¹³C-Aminopyrine Breath Test

¹³ C-Aminopyrine		
H ₃ ¹³ CH ₃ O N N N N N N N N N N N N N N N N N N	Molecular weight: Enrichment: Labeled C-atoms: Dosage:	233.29 g/mol 99 % 2 75 mg

Metabolism

¹³C-Aminopyrine undergoes a two-step N-demethylation by cytochrome P-450 monooxygenases including CYP2C19, CYP1A2 and CYP3A4, yielding formaldehyde and amino-antipyrine¹. The formaldehyde is further oxidized to bicarbonate and exhaled as ¹³CO₂, or deposited in the bicarbonate pool². As N-demethylation occurs exclusively in the liver with a low extraction rate, aminopyrine metabolism reflects the efficiency of aminopyrine metabolism³. It is therefore a good measure of hepatic metabolic capacity, i.e. the "functional hepatic mass".

Applications of ¹³C-Aminopyrine Breath Test

The ¹³C-Aminopyrine Breath Test is very useful for quantitative assessment of liver function in conditions such as established chronic hepatitis and cirrhosis^{4,5}. It can be used for example in Hepatitis C patients to quantify progression of the disease⁶.

The patient should have fasted for 8 hours prior to the test. Smoking should also be avoided at least one hour prior to the test ⁷. The patient should not drink carbonated water or soft drinks prior to the test since that might interfere with the results. In addition, oxygen supplementation should be avoided because increased oxygen content in exhaled breath can influence ¹³CO₂ measurement by NDIRS ⁸.

Test Performance Procedure (see IRIS® Operating Manual for additional information).

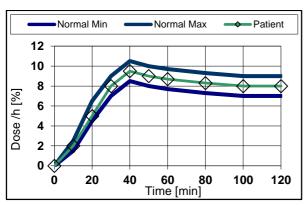
- 1. Collect zero (basal) breath sample as described in manual.
- 2. Patient takes ¹³C-Aminopyrine (75 mg) dissolved in warm water (100 ml).
- 3. Collect additional breath samples as shown below (Table 1).
- 4. Analyze all 10 breath samples with IRIS®-3.

#1 Bag	#2 Bag	#3 Bag	#4 Bag	#5 Bag	#6 Bag	#7 Bag	#8 Bag	#9 Bag	#10 Bag
0 min	10 min	20 min	30 min	40 min	50 min	60 min	80 min	100 min	120 min

Table 1: ¹³C-Aminopyrine Breath Test Sample Collection

Results and interpretation

Typical results for the ¹³C-Aminopyrine Breath Test are presented in Figures 1 to 4. The ¹³C-Aminopyrine test is very sensitive and precise, as can be seen from the very narrow "normal" range. This makes it possible to detect even patients with early stage liver disease ^{6,9,10}.



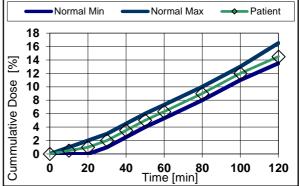
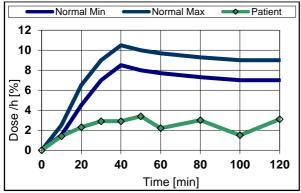


Fig. 1,2: ¹³C-Aminopyrine Breath Test, Dose/h curve and % Cum Dose curve, healthy (normal) subject ¹¹



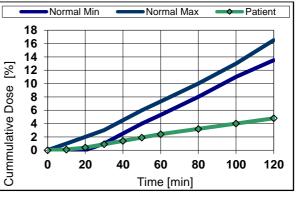


Fig. 3,4: ¹³C-Aminopyrine Breath Test, Dose/h curve and % Cum Dose curve, subject with liver disease ¹¹

For the ¹³C-Aminopyrine Breath Test, cut-off values have been established in a study with 135 patients ¹¹ (see table below).

(555 15615 1575 177							
Condition	dose/hr (‰) at 30 min	% cum. dose at 120 min					
Fibrosis stages 0/1/2	6.62 - 7.10 ± 2.9	9.21 - 10.06 ± 3.8					
Fibrosis stages 3 / 4	2.48 - 3.13 ± 1.2	3.62 - 4.56 ± 2.0					
Cirrhosis, not established	6.77 ± 2.7	9.63 ± 3.6					
Cirrhosis, established	2.48 ± 1.2	3.68 ± 1.9					

Table 2: Cut-off values for ¹³C-Aminopyrine Breath Test ¹¹

References

- 1. Armuzzi, A. et al. Review article: breath testing for human liver function assessment. Aliment. Pharmacol. Ther. 16, 1977–1996 (2002)
- 2. Perri, F., Pastore, M., Annese, V. & Andriulli, A. The aminopyrine breath test. Ital J Gastroenterol 26, 306-317 (1994).
- 3. Nista, E. C. et al. 13C-breath tests in the study of microsomal liver function. Eur Rev Med Pharmacol Sci 8, 33-46 (2004).
- 4. Morelli, A., Narducci, F., Pelli, M. A., Farroni, F. & Vedovelli, A. The relationship between aminopyrine breath test and severity of liver disease in cirrhosis. *Am. J. Gastroenterol.* **76**, 110–113 (1981).
- Giannini, E. et al. 13C-aminopyrine breath test to evaluate severity of disease in patients with chronic hepatitis C virus infection. Aliment. Pharmacol. Ther. 16, 717–725 (2002).
- 6. Rocco, A. *et al.* 13C-aminopyrine breath test accurately predicts long-term outcome of chronic hepatitis C. *J. Hepatol.* **56**, 782–787 (2012).
- 7. Kasicka-Jonderko, A., Loska, D., Jonderko, K., Kaminska, M. & Błonska-Fajfrowska, B. Interference of acute cigarette smoking with [¹³C]methacetin breath test. *Isotopes Environ Health Stud* **47**, 34–41 (2011).
- 8. Riecke, B., Neuhaus, P. & Stockmann, M. Major influence of oxygen supply on 13CO2:12CO2 ratio measurement by nondispersive isotope-selective infrared spectroscopy. *Helicobacter* **10**, 620–622 (2005).
- 9. Merkel, C. et al. Aminopyrine breath test in the prognostic evaluation of patients with cirrhosis. Gut 33, 836–842 (1992).
- 10. Urbain, D., Muls, V., Thys, O. & Ham, H. R. Aminopyrine breath test improves long-term prognostic evaluation in patients with alcoholic cirrhosis in Child classes A and B. *J. Hepatol.* **22**, 179–183 (1995).
- 11. Merz, B. Evaluierung des Aminopyrin-Atemtests bei chronischer Hepatitis C. Hepatologie und Infektiologie, (2005).

