

# Syndromes d'apnées du sommeil et insuffisance cardiaque

M.P. d'Ortho  
Service de Physiologie – Explorations Fonctionnelles  
Hôpital Henri Mondor, Créteil



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## SAS chez les insuffisants cardiaques

- Prévalence, définitions
- Diagnostic
- Physiopathologie
- Prise en charge des SAS obstructifs
- Prise en charge des SAS centraux
- Autres SAS

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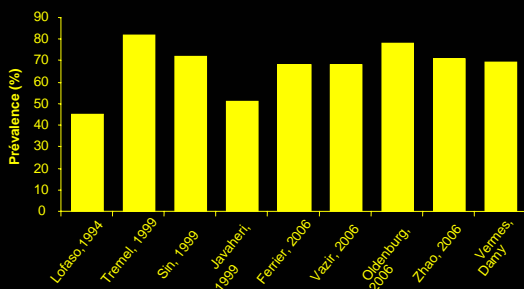
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## Sleep apnea syndromes in heart failure



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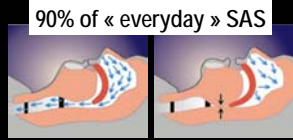
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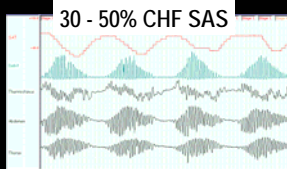
## SAS dans l'insuffisance cardiaque

**Obstructive SAS**  
Upper airway closure



90% of « everyday » SAS

**Central**  
Ventilatory drive instability



30 - 50% CHF SAS

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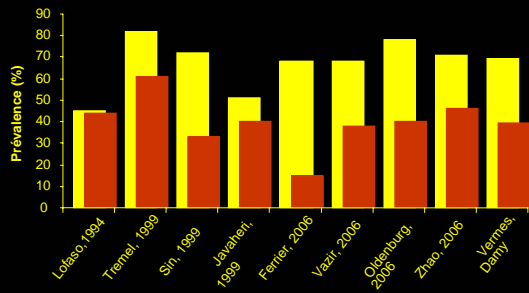
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## Sleep apnea syndromes in heart failure

Prevalence of central SAS and Cheyne-Stokes



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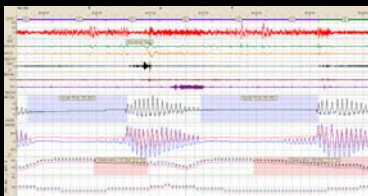
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Apnées obstructives vs apnées centrales :  
ce serait trop simple !



Syndrome d'apnées mixtes

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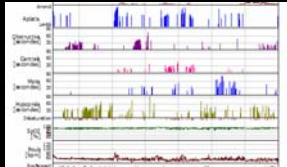
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Apnées obstructives vs apnées centrales :  
ce serait trop simple !



SAS mixte

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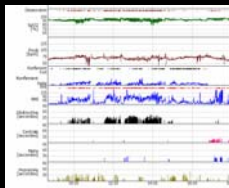
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Apnées obstructives vs apnées centrales  
: ce serait trop simple !



SAS alternant

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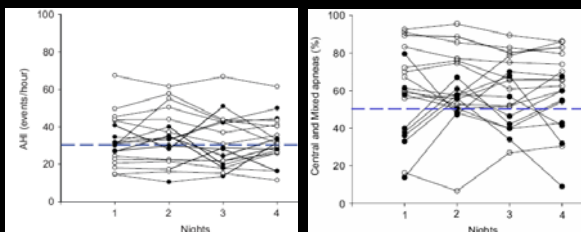
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Apnées obstructives vs apnées centrales :  
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Variation in severity and type of sleep-disordered breathing  
throughout 4 nights in patients with heart failure

*Vazir et al. Respir Med, 2008*




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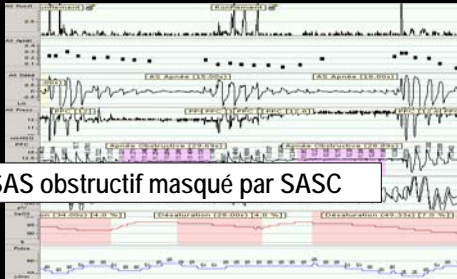
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Apnées obstructives vs apnées centrales :  
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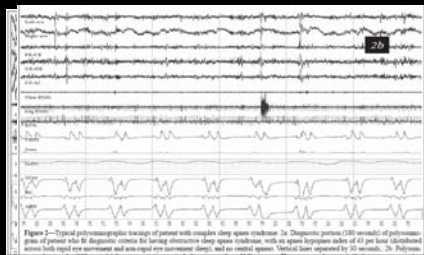
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Apnées obstructives vs apnées centrales :  
ce serait trop simple !



