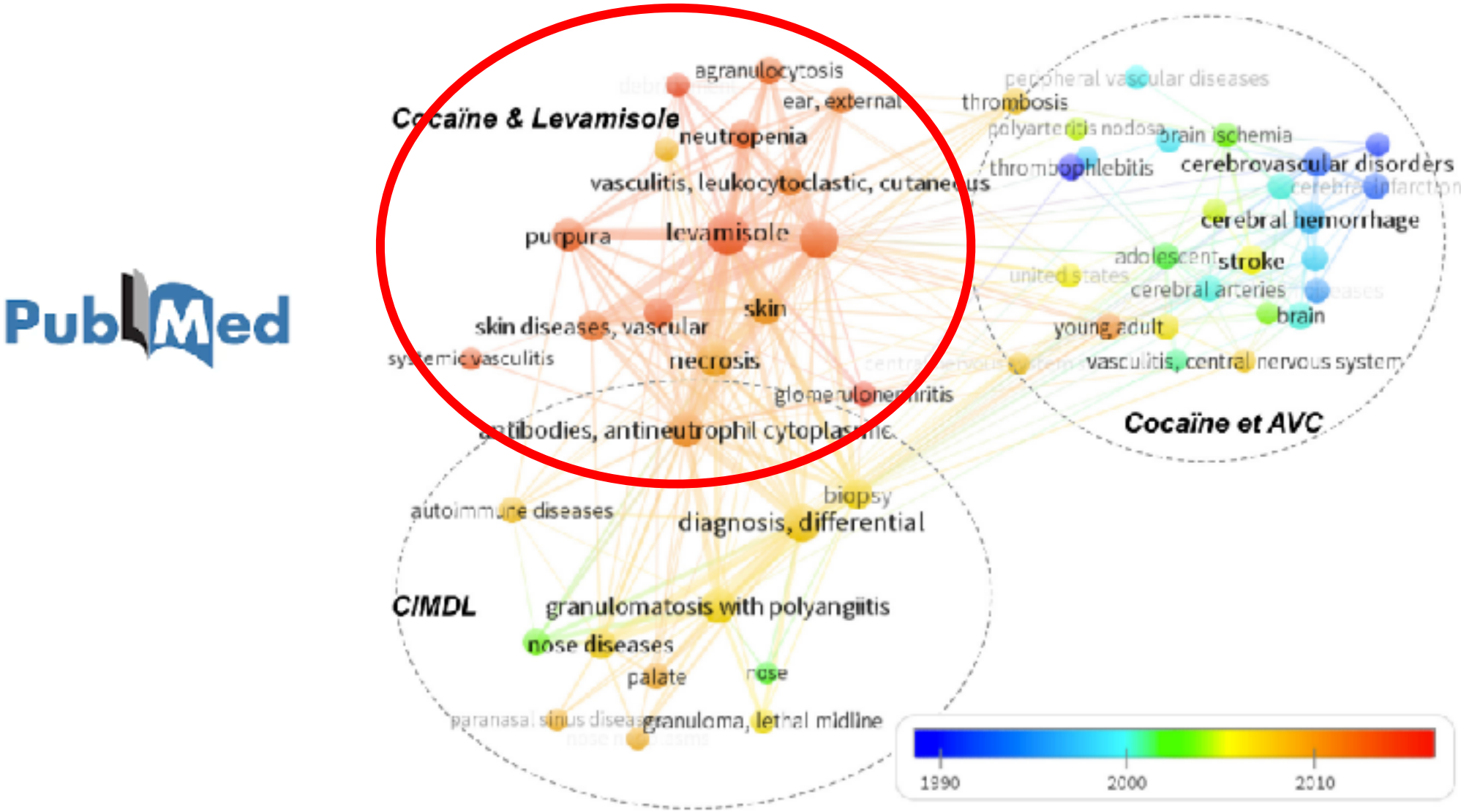
  Human Neutrophil Elastase



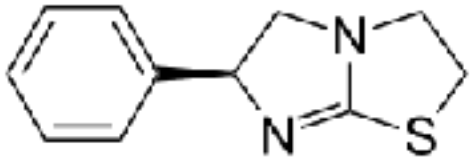
	PR3+ MPO-	PR3- MPO+	PR3+ MPO+	PR3- MPO-
p-ANCA	11	1	1	5
c-ANCA	5	0	0	0
Atypical p-ANCA	1	0	0	1
Atypical c-ANCA	2	0	0	0

Trimarchi M, et al. Medicine 2001
Wiesner O, et al. Arthritis Rheum 2004
Peikert T, et al. Arthritis Rheum 2008
Pendolino AL, et al. Laryngoscope 2024

Vascularite/vasculopathie au Levamisole



Le Levamisole



1966	**Utilisé chez l'homme** (PR, MICI, s. néphrotique de l'enfant, oncologie)
1978	**Première vascularite cutanée nécrosante induite par le lévamisole**
1990s	Enfants traités au long cours : **lésions nécrotiques** des oreilles, joues, cuisses ; AAN, antiphospholipides, ANCA
1998	**Retrait du marché français** : agranulocytose, leuco-encéphalopathie, vasculopathie cutanée
MAIS x 1986	**Médecine vétérinaire** : anti-helminthe

Levamisole: de l'alerte américaine à l'Europe

2003–2007

Lévamisole repéré dans la cocaïne dès 2003 ; < 10 % des échantillons en 2007

2008–2009

De 30 à 70 % des échantillons ; **clusters d'agranulocytose** au Canada et aux États-Unis

CDC, MMWR Dec 2009

2010

Purpura rétiforme nécrotique (membres, nez, oreilles) ; 2 séries de 6 cas, la moitié sans neutropénie

Waller JM, et al. JAAD 2010
Chung C, et al. JAAD 2011
Graf J, et al. Arthritis Rheum 2011

Données CDC

23 cas d'agranulocytose sous cocaïne
~50% lésions cutanées

Vagi SJ, et al. Ann Emerg Med 2013

2014 · France

76 % des prélèvements positifs à la cocaïne contiennent du lévamisole



Pourquoi couper la cocaïne au lévamisole ?

Économique

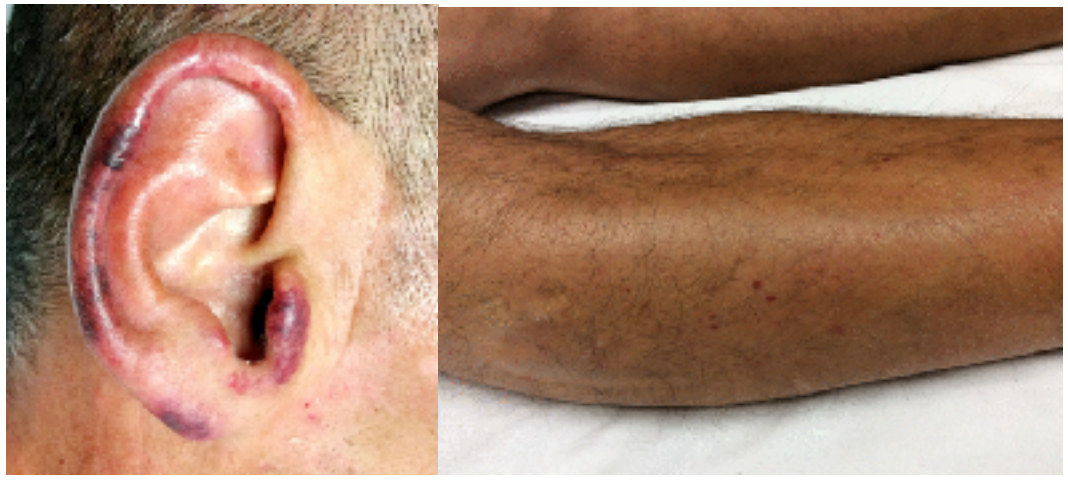
Substance facile à se procurer, aux propriétés physicochimiques proches : augmente les profits

Pharmacologique

Potentialise la cocaïne : effet élévateur de l'humeur, inhibition de la recapture de la noradrénaline, stimulation nicotinique, métabolite amphétamine-like (aminorex)



