PULMONARY FUNCTION TESTS FOR ALLERGOLOGISTS AND CLINICAL IMMUNOLOGISTS

PRACTICE AND INTERPRETATION

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PLAN

- Spirometry: update on technical aspects
- New references for normal values: GLI 2012
- Interpretation of the spirometry
- Volumes measurements: interest and interpretation
- DLCO/KCO measurements

Spirometry
update on technical aspects.

Standardization of spirometry 2019 update
An official ATS/ERS technical statement
(Am. J. Resp. Crit. Care Med 200, 8, Oct.15.2019, e70-e88)

1. THE ROOM AND BASIC EQUIPMENT

- Stable room temperature
- Precise measures of room temperature / barometric pressure/ hygrometry.
- Chair with height adjustment to have patients seated upright with feet flat on the floor.
  (measurements in standing position give identical results but more risk of fall in case of fainting).

- Nose clips
- Disposable mouthpieces

2. THE SPIROMETER

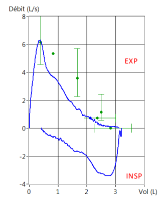
What is for you a good spirometer ?

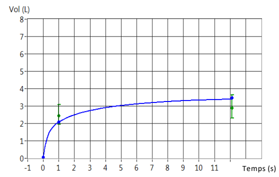
A possible answer: a trustable and practical device with a complete and friendly software…

…but what means «trustable» and «complete» ?

2. THE SPIROMETER

- The device should meet the standard ISO 26782.
- It should be able to measure: - volumes reaching 8l.
  - flow between 0-14 l/s
  - during at least 15s
  - with an accuracy of +/- 2.5%
- Calibration possible with a 3L syringe
- *Auto-measurements of temp. / barom pressure/ hygrometry*
- Dysplay with flow/volume and volume/time curves.



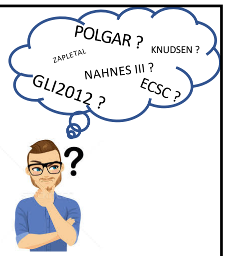


- Calibration with 3L syringe. Max tolerated error at calibration: +/- 2.5%

Potential Reasons for Calibration Verification Failure

- A slight change in spirometer function that requires a subsequent recalibration procedure to adjust the calibration factor.
- A leak in the connection of the spirometer to the calibration syringe
- Air flow through the spirometer during the zero-flow setting procedure
- Failure to fully fill and empty the calibration syringe in one smooth action
- Calibration syringe malfunction (e.g., piston leak or displacement of the piston stop or syringe damaged by dropping)
- Spirometer blockage either by debris in the spirometer sensor or by the operator's hand while holding the spirometer in place
- Improper assembly of the sensor, mouthpiece, filter, and/or breathing tube
- Differences between room temperature and calibration syringe temperature
- Data entry errors in the ambient temperature and/or pressure

3. THE SPIROMETER SETTINGS



You should be able to select:

- the references for normal values
- the ethnicity of the patient
- the best VC, FVC, PEF and FEV_1 of each phase pre / post BD, so that the calculation of FEV_1/FVC or FEV_1/VC can include values from different expirations.
- forced or unforced measurements.

4. THE PATIENT

Enter the following:
- Measured height (1-2% error /cm), weight
- Sex, age, ethnicity

Prior to spirometry:
- No smoke or vaping during 1h before the test.
- No vigorous exercice 1h before
- No too tight clothes
- No chewing gum

In case of a diagnostic procedure, stop the bronchodilator before the test:

Bronchodilator Medication		Withholding Time
SABA	(e.g. albuterol or salbutamol)	4–6 h
SAMA	(e.g. ipratropium bromide)	12 h
LABA	(e.g. formoterol or salmeterol)	24 h
Ultra-LABA	(e.g. indacaterol, vilanterol, orolodaterol)	36 h
LAMA	(e.g. tiotropium, umeclidinium, aclidinium, or glycopyrronium)	36–48 h

5. THE FEV$_1$ and FVC MANEUVER

What do you tell your patient to do ?

5. THE FEV$_1$ and FVC MANEUVER

A. Procedure:

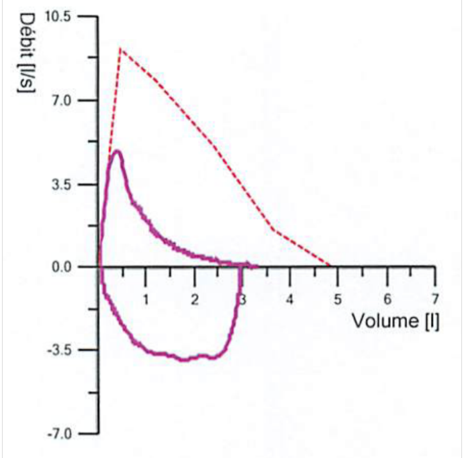
Closed nose with nasal clip.

Normal breathing within the mouthpiece

1. Inhale normally to the maximum possible (pause <2s at TLC)
   (comment: a too slow inspiration or a too long pause before expiration can lead to a diminution of FEV1 and PEF).
2. Exhale with a maximal effort until completely empty and indication of a plateau of flow or an exp. time of max 15 sec. (at least 6 sec.)
3. New complete rapid inhalation to the max. (measure of FIVC)
   (comment: if this second inhalation is correctly done, the comparison of FVC and FIVC can assure that the forced expiration began at full inflation and you can get trustable information about problema of upper airways)
   Repeat at least 3 times, max 8.

The value of the measurement is strongly dependant on the collaboration of the patient

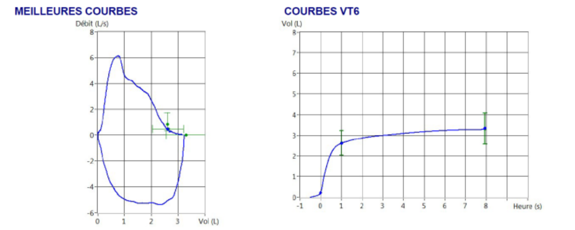
Intensively motivate the patient during the test is very important !



What do you find incorrect in this exam ?

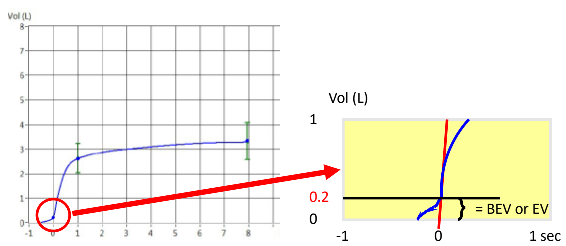
RESULTATS DES TESTS

Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	Plage normale (------) Pré (o) & Post (x) Résultats -4.0 -2.0 0.0 2.0 4.0	plage abs
CV	L		3.47									-
CVF	L	3.30	3.14	95	-0.35						-----o-------	2.56-4.07
VEF1	L	2.63	2.61	99	-0.07						------o------	2.04-3.21
VEF1/CV			0.75									-
VEF1/CVF		0.80	0.83	104	0.46						--------o----	0.69-0.90
DEP	L/s		5.91									-
DEM75	L/s		6.11									-
DEM50	L/s		3.67									-
DEM25	L/s	0.81	1.19	147	0.80						---------o---	0.34-1.75
DEMM	L/s	2.55	3.07	120	0.61						--------o----	1.40-4.05
TEF	s		7.94									-
EV	L		0.21									-
CVIF	L		3.23									-
DIM50	L/s		5.24									-



B. Objective control of the maneuver:

B1.Control of the start of the forced expiration by the back-extrapolated volume (BEV or EV):



BEV = Vol exhaled before time 0, should be <100 ml or <5% FVC.
If too high, FVC and FEV_1 will be too high.