SAS complexe : SAS obstructif,  
devenant SAS central sous PPC

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Les différents syndromes d'apnées du sommeil  
chez les insuffisants cardiaques

SAS central / CS	Pas de SAS
SAS mixtes (C/O/M)	
SAS alternant O/C	
SASO masqué par SASC SAS complexes	
SASO « pur »	

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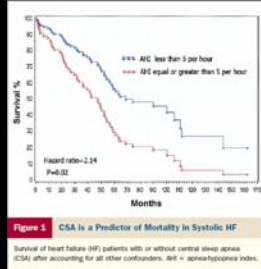
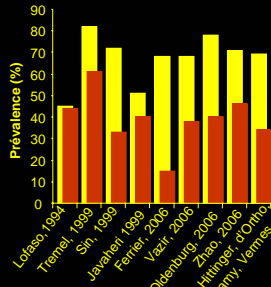
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## SASC et insuffisance cardiaque

Frequent

Mauvais pronostic



Javaheri, JACC, 2007

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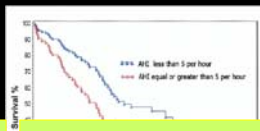
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## SAS et mortalité de l'IC



SAS : il vaut mieux le diagnostiquer ...  
Comment ??

Figure 1 CSA is a Predictor of Mortality in Systolic HF

Javaheri, JACC, 2007

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## Comment faire le diagnostic ?

Arguments cliniques orientent  
Examens complémentaires affirment

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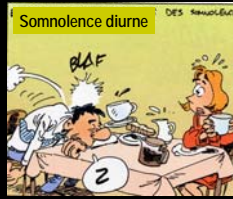
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## SAS obstructifs : orientation clinique



Propension à s'endormir dans des circonstances et des horaires inhabituels

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## SAS centraux : orientation clinique

... rien !!

... dyspnée d'effort ?

... dyspnée d'endormissement ??

Mais le plus souvent : rien

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## Diagnostic = enregistrements nocturnes

Plus simple



Oxymétrie nocturne (taux d'oxygène dans le sang)

Polygraphie nocturne (respiration pendant la nuit)

Polysomnographie nocturne (respiration et sommeil)

Plus compliqué

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## Dépistage : oxymétrie



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## Polygraphie ventilatoire nocturne

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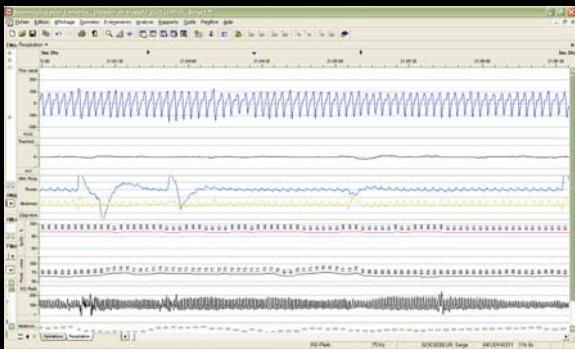
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## DIAGNOSTIC : POLYGRAPHIE NOCTURNE



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# Polysomnographie nocturne

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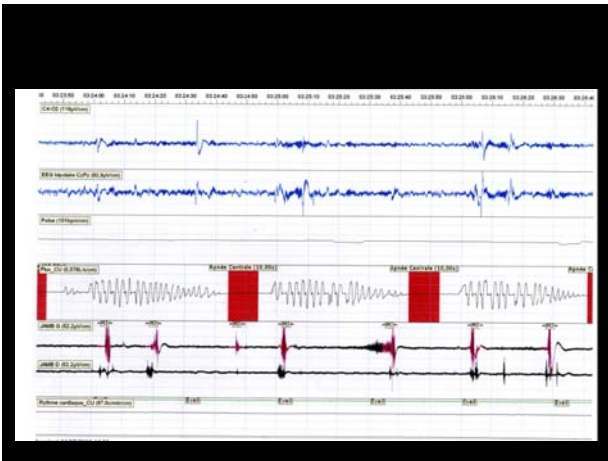
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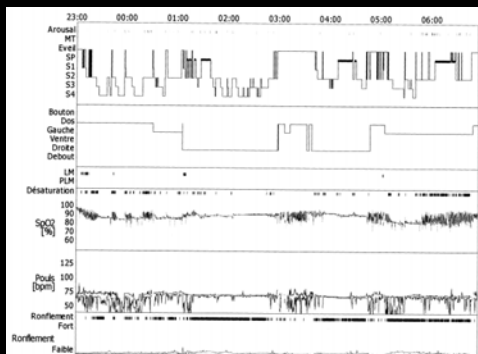
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# Polysomnographie nocturne