Waller JM, et al. JAAD 2010

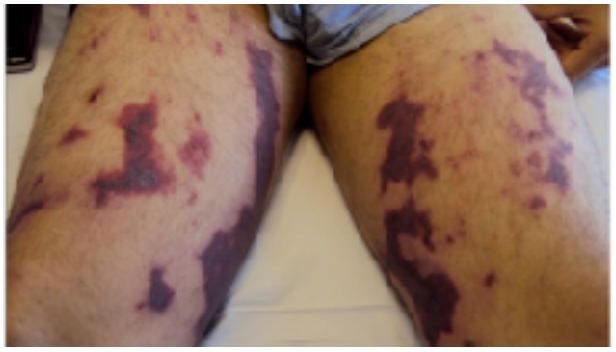


Dherange PA, *et al*. BMJ Case Rep 2015





Lee BL, et al. Art Care Res 2010





Hahn E, et al. J Rheumatol 2015

	All	Adulterated Cocaine[a]	Therapeutic use[b]	P-value
N	302	282 (93)	20 (6.6)	
Demographics				
Female: male ratio	1.48	1.51	1.11	0.6305
Age				
years	43 [35–49]	43 [36–49]	14 [10–49]	0.0029
≤18 years, N (%)	11 (3.6)	0	11 (55)	<0.0001
Organ involvement				
Skin, N (%)	274 (91)	257 (91)	17 (85)	0.4145
Kidney, N (%)	64 (21)	62 (22)	2 (10)	0.2657
Ear-nose-throat, N	44 (15)	44 (16)	1 (5)	0.3291
Lung, N (%)	30 (10)	30 (11)	2 (10)	0.7055
Gastrointestinal tract, N (%)	3 (1.0)	3 (1.1)	0	0.3883
Muscle, N (%)	2 (0.7)	1 (0.4)	1 (5.0)	0.1291
Heart, N (%)	1 (0.3)	1 (0.4)	0	>0.999

Scoglio M, et al. J Autoimmun 2026

Skin (N=274)	
Clinical features	
Skin lesions	
Purpura, N (%)	228 (83)
Necrosis, N (%)	141 (51)
Ulcer, N (%)	70 (26)
Fluid filled lesion, N (%)	68 (25)
Eschar, N (%)	14 (5.1)
Livedo, N (%)	10 (3.6)
Distribution	
Head and neck, N (%)	177 (65)
Ears, N (%)	148 (54)
Cheeks, N (%)	38 (14)
Nose, N (%)	36 (13)
Lower extremities, N (%)	171 (62)
Upper extremities, N (%)	133 (49)
Torso, N (%)	73 (27)

Scoglio M, et al. J Autoimmun 2026

Histologie

Biopsy, N 218

- Biopsy classifiable 187 (86)
  - Thrombotic vasculopathy and vasculitis, 70 (**32**)
  - Thrombotic vasculopathy, 65 (**30**)
  - Leukocytoclastic vasculitis, N (%) 52 (**24**)
- Biopsy unclassifiable 31 (14)

Scoglio M, et al. J Autoimmun 2026

Atteinte rénale

	Sx	Âge	Creat/umol/L	PrU	Histologie rénale	Cut	Art	HIA	Temp	NeP
2011	F	53	492	+++	GN Necr ExtraCap Pl	+	+		+	
2012	F	45	265	3,4	GN Necr ExtraCap Pl	+				
2014	M	60	141	2	GN Necr ExtraCap Pl	+	+			
Id	F	49	646	4,9	GN ExtraCap + FSGSG	+		+		
Id	F	63	287	0,7	GN Necr ExtraCap Pl		+			+
Id	F	43	1238	NS	GN Necr ExtraCap Pl	+				
2015	M	43	347	1,55	GN Necr ExtraCap Pl				+	
2015	M	49	627	1,35	GN Necr ExtraCap + EM	+				
2015	M	40	1839	4,7	GN Mesangiale	+	+			
2015	F	27	292	8,9	GN Necr ExtraCap Pl	+	+			
2016	M	49	403	1,2	GN Necr ExtraCap Pl	+				
2016	F	50	194	1,6	GN Necr ExtraCap + EM	+				
2016	F	34	371	2,4	GN Necr ExtraCap + EM	+				
2016	F	42	NS	NS	GN Necr ExtraCap	+	+			
2016	F	48	280	2,02	GN Necr ExtraCap + dep	+	+			+
2017	M	53	150	1,65	GN Necr ExtraCap + EM	+				
Id	M	35	150	5,24	GN Necr ExtraCap + EM		+	+		
Id	M	34	71	3,97	GN EM	+	+			

Carlson AQ, et al. Medicine 2014; Collister D, et al. Am J Nephrol 2017

Créat 292 µmol/L
RPC 2g/g

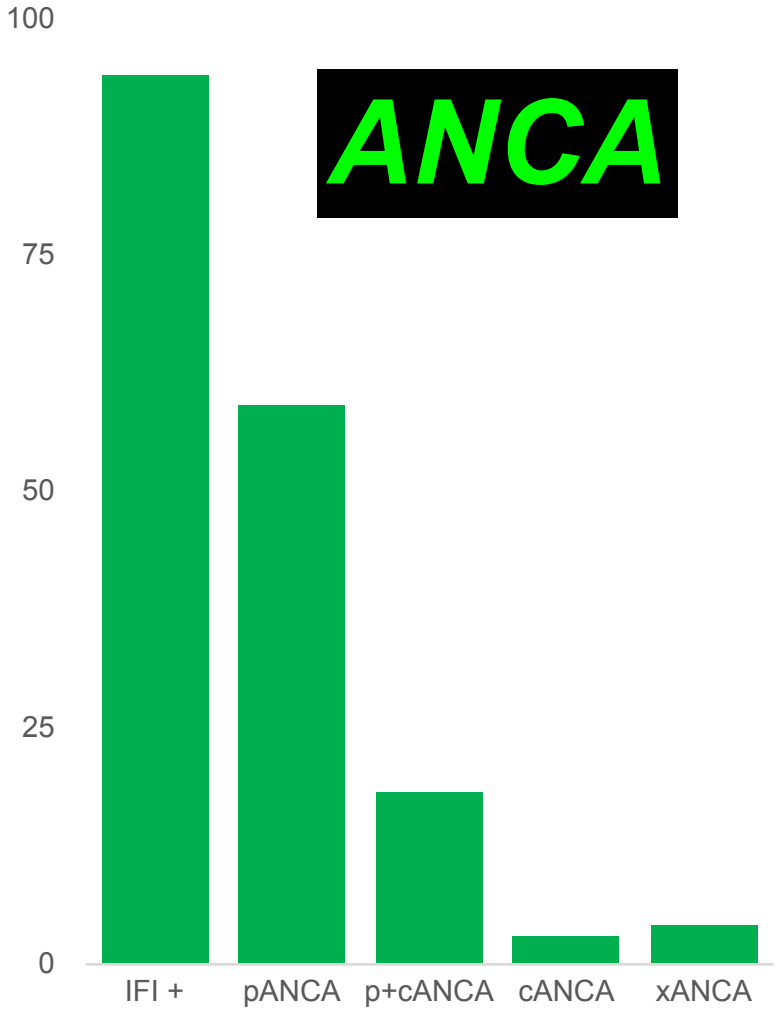
N=18
16 GNEC
1 GEM, 1 Gmes
5 dépots extra-membraneux

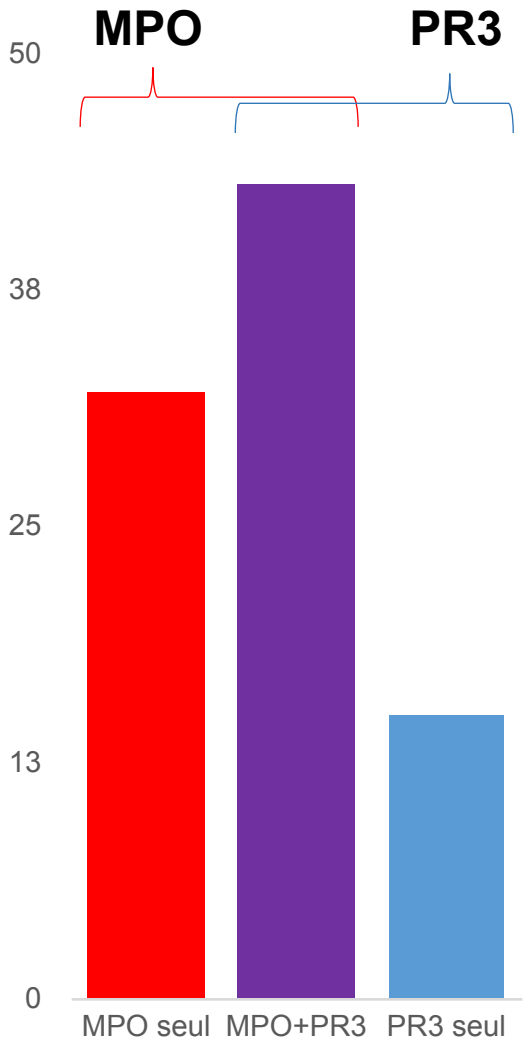
Kidney (N=64)	
Features	
Kidney function deterioration, N (%)	60 (94)
Pathological proteinuria and hematuria, N (%)	51 (80)
Isolated pathological proteinuria, N (%)	4 (6.3)
Isolated pathological hematuria, N (%)	2 (3.1)
Biopsy, N	45
Pauci-immune crescentic glomerulonephritis	18 (40)
Membranous nephropathy	6 (13)
Other glomerulonephritides	14 (31)
Not specified	7 (16)