B2. Control of the end of the forced expiration:
Very important to have a full FVC measurement.
3 possible criteria:

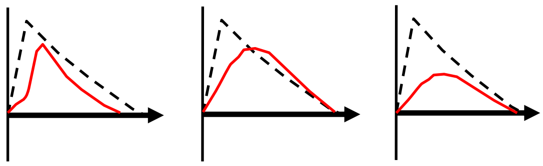
- Less than 0.025 L of volume change for at least 1 sec (= plateau). Should be signaled by the device.
  (comment: about 95% of people achieve to reach a plateau if they can blow out for more than 6 sec).
- Forced expiratory time of 15 sec.
- In the case a plateau cannot be achieved (children, restrictive lung disease), FVC should be repeatedly the same as the best FVC.

Objective control of the maneuver:

B3 Additional remarks:

- When none of these criteria is met, FVC is not trustable
- If FIVC-FVC > 100ml or >5% of FVC, FVC is not trustable
- If cough occurs during the first sec. FEV_1 is not trustable
- Beware of the obstruction of the mouthpiece by the tongue or hand which can alter completely the measures.
- In children 3-6 years who sometimes cannot expire 1 sec, it is useful to record the $FEV_{0.75}$ (ref values in GLI2012)

Common problems

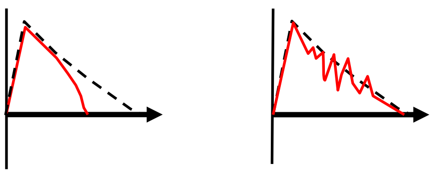


Delayed exhalation

Insufficiently forced (PEF dimished)

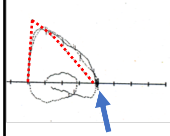
Bad cooperation

Common problems



Premature stop of exhalation

Cough



Spirométrie

		Ref	Pre Mesu	Pre % Ref	Post Mesu	Post % Ref
FVC	Litres	3.82	4.10	107	4.15	109
FEV1	Litres	3.23	3.87	120	3.93	122
FEV1/FVC	%	84	94		95	
DEM50	L/sec	4.36	5.14	118	4.77	109
DPE	L/sec	7.11	6.37	90	6.13	86
CVIF	Litres	3.99	0.16	4	2.77	69
DIM50%	L/sec		0.28		1.33	
VMM	L/min					
Code CDV			000011		000000	

C. Reproducibility of maneuvers:

Acceptable if :

Δ between the 2 best FVC and Δ between the 2 best FEV_1 are:

< 150 ml	> 6 years old
< 100 ml or < 10% of the best	≤ 6 years old

6. The VC maneuver

What do you tell your patient to do ?

6. The VC maneuver

A. Procedure:
Begin with VC maneuvers before FVC maneuvers.
If not, tiredness can diminish the result of VC.

1. Breathe gently at tidal volumes
2. Inhale rapidly to the max
3. Exhale gently but not too slowly and just force at the end to reach maximal expiration and plateau.
This will give the ExpVC

or

2. Exhale gently first to the plateau of max of expiration
3. Inhale rapidly to the max.
This will give the InspVC that can differ from Exp VC in severe obstruction.

B. Objective control of the VC maneuvers:

At least 3 maneuvers and same reproducibility criteria than for FVC.

C. Additional remark:

- The high variability of this measure is normally linked to an incomplete inspiration.
- In obstructive diseases, an air trapping may occur during forced maneuvers, « called dynamic air trapping ». It can be suspected if VC >FVC with Δ>10%.

7. RESPONSIVENESS TO BRONCHODILATOR

- Repeat the forced maneuvers 15 min after 4 puffs of salbutamol with inhalation chamber.
- No consensus on the interest of an additional bronchodilation by ipratropium in BPCO (4 puffs and measures 30-40 min later).

GLI 2012 : new references for normal values

New references for normal values: GLI 2012

Commonly used sets of references values for european countries for adults :

- European coal and steel community (ECSC) for 21-70 years adults
- National health and nutrition examination survey (NHANES III) including whites, afro-american, mexican-american men/women 8-80 years)

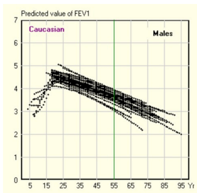
for children:

- Pulgar (modified)
- Quanjer
- Knudsen

Zapletal
Various combinations

Main problems with all these old sets of references

- Predictive equations for normal values are based on mixed observational studies by various authors covering different populations and incompletely the whole spectrum of ages and ethnicities.



Predicted FEV_1 for white males according to 30 authors.

- Precise comparison of different lung functions are not possible if the references sets used are not the same.

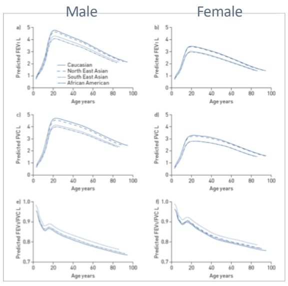
Main problems with all these old sets of references

- Equations are based on false hypothesis like:
  - a linear rise of FEV1 and FVC with growth.
  - a linear diminution of FEV1/FVC with age.

FEV_1

FVC

FEV_1/FVC



FEV_1/FVC diminishes steeply from 3 to 10y, rises from 10 to 16y and then declines
(DATA GLI2012)

Main problems with all these old sets of references

- The transition between equations for children and adults at 18y is problematic with a jump in ref. values:

RESULTS of TEST Miss LZ 17 years 11 month

Polgar	Ref	Val abs	%réf.	Limites 95%
CVF L	3.05	3.68	121%	80-126
VEF1 L	2.90	2.82	97%	80-127
VEF1/CVF	0.95	0.77 *	80% *	88-114

RESULTS of TEST Miss LZ 18 years 1 month

ECSC	Ref	Val abs	%réf.	Limites 95%	
CVF L	3.37	3.68	109%	80-126	-12%
VEF1 L	2.94	2.82	96%	80-127	- 1%
VEF1/CVF	0.84	0.77	91%	88-114	+11%

The Global Lung function Initiative 2012 (GLI2012)

- Standardized measures of lung function in 97’759 healthy non smokers of 72 centers in 33 countries of the world (>150’000 spiro).
- AGE: 2.5 – 95 years
- According to statistical differences of lung function between ethnicities, 5 different set of references values exists (see next page)
- New predictive equation based on these observations, taking into account at all ages: height, age, ethnicity and new limits of normality based on the gaussian distribution of measurements.

The Global Lung function Initiative 2012 (GLI 2012)

- ✓ Caucasians (from Europe, US, Can, Aus, Israel, north Africa, Venezuela, Mexico, Uruguay, Brazil, Chile).
- ✓ Blacks: african-american
- ✓ South-East Asia: Taïwan, South China including Hong-Kong (South of Huaihe River = Yellow river and Quilin mountains), Thaïland.
- ✓ North-East Asia: Korea, North China (north of Huaihe River = Yellow River and Quilin mountains)
- ✓ Others: pooled data from other ethnic groups or mixed ethnic origin.

The Global Lung function Initiative 2012 (GLI 2012)

Predictive value of the new equation GLI compared with other equations in children:

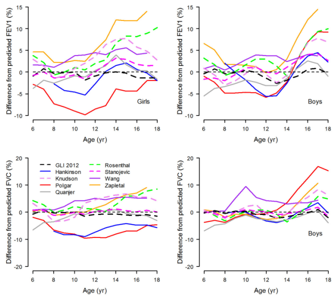


Table 2 – Prevalence rate of airway obstruction according to GLI-2012 and other prediction equations.

	FEV_1/FVC < LLN	
Author	Boys n = 2492	Girls n = 2072
Hankinson	17.8%	14.3%
Knudson	21.0%	10.5%
Quanjer GLI-2012	15.0%	14.0%
Wang	21.6%	16.8%
Zapletal	23.1%	10.9%

The Global Lung function Initiative 2012 (GLI 2012)

The lower limit of normal (LLN)

The hypothesis that the distribution of normal measures will be between +/-20% (usual range of normal measures: 80-120%) of the predicted values is not true in all situations, particularly in older or small people.

The Global Lung function Initiative 2012 (GLI 2012)

The lower limit of normal (LLN) / the higher limit of normal (HLN)

Since 2005 ATS/ERS recommend the use of the LLN which corresponds to the percentile 5 of all measures (in abs.val).

Most of modern spirometers present the LLN and SLN as the P5 and P95.

