LEO AMBARD (1876-1962): THE START OF MEASURED RENAL FUNCTION BY THE URÉO-SECRETOIRE CONSTANTE AT THE UNIVERSITY OF PARIS #865-MP

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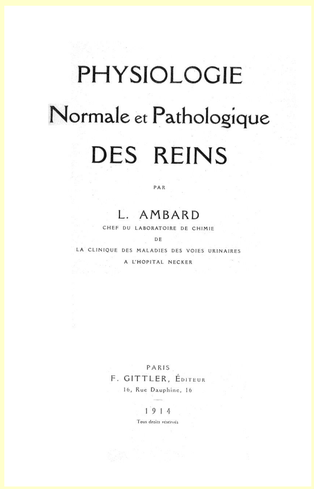
Ambard's life

1876	Born on February 12, in Marseille
1898-1905	Studies at the Medical Faculty of la Sorbonne in Paris: External fellow in 1898, Internal fellow in 1901, MD 1905
1905-1911	assistant to Professor Edward Enriquez (1865-1928) at la Pitié
1911-1914	Chief of the Laboratory of Urology at Necker Hospital at request of Félix Legueu Studies on urea excretion by the kidneys
1914	First edition of Physiologie Normale et Pathologique des Reins
1919	Chair of Phamacodynamics and Experimental Medicine at the University of Strasbourg, which in 1922 was renamed as Chair of Pharmacology and Experimental Medicine
1930	Chair of Medicine B at the University of Strasbourg, as successor of Leon Blum
1930	Correspondent member of the Academy of Medicine in Paris
1939	1st of September the University is moved into the Sanatorium of Clairvivre at Clermont-Ferrand a unique place of French Resistance
1945	1st of October back to the Chair of Medicine B at the University of Strasbourg
1947	Retirement from the university, starts studies on ultrafiltration
1961	L. Ambard and S. Trautman publish Ultrafiltration
1962	Death in Paris on May 19
1970	Henri Jahn (1923-1994)—a fellow of Jules Stahl— becomes Director of the Service of Nephrology and Hemodialysis in Medicine B and in 1971 Full Professor of Nephrology
1987	Henri Jahn and Shaul Massry start the Conférence and the Médaille Léo Ambard. Massry was the first recipient

Léo Ambard



From threshold substances to Ambard's coefficient

Ambard had specialized in renal physiology in order to distinguish between threshold and non-treshold substances. For him non-threshold substances are continually excreted in urine as long as they are present in blood (urea, sulphate).
Threshold substances below a definite and constant blood level, which is specific for each substance, do not appear in urine. The most known substance, sis glucose, was primarily identified by Claude Bernard, who did not speak of threshold and non-threshold substances. This slang was started by Magnus years later. Also chloride is threshold substance, but its threshold is lower than blood concentration. Threshold for Ambard was an entity comparable to the height of a dam. With this expertise he started to experiment on urea.

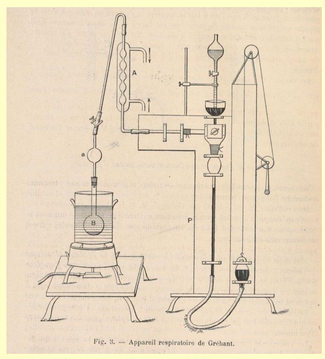


Fig. 3. — Appareil respiratoire de Gréhant.

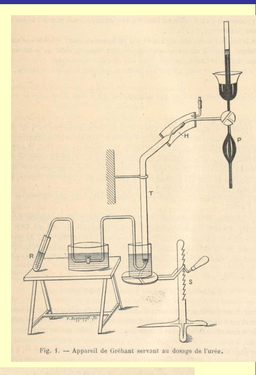


Fig. 1. — Appareil de Gréhant servant au dosage de l'urée.