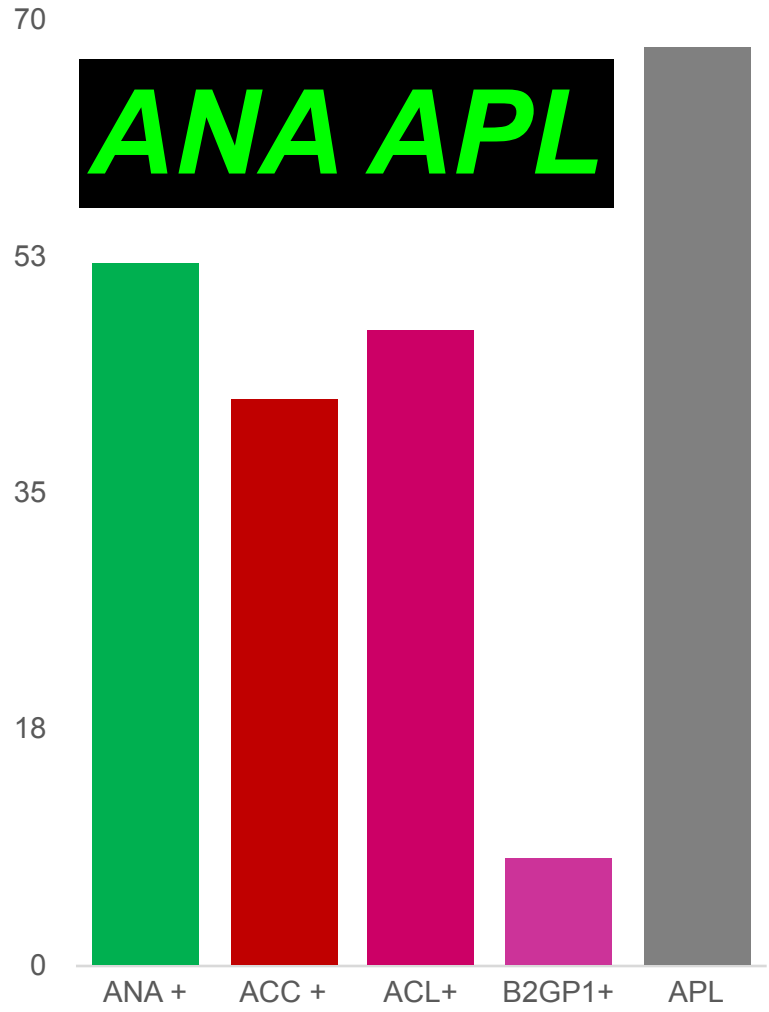
Néel A, Joint Bone Spine 2018

Scoglio M, et al. J Autoimmun 2026

Auto-immunité biologique



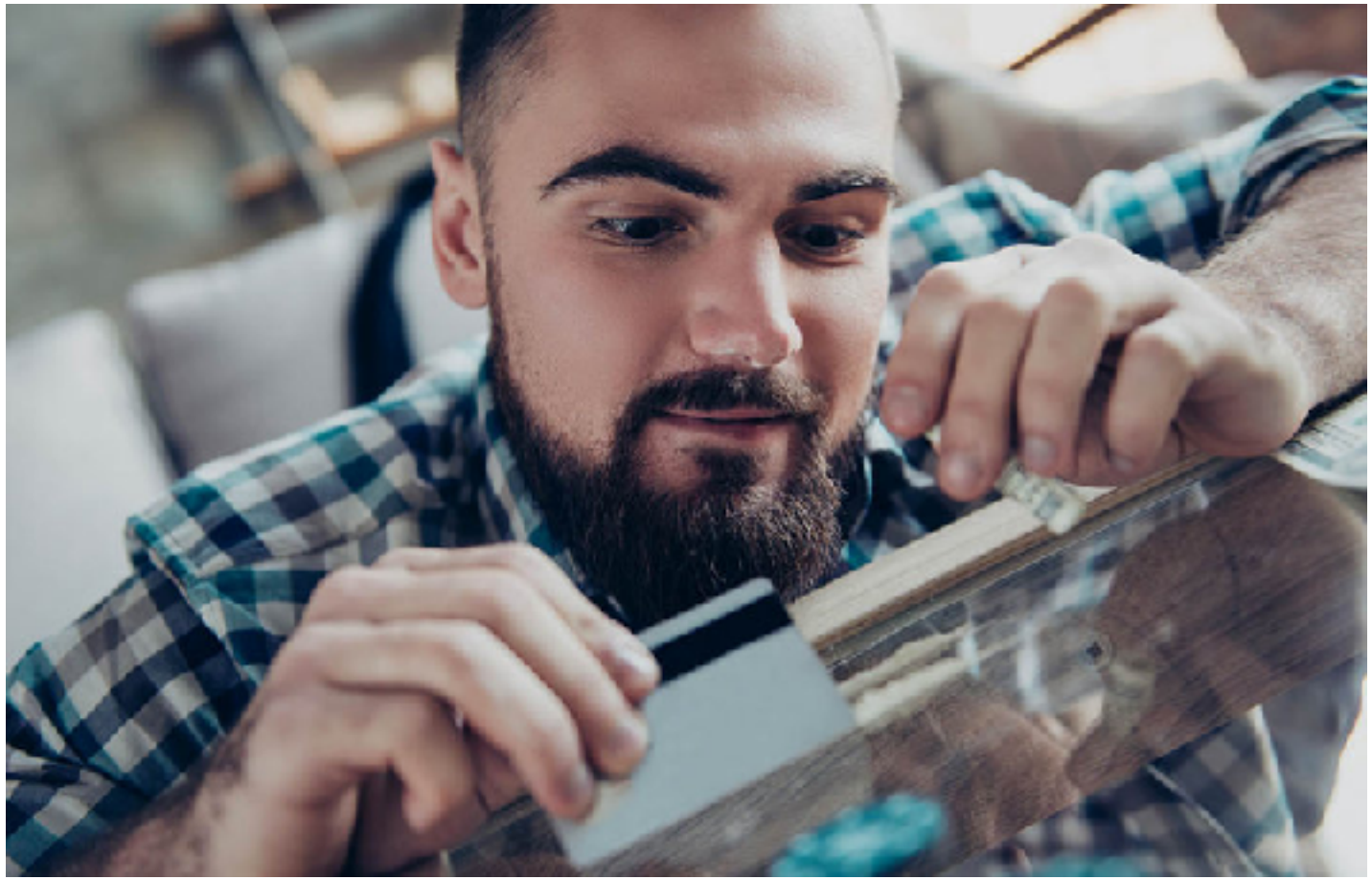


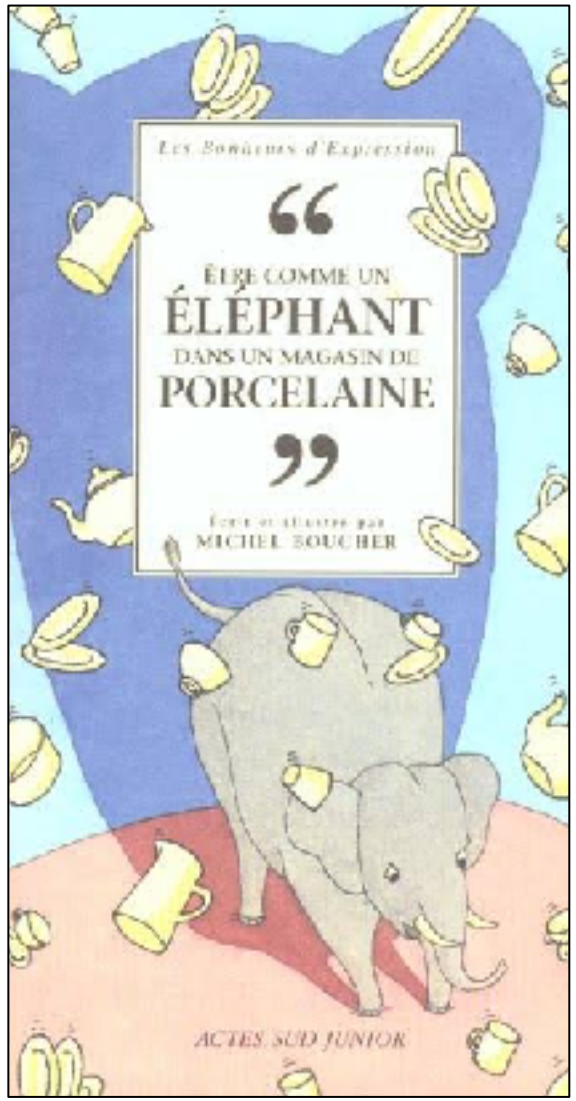


d'après **Dartevel A, et al. Semin Arthritis Rheum 2019**

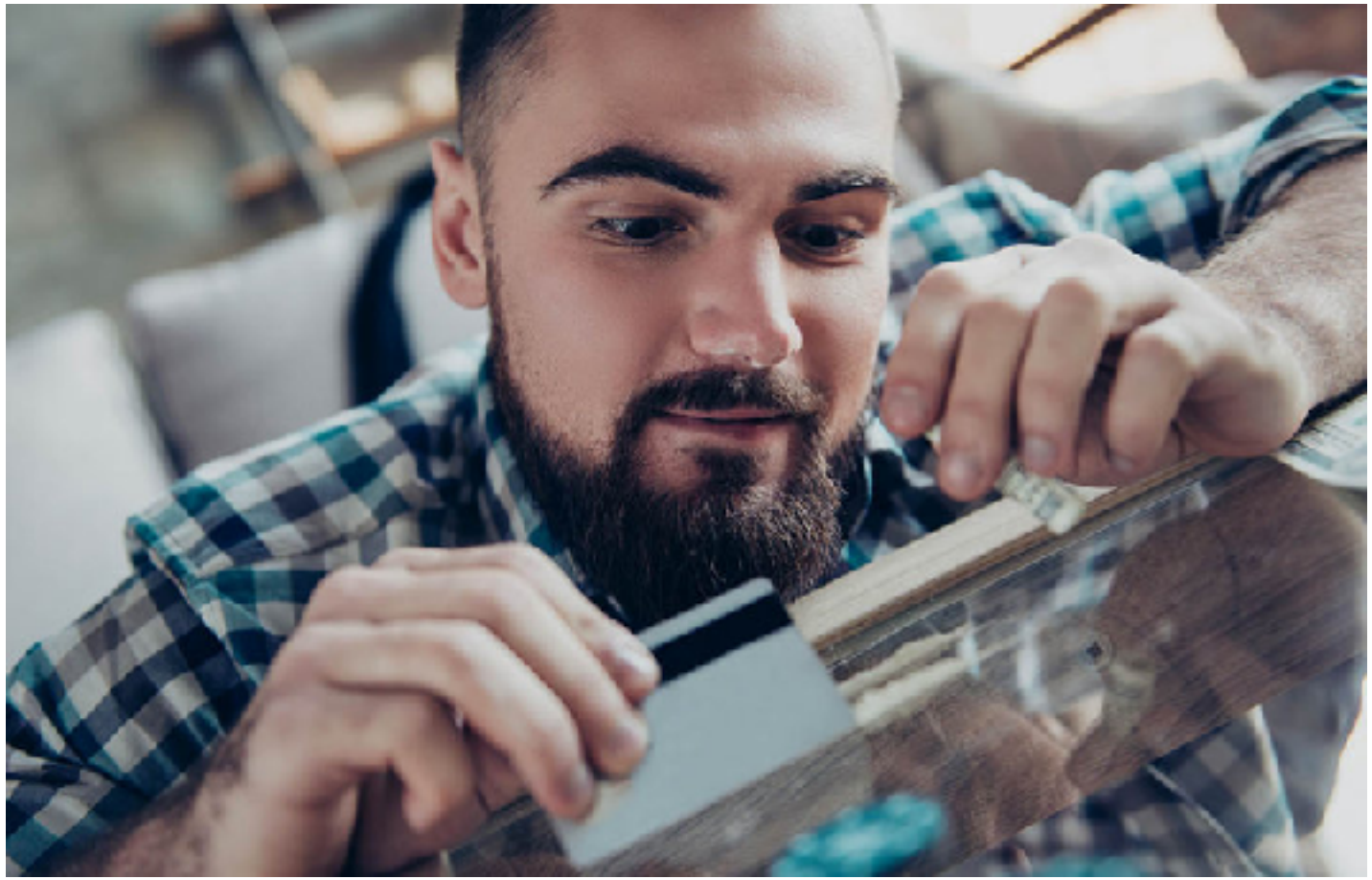
« Vous prenez de la coke » ?

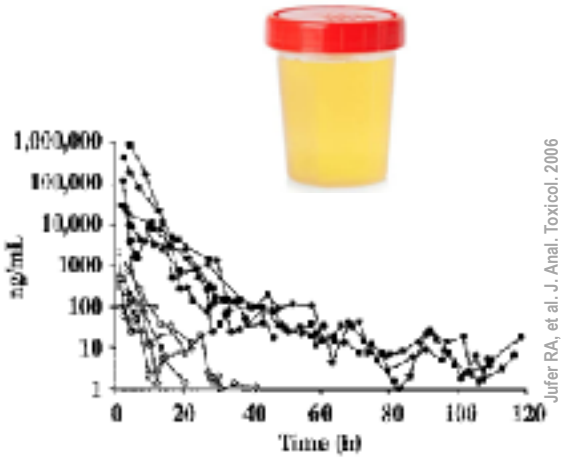