RESULTATS DES TESTS

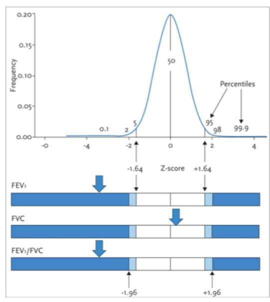
Abr.	Unité	Réf. valeur GLI2012	VALEURS MESUREES test PRE abs	%réf.	score z	test POST abs	%réf.	score z	Différence abs	%pré	Plage normale (-----) Pré (o) & Post (x) Résultats -4.0 -2.0 0.0 2.0 4.0	plage abs
CV	L		3.33									-
CVF	L	3.25	3.41	105	0.31						-------o-----	2.40-4.14
VEF1	L	2.52	2.15	85	-0.92						--o----------	1.85-3.15
VEF1/CV			0.64									-
VEF1/CVF		0.78	0.63	*81	*-1.92						o------------	0.65-0.89
DEP	L/s		6.01									-
DEM75	L/s		3.77									-
DEM50	L/s		1.17									-
DEM25	L/s	0.55	0.31	56	-0.99						--o----------	0.21-1.40
DEMM	L/s	2.10	0.82	*39	*-1.99						o ------------	1.00-3.64
TEF	s		12.13									-
EV	L		0.06									-
CVIF	L		2.81									-

The Global Lung function Initiative 2012 (GLI 2012)

The Z-score: another way to express the deviation from the mean value in a Gaussian distribution.

The Z score is the number of standard deviation between the measured value and the average value in the healthy population.

Z score = 0 measure = average
Z score = -1.64 measure = P5 = LLN
Z score = -1.96 measure = P2.5



The Global Lung function Initiative 2012 (GLI 2012)

The Z score

RESULTATS DES TESTS

Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	Plage normale (-----) Pré (o) & Post (x) Résultats -4.0 -2.0 0.0 2.0 4.0	plage abs
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CVF	L	3.25	3.41	105	0.31						-------o-----	2.40-4.14
VEF1	L	2.52	2.15	85	-0.92						--o----------	1.85-3.15
VEF1/CV			0.64									-
VEF1/CVF		0.78	0.63	*81	*-1.92						o------------	0.65-0.89
DEP	L/s		6.01									-
DEM75	L/s		3.77									-
DEM50	L/s		1.17									-
DEM25	L/s	0.55	0.31	56	-0.99						--o----------	0.21-1.40
DEMM	L/s	2.10	0.82	*39	*-1.99						o ------------	1.00-3.64
TEF	s		12.13									-
EV	L		0.06									-
CVIF	L		2.81									-

Z score = -1.92 The probability that the measure will be found in a normal population is about 3%

Interpretation of spirometry

1. Airway obstruction ?
   Look at FEV_1/FVC or FEV1/ VC

2. If yes, at which degree ?
   Look at FEV_1

Interpretation of spirometry

Airway obstruction is defined by :

FEV_1/FVC or FEV_1/ VC < LLN (<P5) or Z score < -1.64

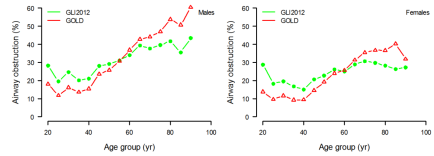


Fig. 28 - Percentage of patients with airway obstruction (FEV_1/FVC < LLN) based on GLI-2012 [23] predicted values, or with GOLD stage 2-4.

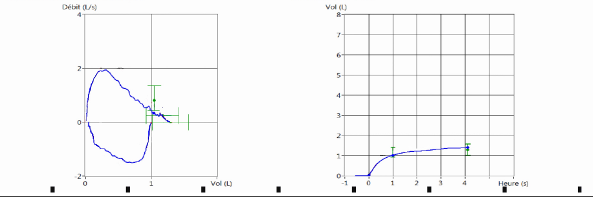
Airway obstruction should not be anymore defined by ~~FEV1/FVC (post BD) <0.7~~ (Definition GOLD for COPD) (Overdiagnosis of obstruction over 60y)

Boy, 5 years, relapsing bronchospasms initially related to viral infections, but more and more independant of viruses. Allergy to dust mites, grasses. No regular TTT.

RESULTATS DES TESTS

Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	Plage normale (-----) Pré (o) & Post (x) Résultats -4.0 -2.0 0.0 2.0 4.0	plage abs
CV	L		1.39			1.26			-0.12	-9		-
CVF	L	1.29	1.30	101	0.07	1.30	101	0.06	-0.00	-0	------*------	1.02-1.57
VEF1	L	1.17	1.03	88	-0.90	1.18	101	0.08	0.15	14	---o--x------	0.92-1.41
VEF1/CV			0.74			0.93			0.19	25		-
VEF1/CVF		0.91	0.79	87	-1.63	0.91	100	-0.05	0.11	14	o-----x------	0.79-1.00
DEP	L/s		1.91			2.10			0.19	10		-
DEM75	L/s		1.92			2.10			0.18	9		-
DEM50	L/s		1.14			1.67			0.53	47		-
DEM25	L/s	0.82	0.48	58	-1.42	0.70	86	-0.43	0.22	47	-o--x--------	0.43-1.36
DEMM	L/s	1.54	0.95	62	-1.60	1.49	96	-0.13	0.53	56	o----x-------	0.94-2.29
TEF	s		4.12			2.49			-1.63	-40		-
EV	L		0.04			0.06			0.02	43		-
CVIF	L		0.95			0.98			0.03	3		-
DIM50	L/s		1.35			1.54			0.19	14		-

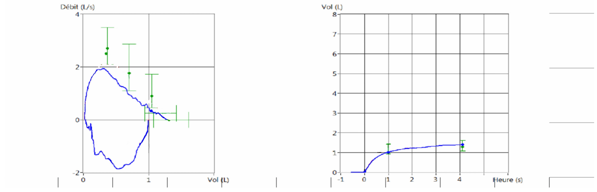
MEILLEURES COURBES **COURBES VT6**



RESULTATS DES TESTS

Abr.	Unité	Réf. valeur Polg. Z	----- VALEURS MESUREES ----- test PRE abs	%réf.	test POST abs	%réf.	Différence abs	%pré	Plage normale (-----) Pré (o) & Post (x) Résultats 20 40 60 80 100 120 140 160 180	95% plage %réf.
CV	L	1.30	1.39	106	1.26	97	-0.12	-9	---x-o----	82-124
CVF	L	1.30	1.30	100	1.30	100	-0.00	-0	----*-----	82-124
VEF1	L	1.15	1.03	90	1.18	103	0.15	14	--o--x----	81-124
VEF1/CV		0.88	0.74	*84*	0.93	106	0.19	25	o---x--	88-115
VEF1/CVF		0.88	0.79	90	0.91	103	0.11	14	o--x--	88-115
DEP	L/s	2.69	1.91	*71*	2.10	78	0.19	10	o x----------	78-130
DEM75	L/s	2.50	1.92	77	2.10	84	0.18	9	o x	-
DEM50	L/s	1.76	1.14	65	1.67	95	0.53	47	-o-----x-------------	62-163
DEM25	L/s	0.89	0.48	53	0.70	78	0.22	47	-o----x-------------------	52-193
DEMM	L/s	1.43	0.95	66	1.49	104	0.53	56	o x	-
TEF	s		4.12		2.49		-1.63	-40		-
EV	L		0.04		0.06		0.02	43		-
CVIF	L		0.95		0.98		0.03	3		-
DIM50	L/s		1.85		1.55		-0.31	-17		-