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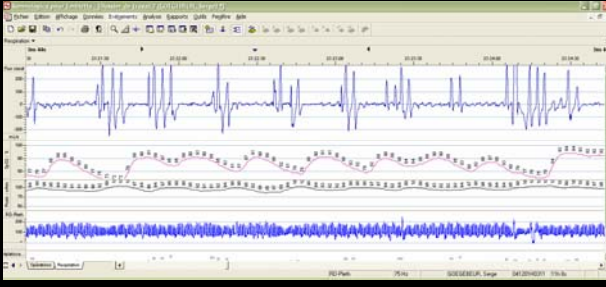
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## Dépistage : autres méthodes qu'oxymétrie

- Lunettes nasale seules
- Lunettes nasales + oxy



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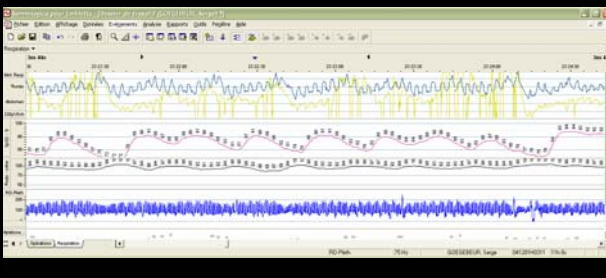
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## Dépistage : autres méthodes qu'oxymétrie

- Ceintures + oxymétrie



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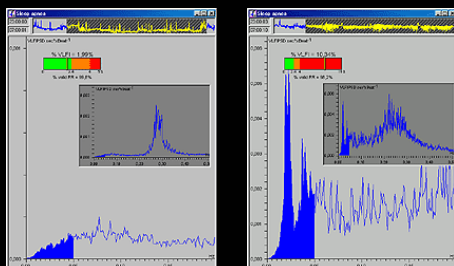
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## Dépistage : autres méthodes qu'oxymétrie

- Analyse de la variabilité de la fréquence cardiaque sur Holter ECG

Roche, Circulation 1999



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## Dépistage : autres méthodes qu'oxymétrie

- Analyse de la variabilité de la fréquence cardiaque sur Holter ECG

Roche, *Circulation* 1999  
Roche, *ERJ*, 2007

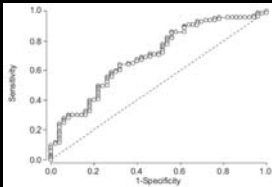


FIGURE 1. Receiver operating characteristic curve for the prediction of obstructive apnoea/hypopnoea syndrome (apnoea/hypopnoea index  $\geq 10$  events/h) from the power spectral density of ectopic interval scores of very low frequencies. Area under the curve=0.70.

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## Dépistage : autres méthodes qu'oxymétrie

- Analyse de la variabilité de la fréquence cardiaque sur Holter ECG, chez l'insuffisant cardiaque

Roche, *Circulation* 1999  
Roche, *ERJ*, 2007

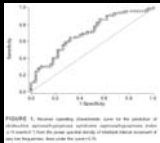


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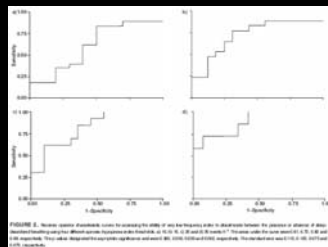


FIGURE 2. Receiver operating characteristic curves for prediction of AHS (area under the curve) in heart failure patients. The panels are ordered as follows: A, power spectral density of ectopic interval scores of very low frequencies; B, power spectral density of ectopic interval scores of very low frequencies; C, power spectral density of ectopic interval scores of very low frequencies; D, power spectral density of ectopic interval scores of very low frequencies. Area under the curve=0.70.

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## Dépistage : autres méthodes qu'oxymétrie

- Analyse de la variabilité de la fréquence cardiaque sur Holter ECG, chez l'insuffisant cardiaque

Damy, Roche, *soumis* 2008

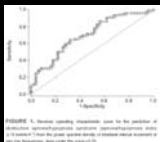


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Holter ECG plutôt peu utile pour le dépistage du SAS chez l'insuffisant cardiaque

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## Accès au dépistage / diagnostic

- Quel équipement ?
- Quelle(s) structure(s)?