« Vous prenez de la coke » ?





« Vous prenez de la coke » ?





Méthode immuno-enzymatique
vs
Chromatographie



48-72h

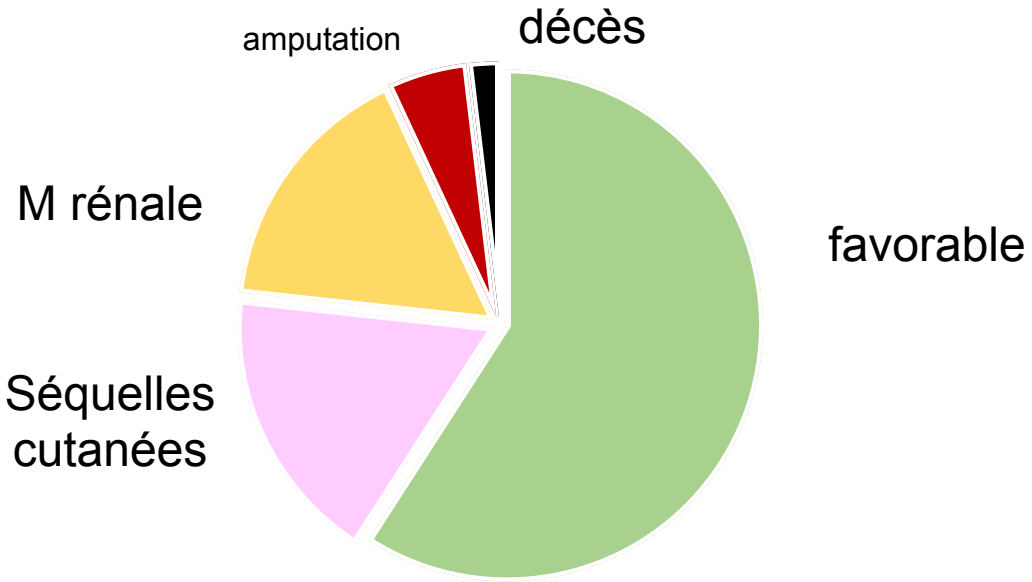
Soins et devenir

- **Levamisole thérapeutique** : régression en 1 mois
- **Cocaïne** : …

  recommandation d'arrêt / PEC addictologique

  Divers traitements immunologiques

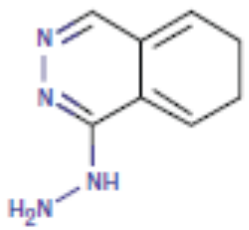
Devenir 159/282 (56%)