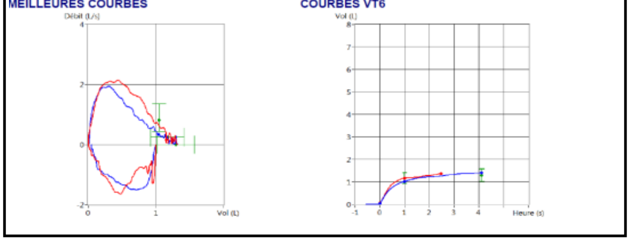
MEILLEURES COURBES **COURBES VT6**



RESULTATS DES TESTS

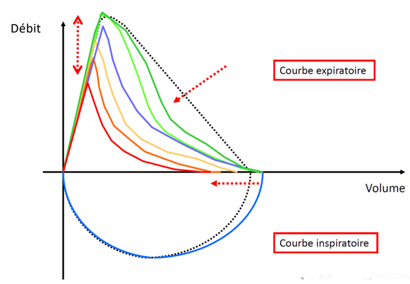
Abr.	Unité	Réf. valeur GLI2012	----- VALEURS MESUREES ----- test PRE abs	%réf.	score z	test POST abs	%réf.	score z	Différence abs	%pré	Plage normale (-----) Pré (o) & Post (x) Résultats -4.0 -2.0 0.0 2.0 4.0	plage abs
CV	L		1.39			1.26			-0.12	-9		-
CVF	L	1.29	1.30	101	0.07	1.30	101	0.06	-0.00	-0	------*------	1.02-1.57
VEF1	L	1.17	1.03	88	-0.90	1.18	101	0.08	0.15	14	---o--x------	0.92-1.41
VEF1/CV			0.74			0.93			0.19	25		-
VEF1/CVF		0.91	0.79	87	-1.63	0.91	100	-0.05	0.11	14	o-----x------	0.79-1.00
DEP	L/s		1.91			2.10			0.19	10		-
DEM75	L/s		1.92			2.10			0.18	9		-
DEM50	L/s		1.14			1.67			0.53	47		-
DEM25	L/s	0.82	0.48	58	-1.42	0.70	86	-0.43	0.22	47	-o--x--------	0.43-1.36
DEMM	L/s	1.54	0.95	62	-1.60	1.49	96	-0.13	0.53	56	o----x-------	0.94-2.29
TEF	s		4.12			2.49			-1.63	-40		-
EV	L		0.04			0.06			0.02	43		-
CVIF	L		0.95			0.98			0.03	3		-
DIM50	L/s		1.35			1.54			0.19	14		-

MEILLEURES COURBES **COURBES VT6**



Interpretation of spirometry

Airway obstruction progression:



Interpretation of spirometry

The severity of the obstruction is defined by the decrease in FEV_1, according to the following scales:

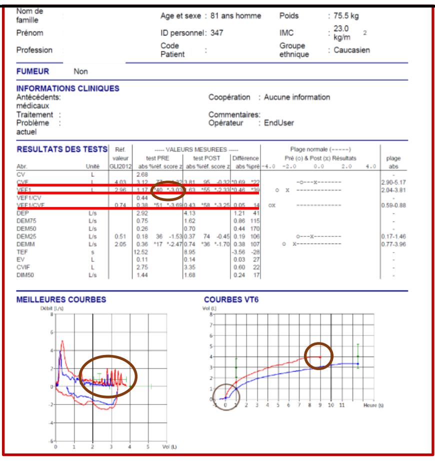
Severity	GOLD	ATS/ERS	Z-score
Mild	>80% pred	>70% pred	Z >= -2
Moderate	50-79% pred	50-69% pred	-3 <= Z < -2
Severe	30-49% pred	35-49% pred	-4 <= Z < -3
Very severe	<30% pred	< 35% pred	Z < -4

The severity grading according to z scores has not been validated. It seems that ATS/ERS grading better correlates with mortality. Z score scale could underestimate the risk of mortality.

Man, 81
Former smoker (50 UPA)
Non allergic
No resp TTT.
Dyspnea NYHA II-III

Reproducibility OK
In pre BD

Not OK for CVF but OK for FEV1 in post BD



Nom de famille		Age et sexe	: 81 ans homme	Poids	: 75.5 kg
Prénom		ID personnel	: 347	IMC	: 23.0 kg/m 2
Profession		Code Patient	:	Groupe ethnique	: Caucasien

FUMEUR Non

INFORMATIONS CLINIQUES
Antécédents: médicaux
Traitement :
Problème : actuel
Coopération : Aucune information
Commentaires:
Opérateur : EndUser

RESULTATS DES TESTS — VALEURS MESUREES — Plage normale (-----) Pré (o) & Post (x) Résultats

Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	plage abs
CV	L		2.68								-
CVF	L	4.03	3.12	77	-1.32	3.81	95	-0.32	*0.69	*22	2.90-5.17
VEF1	L	2.96	1.17	*40	*-3.03	1.63	*55	*-2.33	*0.46	*39	2.04-3.81
VEF1/CV			0.44								-
VEF1/CVF		0.74	0.38	*51	*-3.69	0.43	*58	*-3.25	0.05	14	0.59-0.88
DEP	L/s		2.92			4.13			1.21	41	-
DEM75	L/s		0.75			1.62			0.86	115	-
DEM50	L/s		0.26			0.70			0.44	170	-
DEM25	L/s	0.51	0.18	36	-1.53	0.37	74	-0.45	0.19	106	0.17-1.46
DEMM	L/s	2.05	0.36	*17	*-2.47	0.74	*36	*-1.70	0.38	107	0.77-3.96
TEF	s		12.52			8.95			-3.56	-28	-
EV	L		0.11			0.14			0.03	27	-
CVIF	L		2.75			3.35			0.60	22	-
DIM50	L/s		1.44			1.68			0.24	17	-

Interpretation of spirometry

Utility of FEF 25-75 in adults?

- not to be used for the diagnosis of obstruction.
- Big variability.

Clinical Implications of Having Reduced Mid Forced Expiratory Flow Rates (FEF25-75), Independently of FEV1, in Adult Patients with Asthma.
Riley CM, Wenzel SE, Castro M, Erzurum SC, Chung KF, Fitzpatrick AM, Gaston B, Israel E, Moore WC, Bleecker ER, Calhoun WJ, Jarjour NN, Busse WW, Peters SP, Teague WG, Sorkness R, Holguin F.

- Independantly from a reduced FVC or FEV_1, FEF 25-75 below 32% of predicted gives additional information:
  - more nocturnal symptomes
  - more persistant symptomes
  - more admissions in ICU

Interpretation of spirometry

Utility of FEF 25-75 in adults?
In a sub-group analysis:

- Adults with normal FVC and FEV_1 but reduced FEF25-75, compared to completely normal spirometry have:
  - more nocturnal symptomes
  - more persistant symptomes
  - more admissions in ICU
  - more often serum eosinophilia
  - more often bronchial hyperreactivity

Interpretation of spirometry

Utility of FEF 25-75 in children?

Low FEF 25-75 can precede low FEV_1 and be potentially an early marker of small airways disease.

The utility of forced expiratory flow between 25% and 75% of vital capacity in predicting childhood asthma morbidity and severity.
Devika R. Rao, MD1, Jonathan M. Gaffin, MD, MMSc1, Sachin N. Baxi, MD2, William J. Sheehan, MD2, Elaine B. Hoffman, PhD3, and Wanda Phipatanakul, MD, MS2

In asthmatic children >8y, with normal FEV1 but reduced FEV1/FVC (<85%), the presence also of a reduced FEF 25-75 < 60% is associated with:
- more severe asthma (use of medic, exacerbation,…)
- a better responsiveness to bronchodilator test
- a rise of +30% of the FEF 25-75 identifies 53% more significant response to BD than FEV_1 + 12%.

Interpretation of spirometry

Utility of FEF 25-75 in children?

FEF(25-75) might be a predictive factor for bronchial inflammation and bronchial hyperreactivity in adolescents with allergic rhinitis.
Ciprandi G[1], Tosca MA, Castellazzi AM, Cairello F, Salpietro C, Arrigo T, Miraglia Del Giudice M.

Impaired FEF(25-75) may predict high exhaled nitric oxide values in children with allergic rhinitis and/or asthma.
Ciprandi G[1], Tosca MA, Cirillo I, Lionetti F, Leonardi S, Miraglia Del Giudice M, La Rosa M, Salpietro A, Capasso M, Marseglia GL.