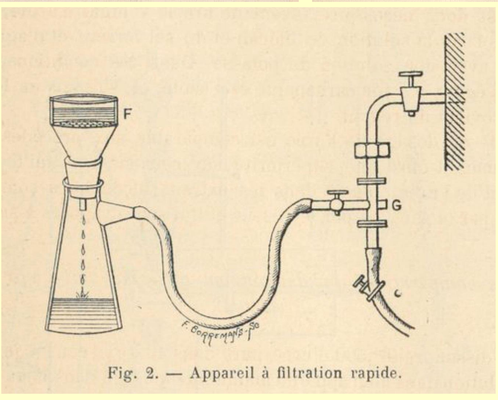


Fig. 2. — Appareil à filtration rapide.

The laws of urea excretion

Ambard's Laws of Kidney Function

1st. "When The kidney is secreting urea at constant concentration, the output varies directly as the square of the concentration of urea in the blood".
1 subject, water intake allowed to keep urea concentration in urine constant, measure of urine output and blood concentration.

$$\frac{U_R}{\sqrt{D}} = K$$

Ur Urea in blood (g/L)
D Urea in urine (g/24 h)
K 0.07±0.01

Urea is given in g/24 hours however its collection lasts less, usually 2 hours
Corrected for body weight

Ambard's Laws of Kidney Function

2nd. "When with a constant concentration of urea in the blood, the subject excretes urea at variable concentration, the output of urea is inversely proportional to the square root of the concentration of urea in urine."

$$\frac{D}{D'} = \frac{\sqrt{C'}}{\sqrt{C}}$$

2 persons, urea constant, C is Urea (g/L) in urine

Ambard's Laws of Kidney Function

3rd. "When all 3 factors , blood urea, output and concentration vary, the output of urea varies in direct proportion to the square of the blood urea, and inversely proportionally to the square root of the concentration of urea in urine".

$$\frac{U_R}{\sqrt{D \cdot \frac{\sqrt{C}}{\sqrt{25}}}} = K \qquad \frac{U_R}{\sqrt{D \cdot \frac{70}{BW} \cdot \frac{\sqrt{C}}{5}}} = K$$

Ur Urea (g/L of plasma)
D Urea (g/24h in urine)
C Urea (g/L urine)
25 Standard concentration of urea in urine
K 0.07± 0.01 (in normal persons)

By correcting for body weight

For threshold substances instead of Ur he used the excess of threshold (the factor driving excretion in urine)

$$\frac{E}{\sqrt{D \cdot \frac{70}{BW} \cdot \frac{\sqrt{C}}{\sqrt{C'}}}} = K$$

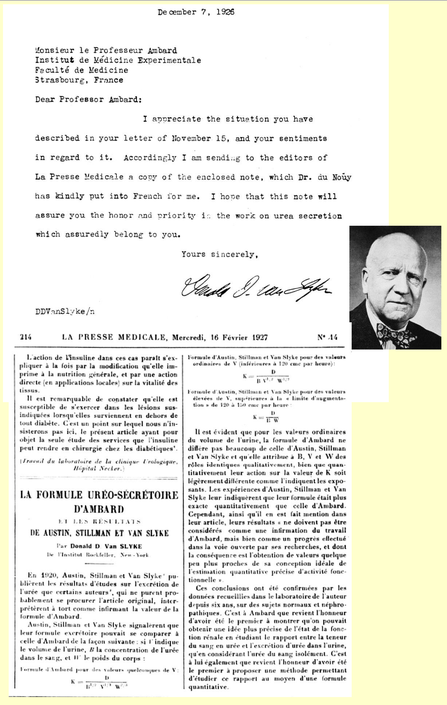
Where
E Excess over the threshold
D g/24 h in urine
W kg body weight
C g/L in urine
C' standard urine concentration isotonic with standard urine concentration of 25 g/L

The destiny of Ambard's coefficient

Austin, Stillman and Van Slyke (46) emphasized the fact that in studies devised to assessing functional capacity of the kidney, urea excretion rate by has been introduced as criterion.
"Ambard and his collaborators (Ambard 1910, 1920), Ambard and Papin (1909), Ambard and Weill (1912), whose work has inspired many investigations including our own".
They have proposed and identified 2 factors. One is represented by urea concentration in plasma, the other was identified in the urea concentration in urine. Ambard held that the excretion rate of urea increases as the square root of the blood urea concentration , i.e. doubling the blood urea quadruples the excretion rate. In that work the first law of Ambard was confirmed. In addition, they developed a new formula which resembled that of Ambard claiming "for greater accuracy than that originally conceived by Ambard". "If this belief is confirmed, the present work is to be regarded not as a disproof of Ambard's, but rather as an accurate advance which has proceeded along the path opened by his researches, and which has resulted in a somewhat closer approximation to his ideal of accurate functional measurement"