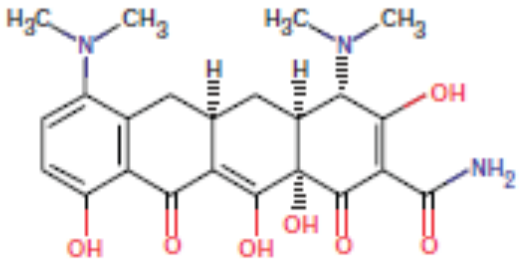


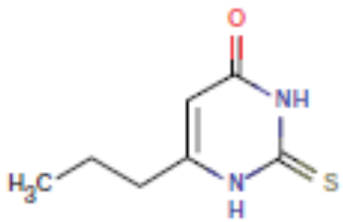
Scoglio M, et al. J Autoimmun 2026

Autres inducteurs

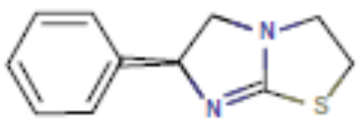
Autres inducteurs



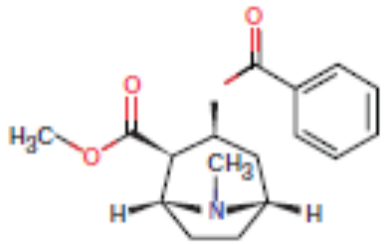




Levamisole

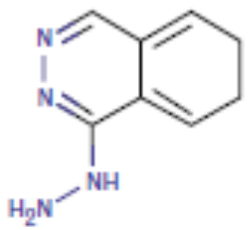


Cocaine

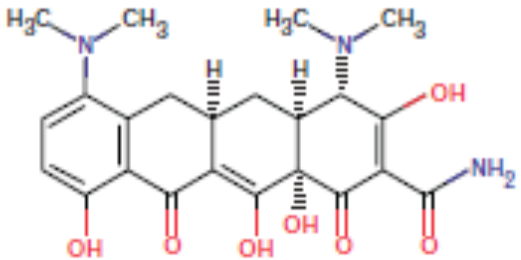


Autres inducteurs

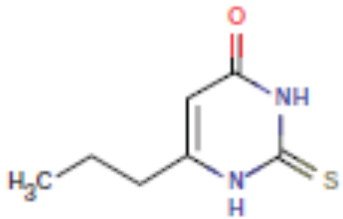
Hydralazine



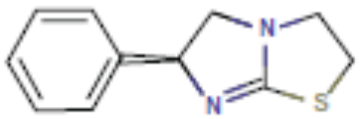
Minocycline



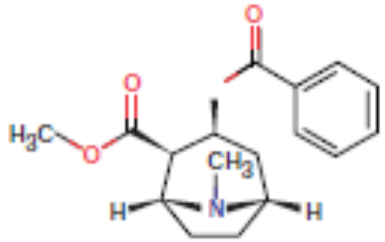
Propylthiouracil



Levamisole



Cocaine



Hydralazine

- Anti-HTA
- 90% Atteinte rénale++ (GNEC pauci-immune)
- 50% poumon
- 30% peau
- ! 20 % ORL

- ANCA anti-MPO svt ANA+

Choi HK, et al. Arthritis Rheum 2000

Anti-thyroidiens

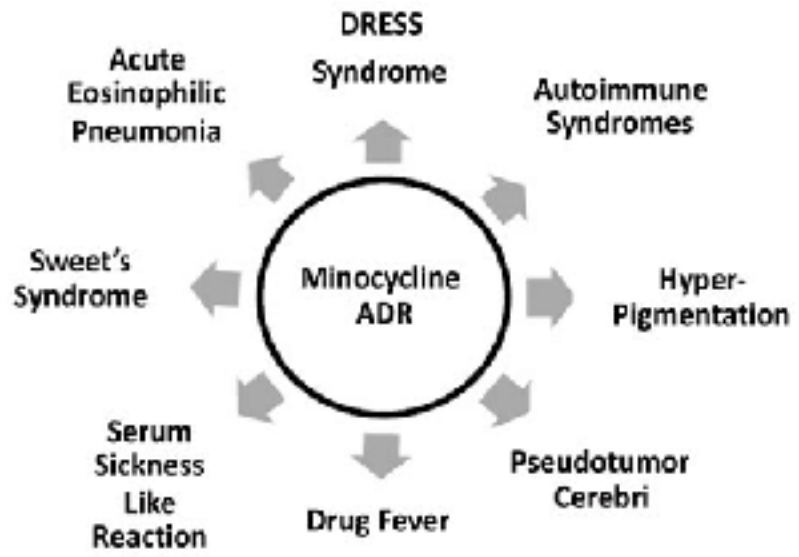
- ++**Propylthiouracile** + Methimazole, autres

- PTU → 20-40% développent des ANCA
- Vascularite : 0-1,4% ?

- 75% atteinte rénale
- 100% anti-MPO (37% MPO+PR3)

Yang J, et al. Thyroid 2017

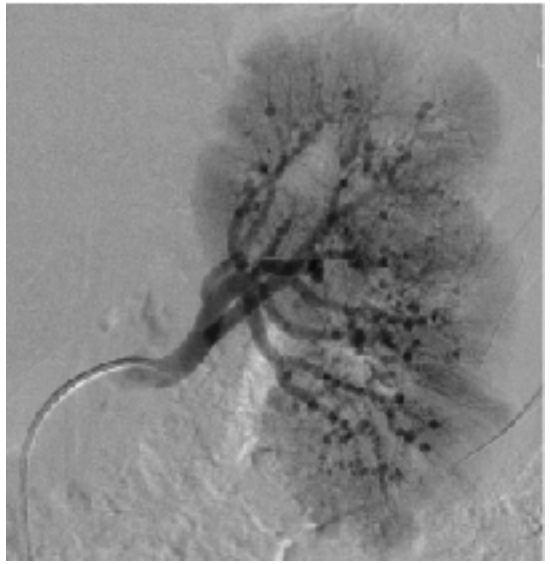
Minocycline



ViDAL

infections microbiologiquement documentées des souches bactériennes résistantes aux autres cyclines et sensibles à la minocycline et pour lesquelles aucun antibiotique par voie orale ne paraît approprié.

- Lupus induit
- Vascularite type PAN
- pANCA +/- anti-MPO



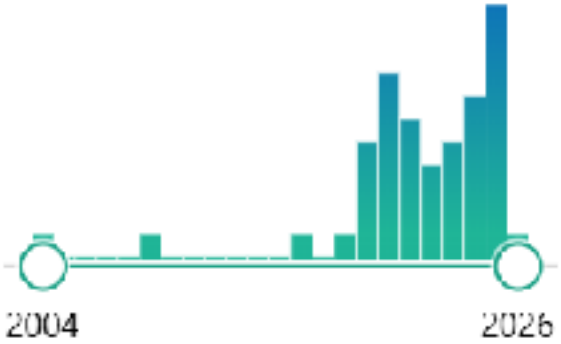
Kermani TA, et al. Semin Arthritis Rheum 2012

Autres ?

Autres ?

Large vessel vasculitis (LVV)/aortitis	- Granulocyte colony-stimulating factor (G-CSF) - Immune check point inhibitors
Medium vessel vasculitis (MVV)	- Minocycline - Empagliflozin - Gemcitabine -Metolazone
Small vessel vasculitis • ANCA-associated vasculitis (AAV)	- Hydralazine - Cocaine - Propylthiouracil -Methimazole - TNF inhibitors - Sulfasalazine - Allopurinol - D-penicillamine - Isoniazid - Phenytoin - immune check point inhibitors
• IgA vasculitis (IgAV)	- Antibiotics - NSAIDs - TNF-inhibitors - Statin - Warfarin
Single organ vasculitis • Leukocytoclastic vasculitis	- NSAIDs - Antibiotics - TNF-inhibitors - Allopurinol - Valproic acid - Sulfonamides - Warfarine - Amiodarone - Anti tuberculosis drugs - Immune checkpoint inhibitors
• Cerebral vasculitis	- Amphetamines - Cocaine - Immune checkpoint inhibitors
• Peripheral vasculitic neuropathy	- Minocycline - Leflunomide - TNF inhibitors - Amphetamines - Immune checkpoint inhibitors - Phenytoin

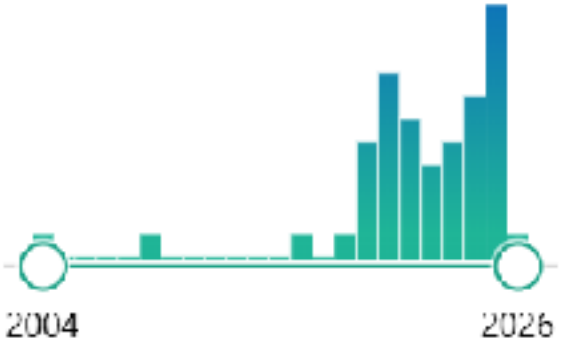
Yaseen K, et al. Curr Rheumatol Rep 2022



Large vessel vasculitis (LVV)/aortitis	- Granulocyte colony-stimulating factor (G-CSF) - Immune check point inhibitors
Medium vessel vasculitis (MVV)	- Minocycline - Empaglifluzin - Gemcitabine -Metolazone
Small vessel vasculitis • ANCA-associated vasculitis (AAV)	Hydralazine - Cocaine - Propylthiouracil -Methimazole TNF inhibitors Sulfasalazine - Allopurinol - D-penicillamine - Isoniazid Phenytoin - immune check point inhibitors
• IgA vasculitis (IgAV)	- Antibiotics - NSAIDs - TNF-inhibitors Statin - Warfarin
Single organ vasculitis • Leukocytoclastic vasculitis	- NSAIDs Antibiotics - TNF-inhibitors - Allopurinol - Valproic acid - Sulfonamides Warfarine - Amiodarone - Anti tuberculosis drugs - Immune checkpoint inhibitors
• Cerebral vasculitis	- Amphetamines - Cocaine - Immune checkpoint inhibitors
• Peripheral vasculitic neuropathy	- Minocycline Leflunomide TNF inhibitors - Amphetamines - Immune checkpoint inhibitors - Phenytoin