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## Physiopathologie

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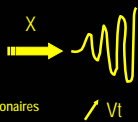
## Mécanismes responsables de la respiration de Cheyne Stokes dans l'insuffisance cardiaque

- L'hypocapnie :

Insuffisance  
cardiaque



- Récepteurs intrapulmonaires juxtacapillaires
- Récepteurs à l'irritation



PaCO<sub>2</sub> ↘

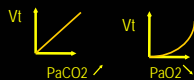
→ Apnée

- L'allongement du temps circulatoire :

Responsable de la durée de la phase hyperpnéique

- L'augmentation du « controller gain » :

Responsable de l'amplitude de l'hyperpnée



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## Prise en charge des SAS obstructifs

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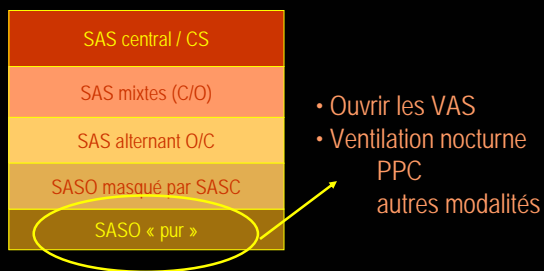
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## Traitement des syndromes d'apnées du sommeil chez les insuffisants cardiaques



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## SYNDROME D'APNEES OBSTRUCTIVES DU SOMMEIL Principes du traitement

Mesures hygiéno-diététiques TOUJOURS  
amaigrissement  
éviton des facteurs favorisants (alcool, benzodiazépines)

Chirurgie ORL / maxillo-faciale  
Orthèse d'avancée mandibulaire

Ventilation nocturne

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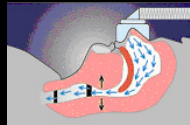
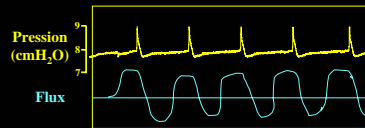
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## Ventilation en pression positive continue nasale (PPC)




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## Déterminer la pression efficace

- « Pression efficace » : compromis entre la pression maximale tolérée et la pression qui abolit
  - Apnées hypopnéées
  - Limitation de débit, ronflement : i.e. les obstructions partielles des VAS
  - Quelque soient le stade de sommeil et la position
- Titration au laboratoire de sommeil
  - Polysomnographie
  - Changement manuel (technicien/médecin) de la pression

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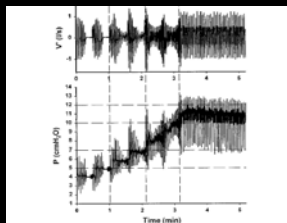
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## Auto-PPC :

- pression sur événements anormaux
- quand respiration stable, normale



Farré, AJRCCM, 2002

Figure 5. Automatic pressure (P) applied by device D2 when connected to a patient model exhibiting a flow (displayed as V) breathing pattern depending on the CPAP applied. P and V are actual pressure and flow, respectively, measured at the entrance of the automatic CPAP device. V<sub>T</sub> = 0.5 l; inspiration, see text for explanation.

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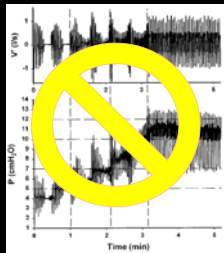
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Pression positive continue (PPC) constante



Pas d'auto-PPC

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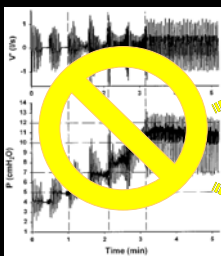
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Pression positive continue (PPC) constante



Tolérance hémodynamique de la PPC  
=> chute de pression artérielle

Induction d'apnées centrales

Pas d'auto-PPC

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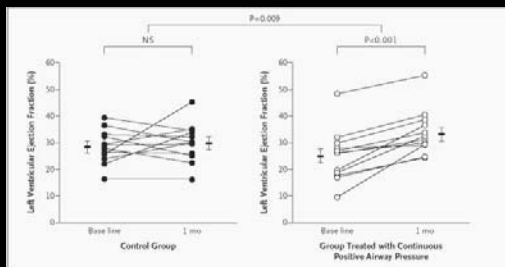
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SAOS : Effet de la PPC sur la fonction VG

Kaneko, N Eng J Med 2003  
24 insuffisants cardiaques, randomisés avec ou sans PPC  
LVEF baseline puis après 1 mois de traitement