A reduced FEF 25-75 < 65% pred. in asthmatic allergic children is associated with a risk of severe bronchial hyperreactivity (OR4.4) and with high Fe(NO) values (>34PPB)

Interpretation of spirometry

RESPONSIVENESS TO BRONCHODILATOR:

Significant. responsiveness

In adults: △ FEV_1: +200ml and +12%
or △ FVC: +200ml and +12%

In children: △ FEV_1: +12%

Complete responsiveness normalization of FEV_1 and FVC.

Partial responsiveness At least one criteria above present but FVC or FEV_1 or FEV_1/FVC not normalized

RESPONSIVENESS TO BRONCHODILATOR

Additonal remarks:

- After BD, a rise of the FVC can be induced simply by a longer forced expiration time (FET) due to a better technique. It is important to compare the FET before and after BD.
- A gain >= 400ml or >15% of initial FEV1 is highly suggestive of asthma.

Man 30y,
Allergic to trees and grasses.
Occasional dyspnea.
Symbicort 400/12 on demand, not since 1 week.

INFORMATIONS PERSONNELLES

Nom de famille :		Date de naiss.	: 28.04.1982	Taille	: 178 cm
Prénom :		Age et sexe	: 30 ans homme	Poids	: 77.3 kg
Profession :		ID personnel	: 2341	IMC	: 24.4 kg/m 2
		Code Patient	:	Groupe ethnique	: Caucasien

FUMEUR Non

INFORMATIONS CLINIQUES

Antécédents: médicaux — Coopération : Aucune information

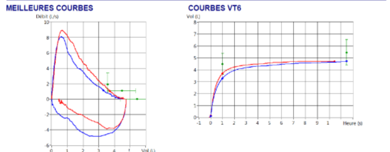
Traitement : Symbicort 400/12 à la demande. Pas depuis 1 sem. — Commentaires:

Problème actuel : — Opérateur : lf

RESULTATS DES TESTS

Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	Plage normale (-----) Pré (o) & Post (x) Résultats -4.0 -2.0 0.0 2.0 4.0	plage abs
CV	L		4.44			4.54			0.10	2		-
CVF	L	5.46	4.56	84	-1.38	4.69	86	-1.18	0.13	3	-+-----------	4.39-6.53
VEF1	L	4.49	3.28	*73	*-2.17	3.69	82	-1.46	*0.40	*12	o x-----------	3.58-5.37
VEF1/CV			0.74			0.81			0.07	10		-
VEF1/CVF		0.83	0.72	87	-1.62	0.79	95	-0.67	0.07	9	o--x---------	0.72-0.92
DEP	L/s		8.11			8.68			0.57	7		-
DEM75	L/s		5.74			7.72			1.98	34		-
DEM50	L/s		2.77			3.91			1.13	41		-
DEM25	L/s	1.90	0.91	*48	*-1.87	1.64	86	-0.40	0.73	80	o----x--------	1.00-3.40
DEMM	L/s	4.56	2.33	*51	*-2.20	3.45	76	-1.00	1.12	48	o --x---------	2.82-6.70
TEF	s		11.47			10.45			-1.02	-9		-
EV	L		0.11			0.14			0.03	32		-
CVIF	L		4.76			4.30			-0.46	-10		-
DIM50	L/s		3.40			2.65			-0.75	-22		-

MEILLEURES COURBES **COURBES VT6**



Woman, 34y
No resp symptomes.
Scleroderma with limited cutaneous Extension,
Scl70 positive

INFORMATIONS PERSONNELLES

Nom de famille	:	Date de naiss.	: 14.09.1975	Taille	: 168 cm
Prénom	:	Age et sexe	: 34 ans femme	Poids	: 69.0 kg
		ID personnel	: 6595	IMC	: 24.4 kg/m 2
Profession	: femme au foyer	Code Patient	:	Groupe ethnique	: Caucasien

FUMEUR Non

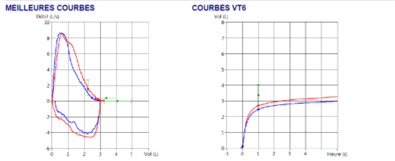
INFORMATIONS CLINIQUES

Antécédents: médicaux
Traitement :
Problème : actuel
Coopération : Aucune information
Commentaires:
Opérateur : LF

RESULTATS DES TESTS

Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	Plage normale (-----) Pré (o) & Post (x) Résultats	plage abs
CV	L		2.88			3.23			0.35	12		-
CVF	L	4.05	2.95	*73	*-2.27	3.23	*80	*-1.68	0.28	10	o x------------	3.24-4.90
VEF1	L	3.36	2.46	*73	*-2.21	2.70	80	-1.62	0.24	10	o x------------	2.69-4.01
VEF1/CV			0.86			0.84			-0.02	-2		-
VEF1/CVF		0.83	0.84	100	0.00	0.84	100	0.05	0.00	0	------*------	0.72-0.93
DEP	L/s		8.39			8.46			0.07	1		-
DEM75	L/s		8.44			8.12			-0.32	-4		-
DEM50	L/s		3.52			5.86			2.34	67		-
DEM25	L/s	1.50	1.02	68	-0.95	1.61	107	0.19	0.59	57	--o----x-----	0.75-2.71
DEMM	L/s	3.56	2.81	79	-0.90	4.19	118	0.69	1.37	49	---o-----x---	2.25-5.12
TEF	s		8.72			10.60			1.88	22		-
EV	L		0.09			0.14			0.05	62		-
CVIF	L		2.79			2.97			0.18	6		-
DIM50	L/s		3.37			3.78			0.41	12		-

MEILLEURES COURBES **COURBES VT6**



Interpretation of spirometry

Restrictive pattern

Suggested by a proportional diminution of FEV1, FVC and VC under LLN and by a FEV_1/FVC >HLN (or >110%).
Flow/vol curve with normal but reduced shape.

Confirmed only by plethysmography if CPT < LLN (P5).

Mixed obstructive-restrictive pattern

Def: FEV_1/VC or FEV1/FVC < LLN (p5) and CPT < LLN (p5)

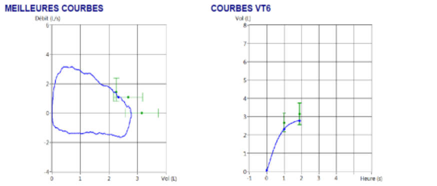
Where is the problem ?

Boy, 12 years,
155 cm, 66 Kg,
BMI 23.3.
Mild chronic rhinitis with house dust mite sensitization

RESULTATS DES TESTS

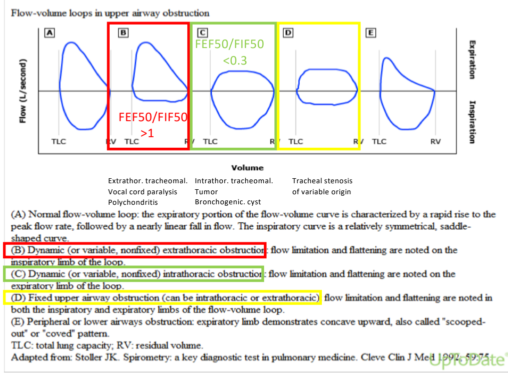
Abr.	Unité	Réf. valeur GLI2012	test PRE abs	test PRE %réf.	test PRE score z	test POST abs	test POST %réf.	test POST score z	Différence abs	Différence %pré	Plage normale (-----) Pré (o) & Post (x) Résultats	plage abs
CV	L		3.01									-
CVF	L	3.15	2.76	88	-1.07						--o----------	2.56-3.74
VEF1	L	2.67	2.32	87	-1.13						--o----------	2.16-3.18
VEF1/CV			0.77									-
VEF1/CVF		0.86	0.84	98	-0.25						-----o------	0.75-0.94
DEP	L/s		3.26									-
DEM75	L/s		3.15									-
DEM50	L/s		2.61									-
DEM25	L/s	1.44	1.64	113	0.39						--------o----	0.79-2.40
DEMM	L/s	3.04	2.34	77	-1.10						--o----------	2.02-4.26
TEF	s		1.89									-
EV	L		0.07									-
CVIF	L		2.77									-
DIM50	L/s		1.32									-