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Aortite induite par le G-CSF



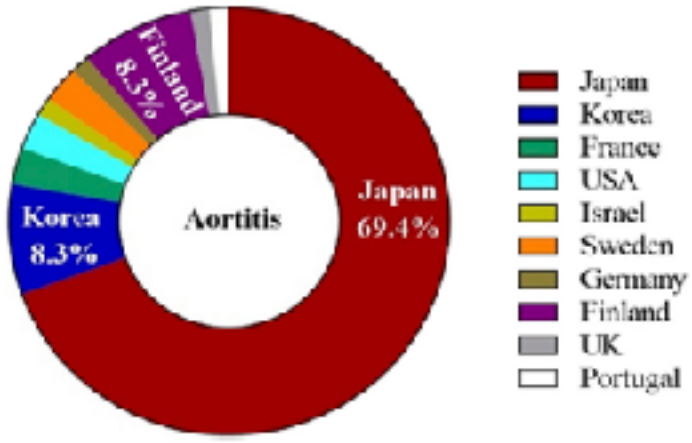
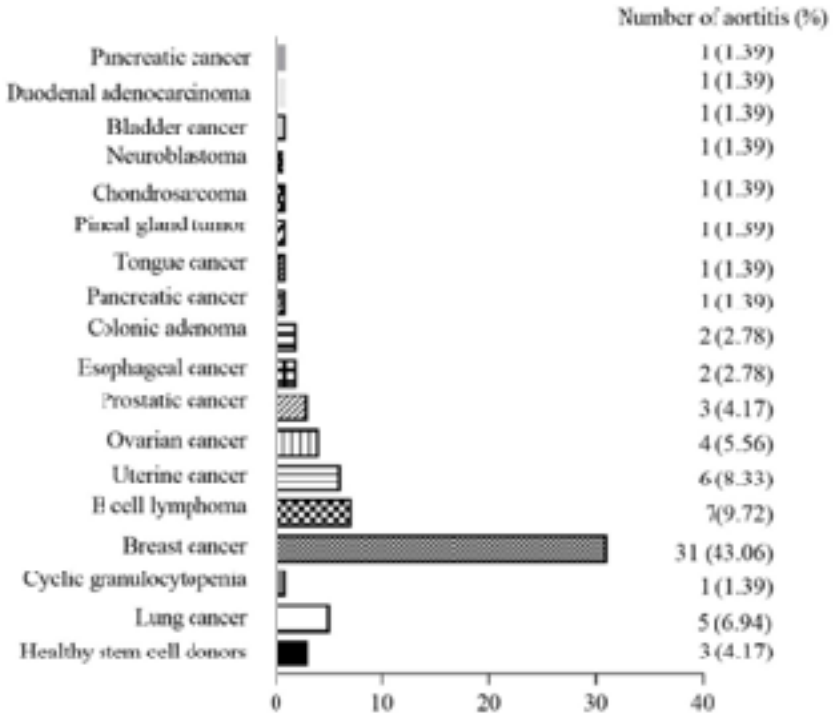
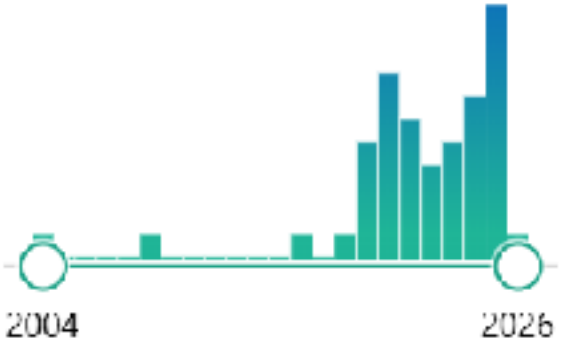


FIGURE 2
The distribution of G-CSF-induced aortitis in countries around the world.

Characteristic	Aortitis (n = 72)
Sex	
Female, n (%)	58 (80.6)
Male, n (%)	14 (19.4)
Age, mean (±SD) years	61.83 (±10.30)
Total no. of G-CSF	
Filgrastim, n (%)	22 (26.8)
Pegfilgrastim, n (%)	52 (63.4)
Lenograstim, n (%)	5 (6.1)
Lipegfilgrastim, n (%)	3 (3.7)



Zhao T, et al. Front Pharmacol 2024

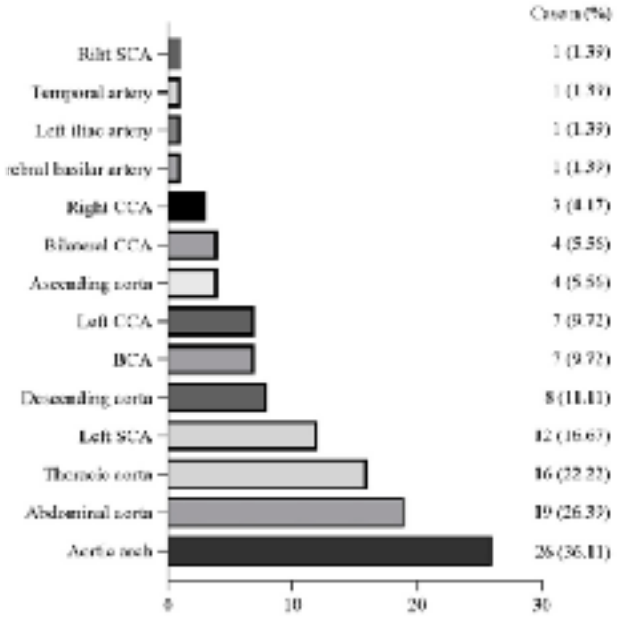


Aortite induite par le G-CSF

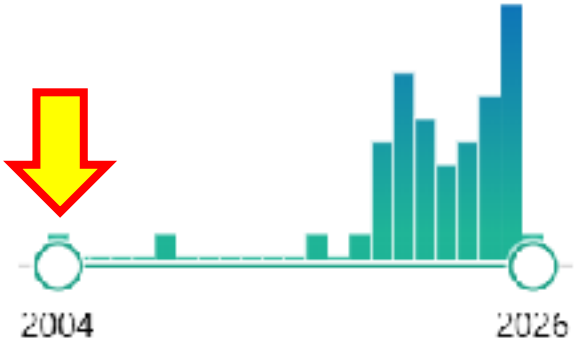
- **Fièvre** Sd inflammatoire++
- **Douleur** Thoracique, rachialgies, douleur abdominale, cervicalgie
- Asymptomatique (4%)

	Filgrastim	Pegfilgrastim	Lenograstim	Lipegfilgrastim
Age, mean (±SD) years	55.05 ± 11.72	60.61 ± 9.66	55 ± 9.93	55 ± 15.01
Sex				
Female	16	42	4	3
Male	6	10	1	0
Time to onset (days ± SD)	11.73 ± 12.72	8.46 ± 4.16	6.67 ± 1.53	6.5 ± 3.10
Body temperature (°C)	38.55 ± 0.7807	38.67 ± 0.6865	39.8[a]	NA
CRP (mg/dL)	26.06 ± 15.39	24.81 ± 9.65	10.45 ± 9.914	NA

SD = standard deviation; CRP = C-reactive protein; NA, No detailed data available.
[a]There is only one detailed data.



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Aortite induite par le G-CSF

AMM filgrastim **1991**
AMM pegfilgrastim **2002**

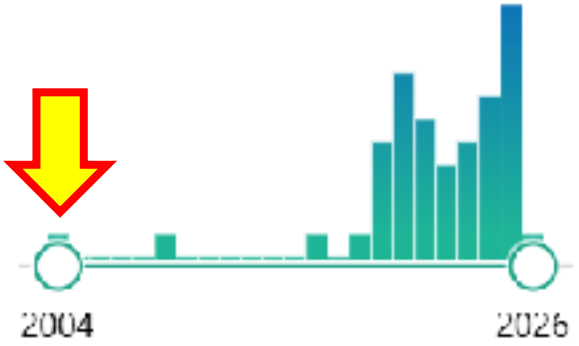
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Sex				
Female	16	42	4	3
Male	6	10	1	0
Time to onset (days ± SD)	11.73 ± 12.72	8.16 ± 4.16	6.67 ± 1.53	6.5 ± 3.10
Body temperature (°C)	38.55 ± 0.7807	38.67 ± 0.6855	39.8[a]	NA
CRP (mg/dL)	26.06 ± 15.39	24.81 ± 9.65	10.45 ± 9.914	NA

SD = standard deviation; CRP = C-reactive protein; NA, No detailed data available.
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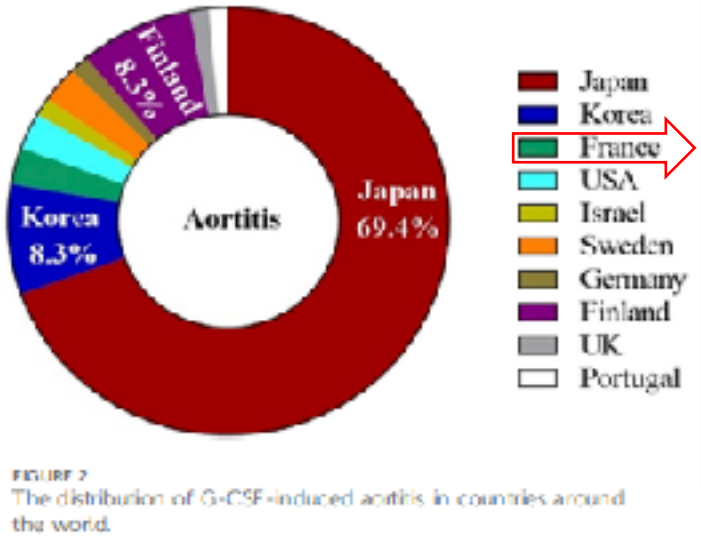


FIGURE 2
The distribution of G-CSF-induced aortitis in countries around the world.