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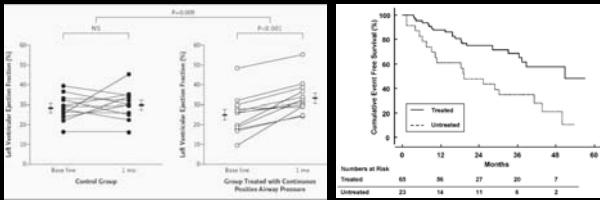
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## OSAS : CPAP benefit on LVEF and survival



Kaneko, *N Eng J Med* 2003  
24 CHF, randomized with or w/o CPAP  
LVEF at baseline vs after 1 month

Kasai, *Chest*, 2007, *epub ahead from print*  
88 CHF, prospective follow-up  
65 treated, 23 untreated

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## SAS obstructif : traitement



Ventilation nocturne  
pression positive continue (PPC) masque nasal  
...  
efficace, mais contraignant

Observance :  
288 ± 129 min à 360 ± 110 min après 1 mois, stable pdt 3 mois  
patient compliant (>4h/j, > 5j/sem) : 72 à 80 %  
⇒ 20-30% des sujets ne suivent pas leur traitement

Pépin, *AJRCCM*, 1999

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## L'éducation et le suivi

- Partenariat prestataire – médecin
- Mesures additionnelles
  - Suivi infirmier (Royaume-uni)
  - Evaluation d'une consultation « technicien », groupe de parole  
Créteil, H Hchikat, L Margarit
  - Matériel pédagogique destiné aux patients  
Jean Wiese, *Sleep Med*, 2005
- Fréquence du suivi
  - Intérêt d'une consultation précoce
  - Au minimum suivi téléphonique précoce




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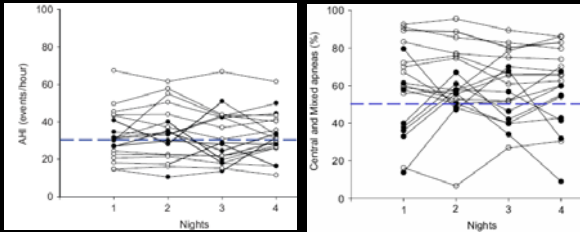
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Variation in severity and type of sleep-disordered breathing  
throughout 4 nights in patients with heart failure

Vazir et al. Respir Med, 2008




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## Apnées obstructives vs apnées centrales : ce serait trop simple !

Variation in severity and type of sleep-disordered breathing  
throughout 4 nights in patients with heart failure

2008

Un traitement « classique » du SAS obstructif  
peut ne pas être efficace  
- d'une nuit à l'autre  
- au cours du temps (évolution de la cardiopathie)




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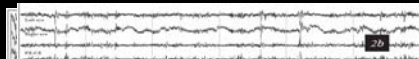
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## Apnées obstructives vs apnées centrales : ce serait trop simple !



Un traitement par PPC du SAS obstructif  
peut induire des apnées centrales :  
=> Il FAUT faire un contrôle PG/PSG d'efficacité

devenant SAS central sous PPC

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## Prise en charge des SAS centraux avec Cheyne-Stokes

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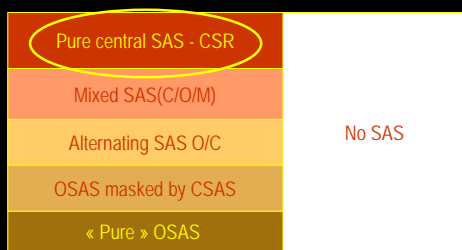
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## Sleep apnea syndrome in CHF patients




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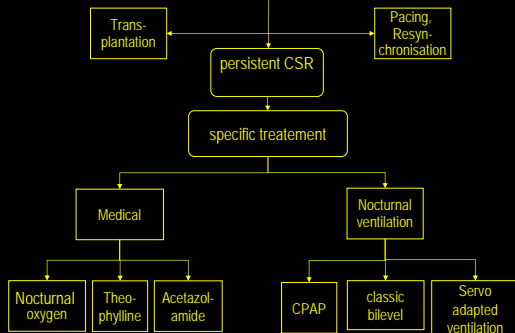
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Optimize medical treatment!  
ACEI;  $\beta$ -Blockers; Digoxin;  
Diuretics; Spironolactone




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### Mechanisms by which Optimal Medical Treatment of Heart Failure may Improve CSA/CSR

1. Normalization of PCO <sub>2</sub>	↓ PCWP and ↓ RR	Diuretics β-Blockers ACEI
2. Increase of functional residual capacity	↓ Cardiac size ↓ Pleural effusion ↓ Lung water	Diuretics ACEI β-Blockers
3. Reduction of circulation time	↑ Stroke volume ↓ Lung water ↓ Cardiac size	ACEI Diuretics β-Blockers
4. Increase in upper airway size	↓ Tissue water	Diuretics

adapted from Javaheri, Sem Respir Crit Care Med 2005;26,44

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### CSA/CSR & CHF: Response to Drugs