Addis T and Watanabe CK.
The rate of urea excretion.
Criticism of Ambard and Weill's laws of urea excretion.
J Biol Chem 1916; 24: 203-220

"The approximate constancy of the combined formula which after all is roughly approximate, is due in part to the tendency for increased urea concentration in the blood to be accompanied by increased rate of urea excretion. But in large part is to be ascribed to its mathematical construction. The more variable factors—the concentration in the urine, the volume of urineand the amount of urea in the urine occur as the square or the fourth roots of their values. Their disturbing effect on the constancy of the resultant of the formula is thus greatly reduced, while the only factor used without such modifications—the concentration in the blood—is itself the most constant quantity used".



December 7, 1926

Monsieur le Professeur Ambard
Institut de Médicine Experimentale
Faculté de Medicine
Strasbourg, France

Dear Professor Ambard:

I appreciate the situation you have described in your letter of November 15, and your sentiments in regard to it. Accordingly I am sending to the editors of La Presse Medicale a copy of the enclosed note, which Dr. du Noüy has kindly put into French for me. I hope that this note will assure you the honor and priority in the work on urea secretion which assuredly belong to you.

Yours sincerely,

DDVanSlyke/n

214 LA PRESSE MEDICALE, Mercredi, 16 Février 1927 N° 14

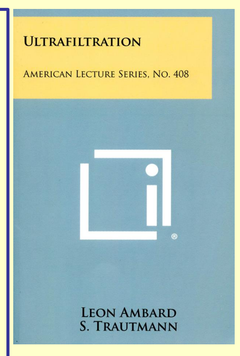
LA FORMULE URÉO-SÉCRÉTOIRE D'AMBARD
ET LES RÉSULTATS
DE AUSTIN, STILLMAN ET VAN SLYKE
Par Donald D Van SLYKE
De l'Institut Rockfeller, New-York

Preface of Professor Félix Legueu to Léo Ambard's *Physiologie normale et pathologique des reins*. 1914, pp.332

"There was no need of a preface, but it gives me the privilege to attest my high esteem and the appreciation for his collaboration and to explain the reasons for which I have asked him to write this book.
After Ambard took the direction of the Laboratory of the Division of Urology , works of high originality have been delivered by his brainy activity. By studying the concentration of urea in blood and urine he discovered that urea excretion occurs following precise mathematical rules and that a constant number represents this physiological ratio.
From the practical point of view the excretory coefficients for urea and chloride are used for studying renal function at Necker Hospital, and represent a rigorous precise method, more accurate than any other, to understand the functional state of the kidneys.
For this work Academy of Science has assigned to Mr. Ambard one of the six Montoya prices and award, the highest sign of distinction which in our country crowns scientific research.
On my arrival at Necker I have asked Mr. Ambard to give a course on physiological and pathological function of the kidneys, two times a year for the fellows of the clinic and for those joining our group to study the complexity of the kidney function. For their interest I asked him to vulgarize those seminars for a larger audience and give him the possibility to explain his vision and ideas about normal and pathological function of the kidneys. "
January 30, 1914

The last book

Ultrafiltration is the last book by Ambard and Trautman, indicating that he continued to work till the end of life. One can say that the data, the work done before getting the chair in Strasbourg, may be considered a paradigm. He used his knowledge on threshold and non-threshold substances in order to develop a tool capable of allowing the renal prognosis of patients undergoing surgery for urological problems. His findings were highly original and opened a field. He was able to put scientists from all over the world to work . His experiments were repeated, discussed and of course acquired a new light.



54 ERA
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History of nephrology
Natale De Santo
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