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Communication brève

Aortite après injections de G-CSF

Aortitis after G-CSF injections

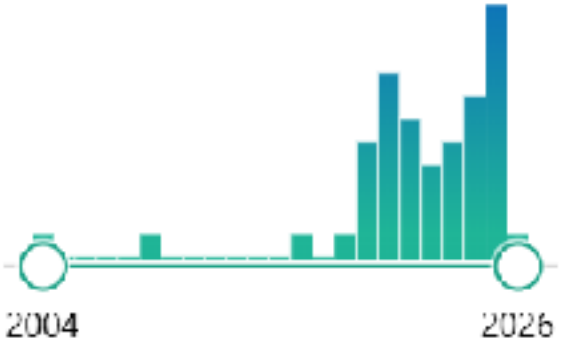
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[a] Service de cardiologie, hôpital de Valence, 179, boulevard du Maréchal Juin, 26953 Valence cedex 9, France
[b] Service de radiologie, hôpital de Valence, 179, boulevard du Maréchal-Juin, 26953 Valence cedex 9, France
[c] Service de médecine interne, hôpital de Valence, 179, boulevard du Maréchal Juin, 26953 Valence cedex 9, France
[d] Service des urgences, hôpital de Valence, 179, boulevard du Maréchal-Juin, 26953 Valence cedex 9, France

Reçu le 28 juin 2003 ; accepté le 3 octobre 2003

Darie C, et al. Rev Med Interne 2004

Aortite induite par le G-CSF



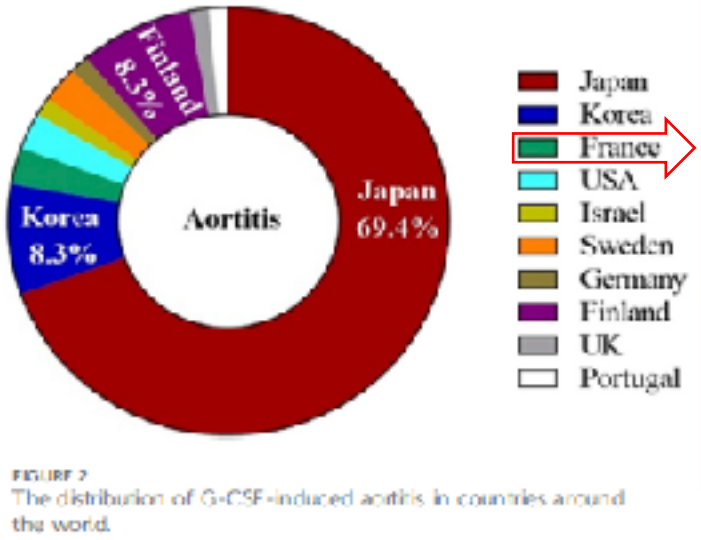


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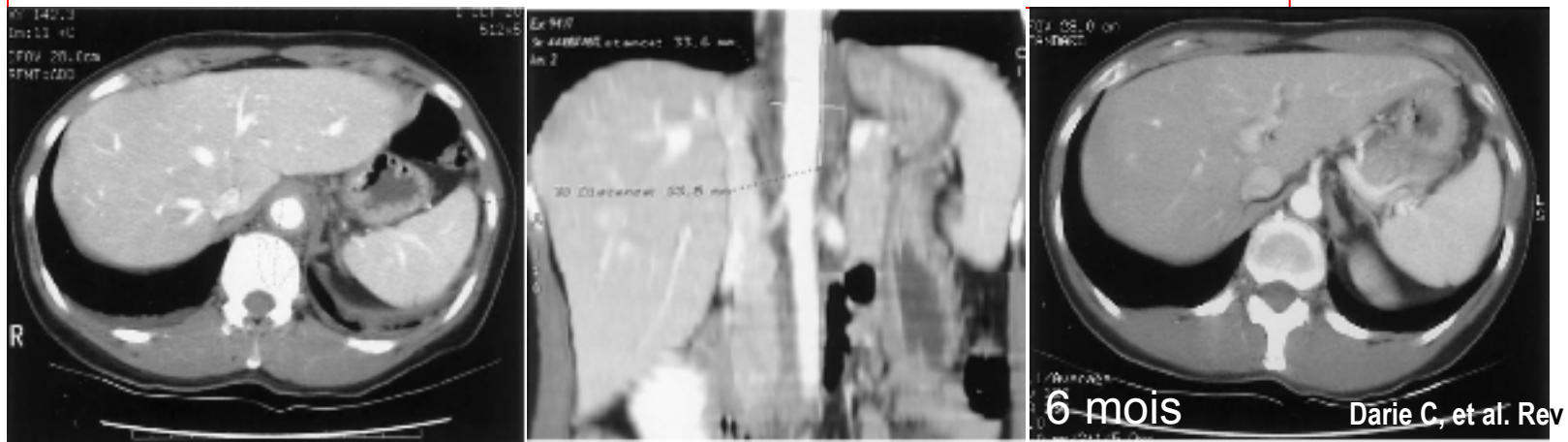
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Reçu le 28 juin 2003 ; accepté le 2 octobre 2003



55 ans
Recueil CSHP
G-CSF du 21 au 25/09

27/09 : **DI abdo, 39°C**
CRP 300mg/L
GB 14 G/L, PN 12,8 G/l
Hb 9,9g/dL

Darie C, et al. Rev Med Interne 2004



AAV dans VigiBase (OMS)



	Drug	No. of ICSRs	No. (%) fatal reactions	IC_{025}/IC	ROR (95% CI)	Time from introduction of the drug to onset of AAV, median (Q1–Q3) days/no. with data available
✓	Hydralazine	208	19 (9)	8.2/8.4	2,683.5 (2,269.3–3,173.3)	1,277/1
✓	Propylthiouracil	108	4 (4)	7.2/7.5	1,201.5 (974.8–1,480.9)	1,003 (425–1,959)/19
✓	Thiamazole	40	5 (13)	5.2/5.6	138.7 (100.7–191.1)	411 (58–966)/6
✗	Sofosbuvir	46	0 (0)	4.9/5.3	74.6 (55.3–100.8)	NA
✓	Minocycline	17	0 (0)	3.8/4.6	72.4 (44.7–117.3)	NA
✓	Carbimazole	6	0 (0)	2.0/3.4	44.9 (20.1–100.4)	92/1
✗	Mirabegron	7	2 (29)	1.5/2.7	11.1 (5.3–23.3)	291 (289–415)/3
✗	Nintedanib	6	2 (33)	1.4/2.8	14.2 (6.3–31.7)	56 (36–132)/4
✓	Penicillamine	4	1 (25)	1.4/3.1	170.3 (63.5–456.3)	NA
	Influenza vaccine	29	2 (7)	1.3/1.9	4.1 (2.8–6.0)	24 (20–26)/7
✓	Allopurinol	7	2 (29)	1.2/2.4	8.0 (3.8–16.8)	NA
✓	Rifampicin	7	2 (29)	0.6/1.9	4.7 (2.2–9.8)	NA
	PEGylated interferon alfa-2b	4	0 (0)	0.3/2.1	7.0 (2.6–18.6)	98/1
✓	Montelukast	4	4 (100)	0.2/1.9	5.8 (2.2–15.5)	NA
	Rosuvastatin	6	0 (0)	0.1/1.5	3.4 (1.5–7.5)	NA

* AAV = antineutrophil cytoplasmic antibody–associated vasculitis; IC_{025} = lower end of the 95% credibility interval for the information component; ICSRs = individual case safety reports; ROR = reporting odds ratio; 95% CI = 95% confidence interval; Q1 = quartile 1; NA = not available.