MEILLEURES COURBES **COURBES VT6**



Interpretation of spirometry

Upper airways obstruction patterns:

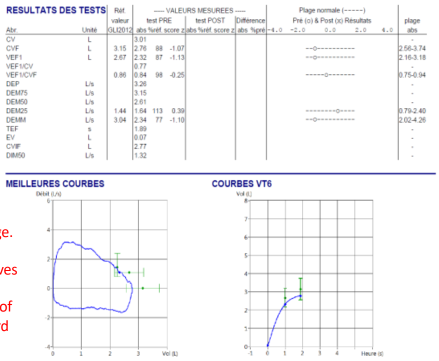


(A) Normal flow-volume loop: the expiratory portion of the flow-volume curve is characterized by a rapid rise to the peak flow rate, followed by a nearly linear fall in flow. The inspiratory curve is a relatively symmetrical, saddle-shaped curve.
(B) Dynamic (or variable, nonfixed) extrathoracic obstruction: flow limitation and flattening are noted on the inspiratory limb of the loop.
(C) Dynamic (or variable, nonfixed) intrathoracic obstruction: flow limitation and flattening are noted on the expiratory limb of the loop.
(D) Fixed upper airway obstruction (can be intrathoracic or extrathoracic): flow limitation and flattening are noted in both the inspiratory and expiratory limbs of the flow-volume loop.
(E) Peripheral or lower airways obstruction: expiratory limb demonstrates concave upward, also called "scooped-out" or "coved" pattern.
TLC: total lung capacity; RV: residual volume.
Adapted from: Stoller JK. Spirometry: a key diagnostic test in pulmonary medicine. Cleve Clin J Med 1992; 59:75.

Where is the problem ?

Boy, 12 years, 155 cm, 66 Kg, BMI 23.3. House dust mite sensitization

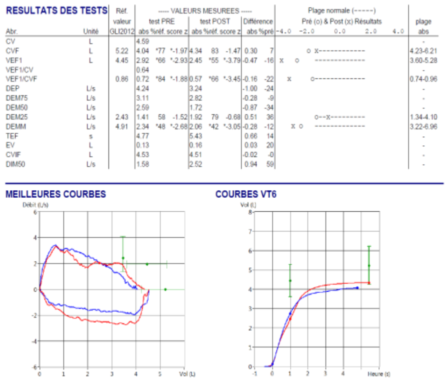
S/P op cerebral trunk tumor at 4 months of age. Sequellae: Partial palsy of cran.nerves 9, 10, 11 with open rhinolalia, hemiatrophy of tongue, partial vocal cord palsy. Diaphragm ?



FEF 50 /FIF 50 : 1,9 (N<=1)

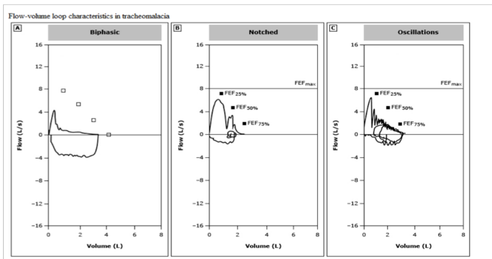
Same guy, age 19, 175 cm, 99.3 Kg, BMI 32.4. Allergy. to HDM, grass, trees.
Mild rhinitis,
Rare asthma.
No sport.

Fe(NO) 25 PPB



Interpretation of spirometry

Patterns of tracheo-bronchomalacia (variable intrathoracic obstr.)

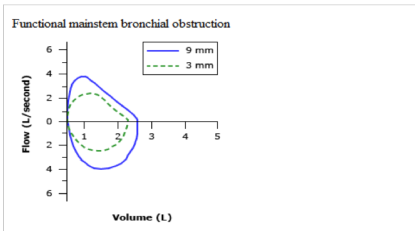


(A) Flow-volume loop in a patient with tracheomalacia demonstrating biphasic morphology with typical obstructive pattern.
(B) A notched expiratory loop in a different patient is shown.
(C) Expiratory oscillations from a third patient are shown.
FEF: forced expiratory flow.
Reproduced with permission of the American Association for Respiratory Care, from: Majid A, Sosa AF, Ernst A, et al. Pulmonary function and flow-volume loop patterns in patients with tracheobronchomalacia. Respir Care 2013; 58:1521; permission conveyed through Copyright Clearance Center, Inc. Copyright © 2013.

UpToDate

Interpretation of spirometry

Patterns of unilateral mainstem bronchial obstruction



Maximal expiratory and inspiratory flow-volume loops before (inner dashed-line loop) and after (outer solid-line loop) surgery in a patient with mainstem bronchial obstruction. The diameter of the orifice at the site of maximal obstruction both before and after treatment is shown in relation to the corresponding flow-volume loop. Note the relatively parallel rightward shift of the descending limb of the maximal expiratory flow-volume curve after treatment.

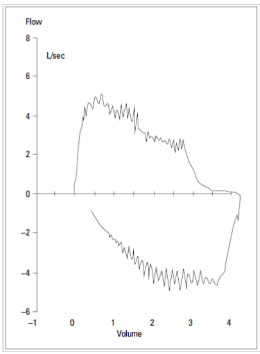
UpToDate

Interpretation of spirometry

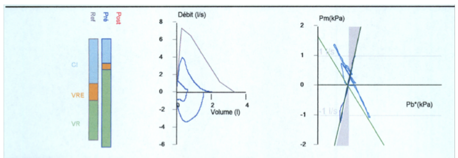
Sawtooth pattern:

Can be seen in:

- neuromuscular diseases
- Parkinson disease
- laryngeal dyskinesia.
- pedunculated tumors of the upper airway
- tracheobronchomalacia.
- upper airway burns
- obstructive sleep apnea



Man 63 y,
asthma and
bronchiectasis



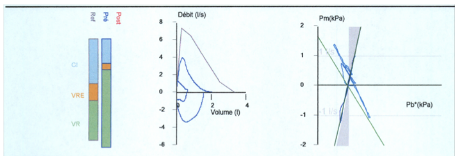
SPIROMETRIE	Paramètre	Unité	Ref	Pré	%Ref	ZScore
	FEV1	l	2,81	1,53	54	
	FVC	l	3,60	2,07	58	
	FEV1/FVC	%	78	74		
	FEV1/VC	%	78	74		
	DEP	l/s	7,39	3,98	54	
	DEM25	l/s	1,25	0,32	26	
	DEM50	l/s	3,84	1,26	33	
	DEM75	l/s	6,55	3,54	54	
	DEM 25-75	l/s	3,13	0,93	30	
	tex	s		8,9		

Is this a restrictive syndrome ?

Lung volumes

(no GLI reference values)

Man 63 y,
asthma and
bronchiectasis



SPIROMETRIE	Paramètre	Unité	Ref	Pré	%Ref	ZScore
	FEV1	l	2,81	1,53	54	
	FVC	l	3,60	2,07	58	
	FEV1/FVC	%	78	74		
	FEV1/VC	%	78	74		
	DEP	l/s	7,39	3,98	54	
	DEM25	l/s	1,25	0,32	26	
	DEM50	l/s	3,84	1,26	33	
	DEM75	l/s	6,55	3,54	54	
	DEM 25-75	l/s	3,13	0,93	30	
	tex	s		8,9		

VOLUMES	Paramètre	Unité	Ref	Pré	%Ref	ZScore
	CV	l	3,47	2,07	60	
	CI	l	2,59	1,55	60	
	FRC	l	3,27	4,88	149	
	TLC	l	5,86	6,29	107	
	RV	l	2,28	4,51	198	
	RV/TLC	%	39	72	186	

Lung volumes

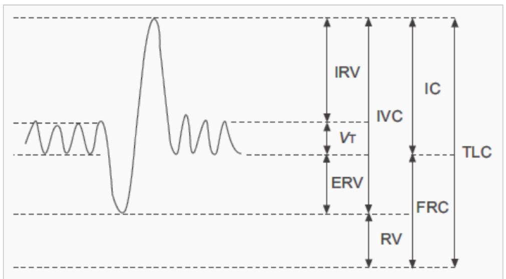
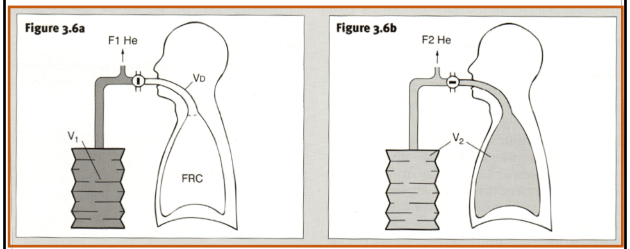


FIGURE 1. Static lung volumes and capacities based on a volume–time spirogram of an inspiratory vital capacity (IVC). IRV: inspiratory reserve volume; *V*T: tidal volume (TV); ERV: expiratory reserve volume; RV: residual volume; IC: inspiratory capacity; FRC: functional residual capacity; TLC: total lung capacity.