- 4 weeks captopril: AHI 35->20 / hr  
- Walsh, British Heart J, 1995
- 3 months medical optimization in RCT: AHI 33-> 27 / hr  
- Naughton, AJRCCM 1995
- 4 months optimized treatment: AHI 39-> 19 / hr  
- Solin, Circulation, 1999
- 2 months medical optimization: only 2 of 21 improved  
- Tremel, Eur Heart J, 1999
- 4 weeks optimized treatment: AHI 45-> 40 / hr  
- Teschler, ERJ, 2002

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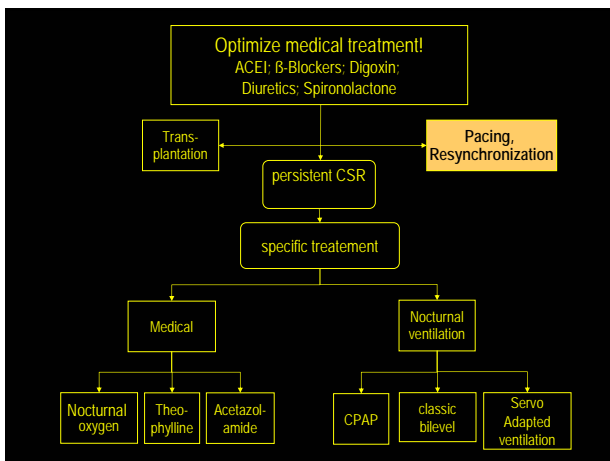
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## Théophylline

VARIABLE	BASE LINE	PLACEBO	THEOPHYLLINE	P VALUE†
mean ± SD				
Breathing event (no. of episodes/hr)				
Apnea-hypopnea	47±21	37±23	18±17	<0.001
Central apnea	26±20	26±21	6±14	<0.001
Obstructive apnea	2±6	2±3	2±5	0.7
Mixed apnea	2±3	2±4	1±1	0.06
Hypopnea	17±13	7±6	9±11	0.06
Arousal due to disordered breathing	24±11	17±15	8±10	<0.001
Oxygenoglobin saturation‡				
Base line (%)	95±2	94±2	95±2	0.7
Lowest value (%)	78±10	79±9	82±11	0.038
<90% (% of total sleeping time)	14±14	23±37	6±11	0.036
Partial pressure of oxygen (mm Hg)‡	83±8	82±12	84±12	0.7

S. Javaheri et al. NEJM 1996

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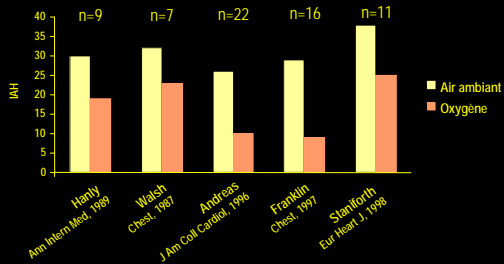
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## Oxygénothérapie nocturne




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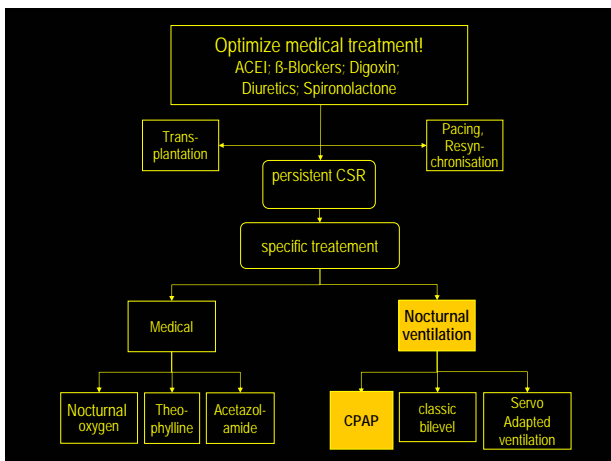
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## LA VENTILATION NOCTURNE EN PRESSION POSITIVE

- Buts:
  - Améliorer l'oxygénation des tissus et notamment du muscle cardiaque durant le sommeil
  - Améliorer l'hémodynamique cardiaque en réduisant la pression artérielle mais aussi la fréquence cardiaque.
  - Limiter la stimulation sympathique
  - Réduire la pression ventriculaire transmurale et la précharge.