Deshayes S, et al. Arthritis Rheum 2022

Mirabegron ? BETMIGA ®

Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.7653-26
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Yumi Kawamoto[1,2], Shinjiro Kaieda[2], Yuri Hasuo[1,2] and Tomoaki Hoshino[2]

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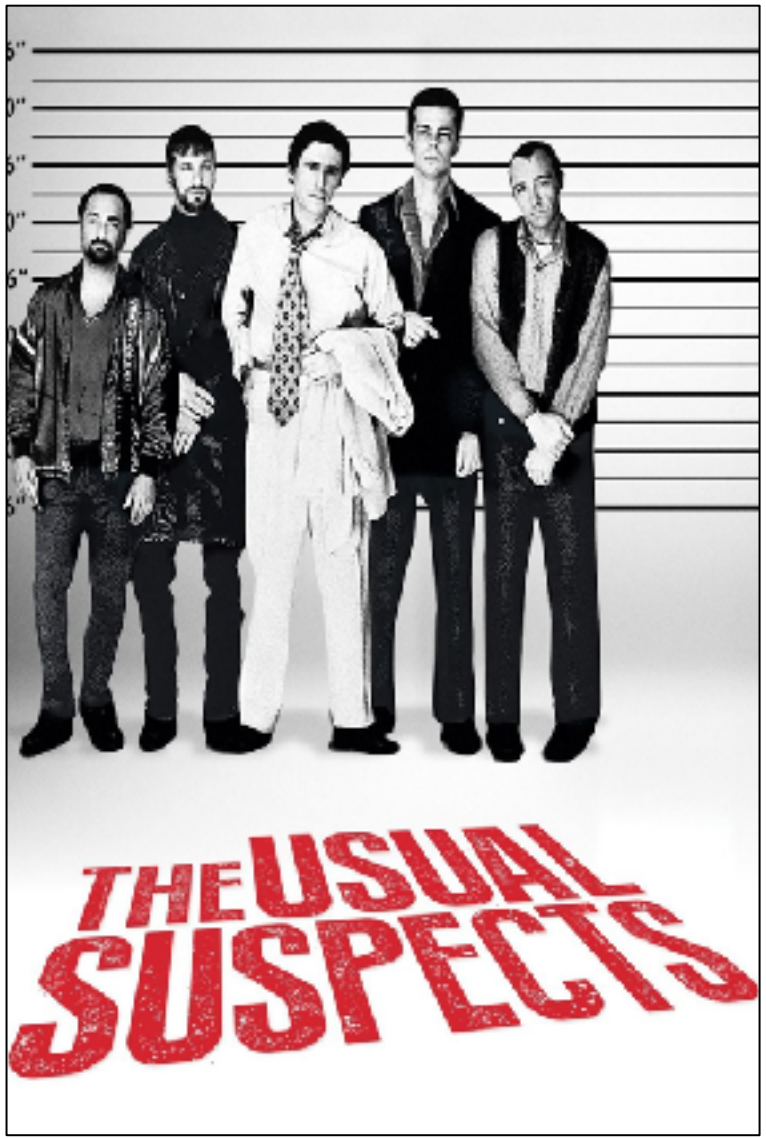
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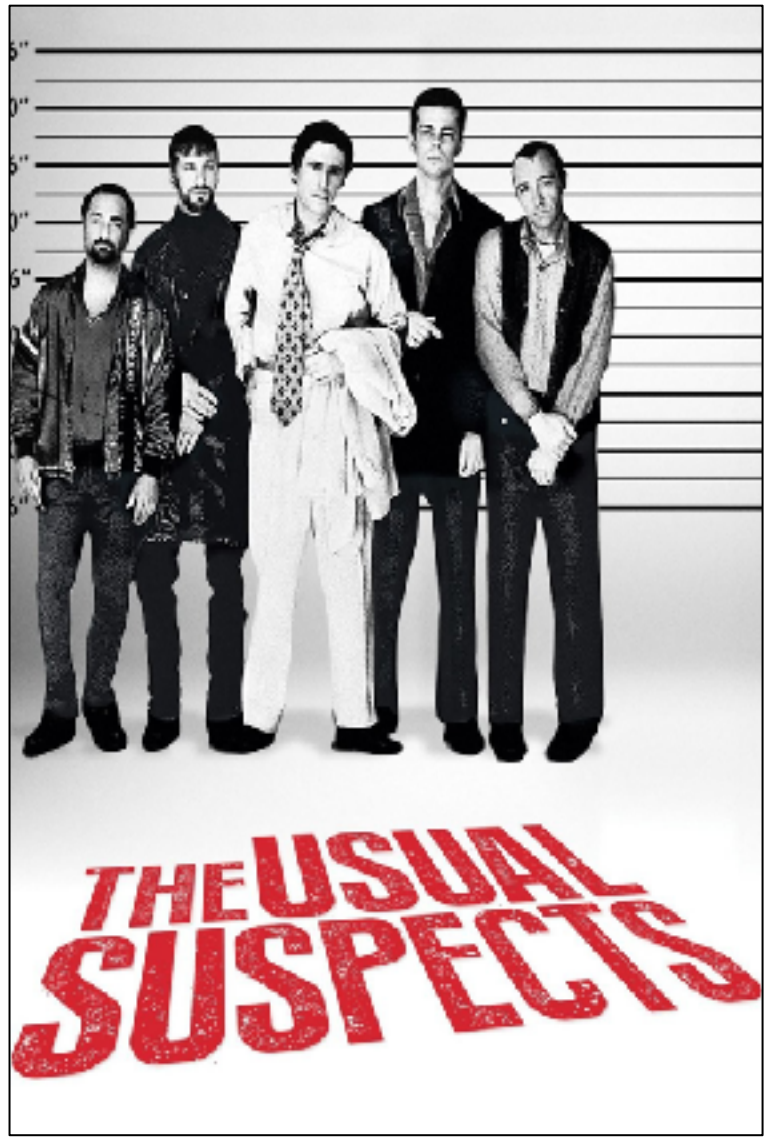


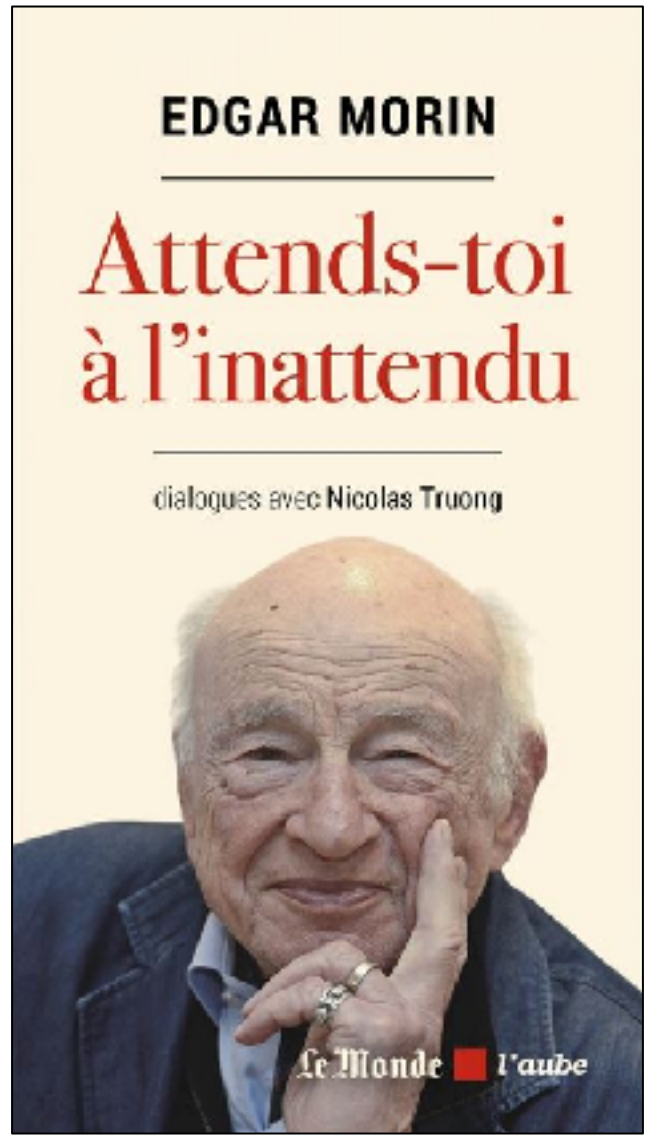


Conclusion



Conclusion


THE USUAL SUSPECTS


EDGAR MORIN
Attends-toi à l'inattendu
dialogues avec Nicolas Truong
Le Monde
l'aube