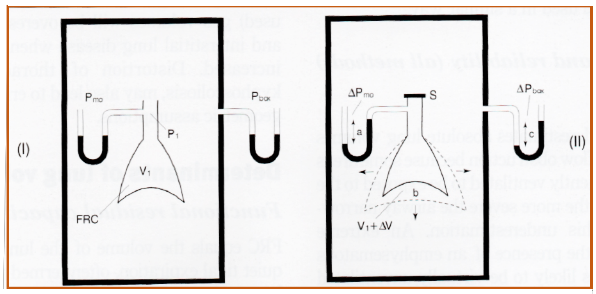
Volumes : dilution (He)



Measurement of the FRC

From JMB Hugues and Pride Lung Fonction Tests (2000)

Volumes : plethysmography



Measurement of the FRC derived from Boyle's law : $V1\Delta P = P1\Delta V$

From JMB Hugues and Pride Lung Fonction Tests (2000)

Measured volumes

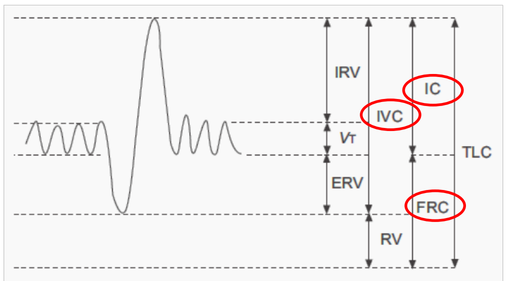
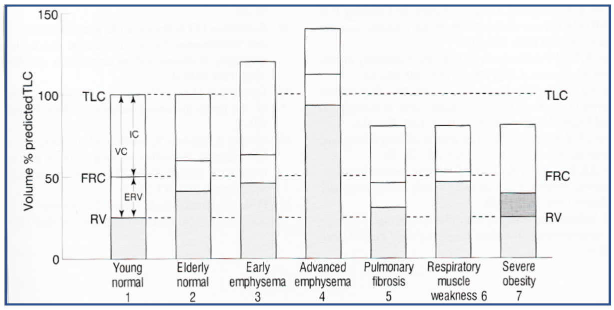


FIGURE 1. Static lung volumes and capacities based on a volume–time spirogram of an inspiratory vital capacity (IVC). IRV: inspiratory reserve volume; *V*T: tidal volume (TV); ERV: expiratory reserve volume; RV: residual volume; IC: inspiratory capacity; FRC: functional residual capacity; TLC: total lung capacity.

Measured volumes



- Restrictive syndrome : TLC < 5th percentile or < 80% predicted value
- Air trapping : RV/TLC > 130%
- Hyperinflation : FRC > 120-130% of predicted value except if TLC is harmoniously increased

Causes of reduced TLC

- **Intrapulmonary**
  - Pneumonectomy
  - Collapsed lung
  - Consolidation
  - Oedema
  - fibrosis

From JMB Hugues and Pride Lung Fonction Tests (2000)

Causes of reduced TLC

- **Extrapulmonary**
  - Pleural disease (effusion, PNO)
  - Rib cage deformity
  - Respiratory muscle weakness
  - Gross abdominal enlargement
  - Severe obesity

From JMB Hugues and Pride Lung Fonction Tests (2000)

Causes of increased RV

- **Intrapulmonary**
  - Generalized airway obstruction
  - Pulmonary vascular congestion
  - Mitral stenosis
- **Extrapulmonary**
  - Expiratory muscle weakness (myopathies, etc)

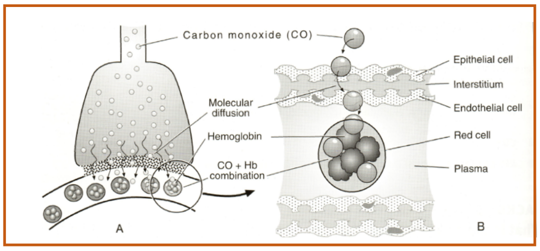
From JMB Hugues and Pride Lung Fonction Tests (2000)

Diffusion

Diffusion

- Diffusing capacity for CO = D_LCO (US)
  Transfer factor for CO = T_LCO (Europe)
- Unique non-invasive window on pulmonary microcirculation

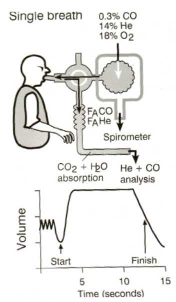
Diffusion
Alveolar—capillary transfer of carbon monoxide (CO)



The T_LCO measures the rate of transfer of CO from the alveoli to the blood.
CO has a very high affinity for Hb
Transfer of CO only limited by diffusion

From JMB Hugues and Pride Lung Fonction Tests (2000)

Diffusion
Single breath DLCO/TLCO measurement



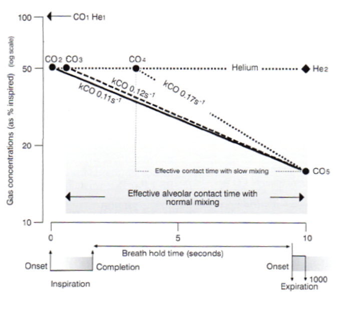
Gas mixture : CO (diffusion)
CH_4 or He (inert gas)
O_2 and N_2

The patient exhales then takes a rapid (<3s) and full inspiration (VC). Breath is held for 10s then a full exhalation is made

CO and CH4 measurements performed following the first 750 ml of exhaled gas

From JMB Hugues and Pride Lung Fonction Tests (2000)

Diffusion
Alveolar—capillary transfer of carbon monoxide (CO)



- $VA = V_I \times \frac{F_I He}{F_A He}$
- $kCO = \frac{\log_e(FACO2/FACO5)}{t}$
- $T_L CO = \frac{V_A \times kCO}{P_b - PH_{2O}}$

VA = alveolar volume

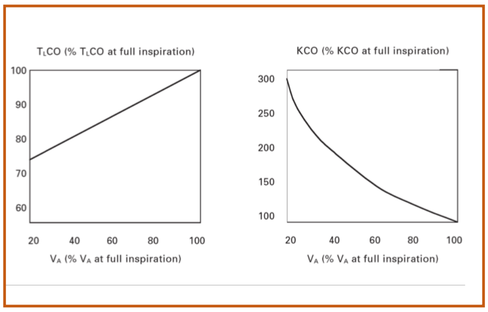
V_I=inspired volume

kCO = rate constant for alv-cap. CO transfer

Pb=barometric pressure (driving pression for diffusion)

From JMB Hugues and Pride Lung Fonction Tests (2000)

Diffusion
Determinants of single breath DLCO in normal subjects



KCO = CO transfer coefficient = kCO/(P_b-P_{H2O}) => KCO = T_LCO/VA
mmol CO x min^{-1} x kPa^{-1} x L^{-1}

Diffusion
Determinants of single breath DLCO in normal subjects

Components of T_LCO :

- *membrane conductance* (D_M) = diffusion component
- *reactive conductance* ($\theta \times Q_c$) = rate of CO with Hb