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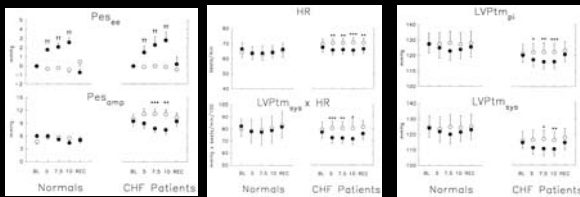
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## Effets hémodynamiques de la PPC

Diminution de la post-charge du VG

- ➔ dépression intrathoracique = ➔ pression transmurale VG
- ➔ de FC : correction de l'hypoxémie, augmentation CRF  
correction des décharges sympathiques



Naughton, *Circulation*, 1995

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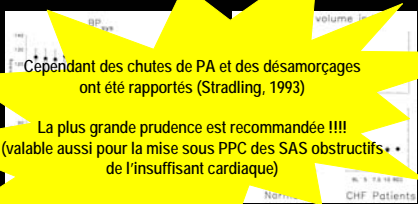
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## Effets hémodynamiques de la PPC

Diminution de la post-charge du VG

sans affecter la pression artérielle ni le volume dejection / index cardiaque



Cependant des chutes de PA et des désamorçages ont été rapportés (Stradling, 1993)

La plus grande prudence est recommandée !!!!  
(valable aussi pour la mise sous PPC des SAS obstructifs de l'insuffisant cardiaque)

Naughton, *Circulation*, 1995

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## Does CPAP treatment improve heart function and outcome ?

**YES !**

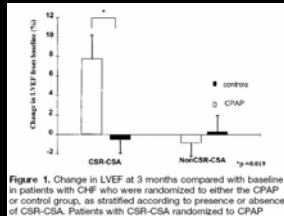


Figure 1. Change in LVEF at 3 months compared with baseline in patients with CHF who were randomized to either the CPAP or control group, as stratified according to presence or absence of CSD-CSDA. Patients with CSD-CSDA randomized to CPAP.

66 patients, randomized study  
Sin, Circulation, 2000

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## Does CPAP treatment improve heart function and outcome ?

**YES !**

**NO !**

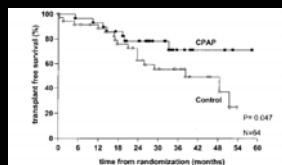


Figure 2. Treatment analysis revealed that overall transplant-free survival was significantly greater in patients randomized to CPAP who complied with therapy than in control subjects.

66 patients, randomized study  
Sin, Circulation, 2000

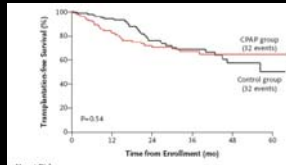


Figure 3. Heart Transplantation-free Survival.

258 patients, randomized  
Bradley, NEJM, 2005

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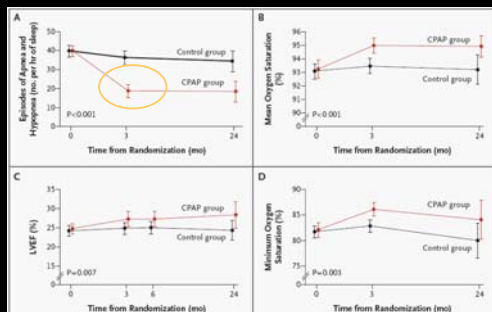
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Not all patients were efficiently treated,  
CPAP benefits were higher in responders  
Events (death/transplantation) were higher in CPAP drop outs

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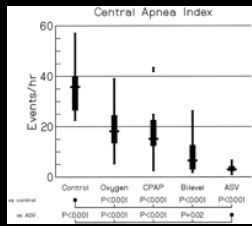
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## Adapted servo-ventilation : efficacy



	Change with Therapeutic ASV (n = 15)	Change with Subtherapeutic ASV (n = 15)	p Value
Daytime sleepiness			
Ordis, min	+7.9 (2.9)	-1.0 (1.7)	0.014
BNP, pg/ml	-56.0 (-238--16.0)	0.0 (-24.0+73.0)	0.001
Metadrenaline, nml/nml creatinine			
Metroradrenaline, nml/nml creatinine	-15.4 (4.6)	+5.3 (6.8)	0.018
Metroradrenaline, nml/nml creatinine	-36.6 (21.3)	-2.3 (13.7)	0.19

ASV reduced

- BNP
- Urinary catecholamine

Randomized, over 1 month  
Pepperrell, *AJRCCM* 2003

O<sub>2</sub> < CPAP < ASV = Bilevel  
Randomized, over 1 night  
Teschler, *AJRCCM*, 2001