θ = rate of reaction of CO with Hb
Q_c= blood volume in the pulmonary capillaries

Diffusion
Determinants of single breath DLCO in normal subjects

- θ is decreased in anemia
  => T_LCO should be corrected for Hb
- Altitude : competition between O_2 and CO for Hb (↑θ)
  => 0.31% increase of T_LCO per mmHg decrease of PO_2
- H_bCO decreases T_LCO (↓1%T_LCO per ↑1%H_bCO)
  => no smoking 24h before the measurement…
- O2 supply decreases T_LCO
  => 0.35% decrease of T_LCO per mmHg increase of PO_2

Diffusion
Normal values

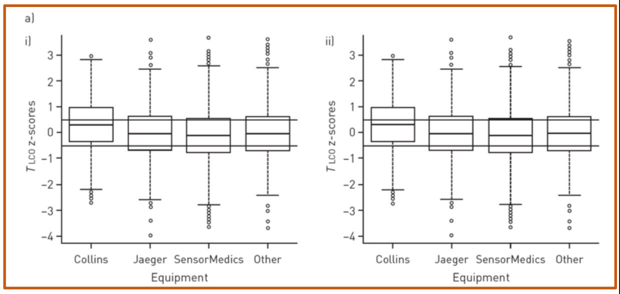
Official ERS technical standards: Global Lung Function Initiative reference values for the carbon monoxide transfer factor for Caucasians

Sanja Stanojevic[1,2], Brian L. Graham[3], Brendan G. Cooper[4], Bruce R. Thompson[5], Kim W. Carter[6,7], Richard W. Francis[6,7] and Graham L. Hall[7,8,9] on behalf of the Global Lung Function Initiative *T*LCO working group[10]

Eur Respir J 2017; 50: 1-13

- 12660 TLCO measurements from asymptomatic, lifetime nonsmokers (85% Caucasians 5-85 y)
- Uncorrected for Hb concentration.
- Adjustments for elevation above sea level

Diffusion
Normal values : differences between equipments



Diffusion
Normal values : differences between studies

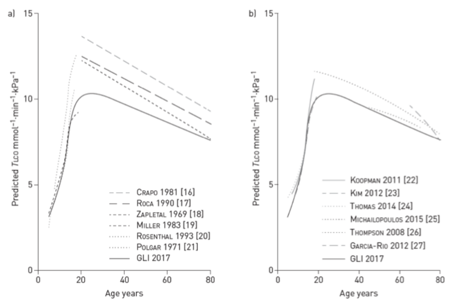
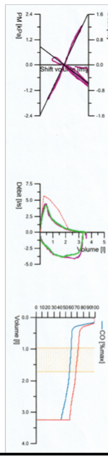


FIGURE 4 Comparison of transfer factor of the lung for carbon monoxide (*T*LCO) reference equations to the current Global Lung Function Initiative (GLI) equations. Equations found in a) most commercially available equipment and b) more recently published studies.

Female 65 y,
Ex-smoker,
Primary sclerosing cholangitis,
severe dyspnea



Volumes pulmonaire	Unité		Théor.	Pre	%Pred.
CVL	l	(1)	2.49	3.65	147%
CI	l	(3)	2.11	2.31	110%
TLC	l	(1)	4.70	6.80	145%
FRC	l	(1)	2.62	4.49	171%
RV	l	(1)	1.89	3.15	167%
RV/TLC	%	(1)	40	46	116%
RVA	kPa/(l/s)	(1)	0.30	0.37	125%
sGaw	1/(kPa*s)	(36)	1.64	0.56	34%

Spirométrie	Unité		Théor.	Pre	%Pred.	Z Score	Ventolin (4 bouffées)	%Pred.	Z Score	%Change
FEV1	l	(35)	2.30	1.80	78%	-1.44	1.86	81%	-1.25	+3.7%
VEM6	l	(15)	2.93	3.10	106%		3.18	108%		+2.4%
FVC	l	(35)	2.92	3.61	124%	1.49	3.66	125%	1.59	+1.3%
FEV1/FVC	%	(35)	79	50	63%	-3.43	51	64%	-3.32	+2.4%
FEV1/VC	%	(1)	77	49	64%	-4.30	51	66%	-4.04	+3.5%
DEM25-75	l/s	(35)	2.08	0.57	28%	-2.67	0.61	29%	-2.56	+7.0%
DEM/DIM50				0.20			0.21			+7.2%
DEP	l/s	(1)	5.75	4.57	80%	-1.30	4.67	81%	-1.20	+2.1%
VMM	l/min	(3)	85.8							

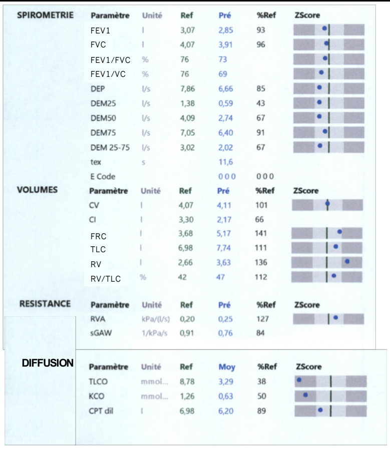
DIFFUSION	Unité		Théor.	Pre	%Pred.	Z Score
DLCO	mmol/kPa/min	(42)	6.38	1.75	27%	
DL corr.	mmol/kPa/min	(42)	6.38	1.74	27%	
KCO	mmol/kPa/min/l	(42)	1.43	0.37	26%	-6.84
KCO corr.	mmol/kPa/min/l	(42)	1.43	0.37	26%	-6.87
VA	l	(42)	4.50	4.74	105%	0.40
CVI	l	(1)	2.49	3.68	148%	2.82
Hb	g/l			137.0		

Main pathological profiles of diffusion capacity

Condition	VA	KCO	DLCO	Examples
Incomplete expansion	↓↓↓	↑↑	↓	Pleural, skeletal, neuromuscular diseases, obesity
Localized loss of unit	↓↓↓	↑	↓↓	Resection, atelectasis
Diffuse loss of unit	↓↓	↓	↓↓↓	Fibrosis
Emphysema	↓	↓↓	↓↓↓	COPD
Pulmonary vascular disease	Normal	↓↓	↓↓	PAH, chronic thromboembolic disease, vasculitis, sickle cell anemia, hepatopulmonary syndrome
High blood flow	Normal	↑	↑	High cardiac output, left-right shunt
Alveolar hemorrhage	↓	↑↑↑	↑↑	Anti-GBM disease, vasculitis, SLE

A. Pasche and J.-W. Fitting. Swiss Medical Forum 2012;12:525

Man 72 y,
Sclerodermia
Ex-smoker



SPIROMETRIE	Paramètre	Unité	Ref	Pré	%Ref	ZScore
	FEV1	l	3,07	2,85	93	
	FVC	l	4,07	3,91	96	
	FEV1/FVC	%	76	73		
	FEV1/VC	%	76	69		
	DEP	l/s	7,86	6,66	85	
	DEM25	l/s	1,38	0,59	43	
	DEM50	l/s	4,09	2,74	67	
	DEM75	l/s	7,05	6,40	91	
	DEM 25-75	l/s	3,02	2,02	67	
	tex	s		11,6		
	E Code			0 0 0	0 0 0	

VOLUMES	Paramètre	Unité	Ref	Pré	%Ref	ZScore
	CV	l	4,07	4,11	101	
	CI	l	3,30	2,17	66	
	FRC	l	3,68	5,17	141	
	TLC	l	6,98	7,74	111	
	RV	l	2,66	3,63	136	
	RV/TLC	%	42	47	112	

RESISTANCE	Paramètre	Unité	Ref	Pré	%Ref	ZScore
	RVA	kPa/(l/s)	0,20	0,25	127	
	sGAW	1/kPa/s	0,91	0,76	84	

DIFFUSION	Paramètre	Unité	Ref	Moy	%Ref	ZScore
	TLCO	mmol...	8,78	3,29	38	
	KCO	mmol...	1,26	0,63	50	
	CPT dil	l	6,98	6,20	89