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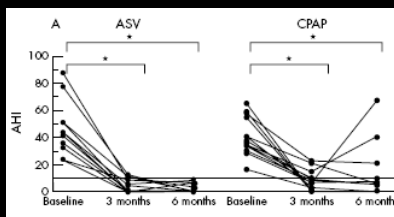
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## ASV AutosetCS® versus CPAP



25 patients, randomized, over 6 months

Philippe, *Heart*, 2005

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## ASV AutosetCS® versus CPAP

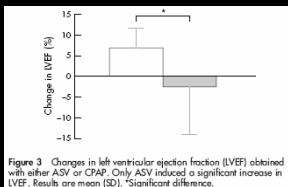
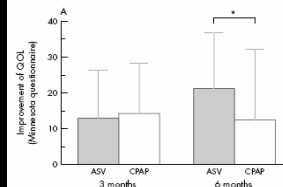


Figure 3 Changes in left ventricular ejection fraction (LVEF) obtained with either ASV or CPAP. Only ASV induced a significant increase in LVEF. Results are mean (SD). \*Significant difference.



25 patients, randomized, over 6 months  
Greater benefit from ASV than CPAP  
But small study that requires confirmation

Philippe, *Heart*, 2005

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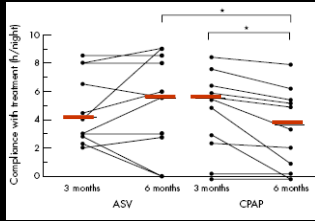
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## ASV AutosetCS<sup>®</sup> versus CPAP



25 patients, randomized, over 6 months  
Satisfactorily compliance

Philippe, *Heart*, 2005

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## 5 years follow-up of heart failure patients treated with ASV<sup>®</sup>

- **Aim of the study :**
  - Describe characteristics, compliance and outcome of patients treated for central sleep apnea syndrome with ASV<sup>®</sup>
- **Design of the study,**
  - Retrospective analysis of patient files
  - Patients identified in a homecare provider database
  - Between 1st Janv. 2001 – 31 Oct. 2005
  - Exclusion criteria
    - ASV treatment for CS-CSA due to other causes than CHF
- **Results**
  - 141 patients, 40 excluded
    - 17 neurologic CS, 19 TT < 2 weeks, 14 impossibility to access medical files

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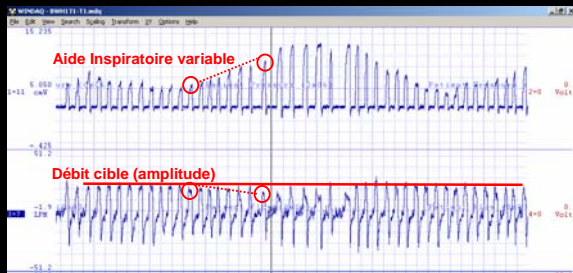
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## Ventilations asservies




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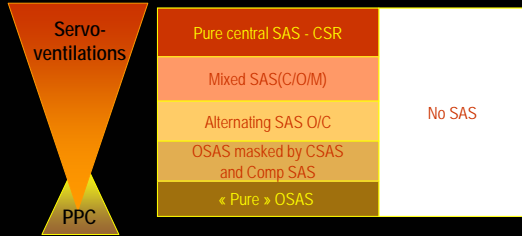
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## Sleep apnea syndrome treatment with NIV in CHF patients



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## To conclude

- SAS, especially Central SAS with Cheyne-Stokes in CHF,
  - Is frequent
  - Poor prognosis
- Should be treated
  - CPAP ?
  - ASV : first studies suggest that ASV improves heart function and outcome
  - Compliance is not a problem
- More data are needed

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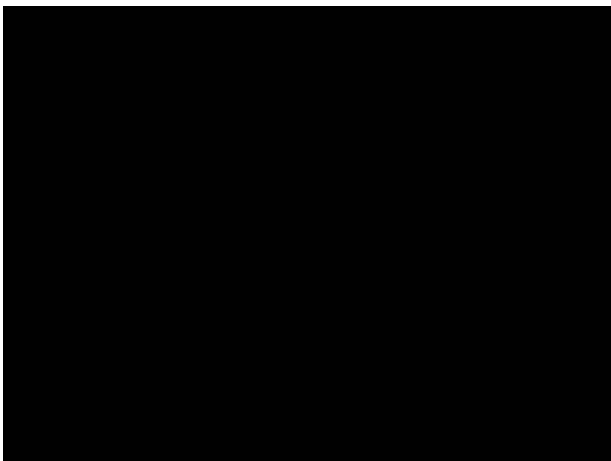
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