# Alberto C. Taquini and the 'links' that led to the discovery of angiotensin: on the 100th anniversary of his birth

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Dr Alberto C. Taquini (1905–1998) was a member of the Braun Menéndez' team that discovered the renin–angiotensin system, and the last surviving scientist of both the Argentine [1,2] and the American [3,4] groups involved in that achievement [5].

On the basis of Taquini's autobiographical notes [6] and some unpublished documents found by myself at the time of taking charge as the Director of the Instituto de Investigaciones Cardiológicas 'Prof. Dr. Alberto C. Taquini', I shall attempt to make known some ignored aspects of the 'links' that led to the discovery of angiotensin. Notably, the manuscripts, letters and documents related to this report had been kept in one of the drawers of Taquini's desk as a valuable treasure.

As emphasized in the review by Basso and Terragno [7], in their tribute to the 'Sixtieth Anniversary of Angiotensin' [8], and 'In Memoriam' by Basso and Schiffrin [9], Dr Taquini was a pioneer and an outstanding figure in cardiovascular and clinical research for more than 60 years.

The contributions of Dr Taquini in the field of clinical and experimental hypertension began in 1931 during his short visit to Dr Volhard's laboratory as a member of the research group of Dr Bernardo Houssay (Nobel Prize, 1947). Dr Volhard was the first to postulate that the kidney releases an agent having a direct vasoconstrictor effect.

Dr Taquini narrated the circumstances as follows [10]:

> In 1931, when I was initiated in cardiology, I had had the privilege of listening personally to Franz Volhard postulating that vasospasms, characteristic of pale hypertension, were produced by a vasoconstrictor substance released by the kidney, which was still under study.

Goldblatt's classical report [11] showing that partial occlusion of the renal arteries produces sustained hypertension in dogs similar to that seen in human beings, plus some additional evidences denying its reflex origin [12], led Houssay, mainly an endocrinophysiologist, to foresee the presence of a humoral mechanism. In 1936 he put Fasciolo, a recent medical graduate, in front of the challenge of reproducing Goldblatt's dogs which he prosecuted with praiseworthy skill. Then, using the grafting technique, Houssay with Fasciolo [13] were able to show that in fact the ischemic kidneys released a pressor substance that increased the recipient's blood pressure.

At the time Houssay and Fasciolo performed their experiments, I was head of the Cardiovascular Laboratory of the Institute and, with Volhard's hypothesis in mind, I discussed with them the possibility that the pressor substance released by the ischemic kidney might act directly on the vessels. Houssay firmly supported this hypothesis and advised me to test it with the Löwen Trendelenburg technique, which I did with positive results. In fact, the plasma of blood leaving the clamped kidney proved to have a definite constrictor effect on the isolated vessels of the toad's legs [14].

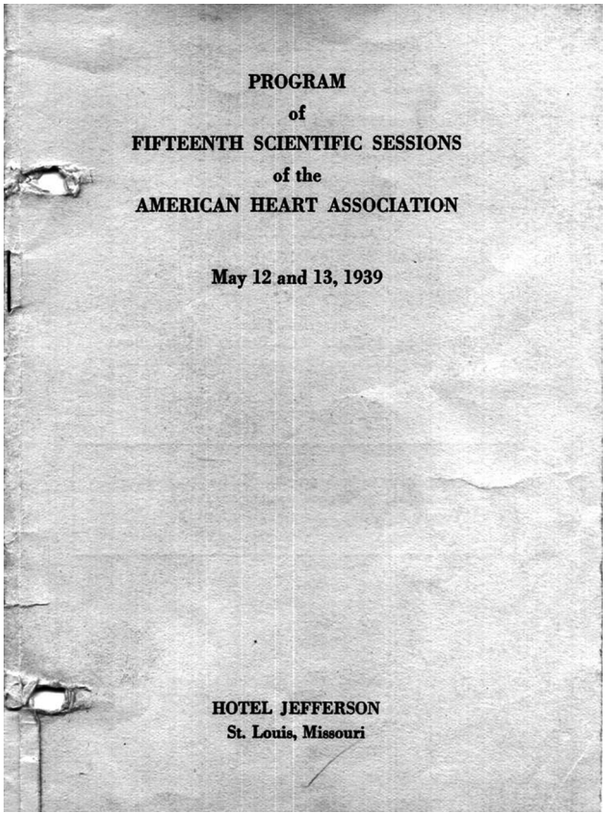
Thus, Houssay's, Fasciolo's and my experiments led to affirm that Goldblatt's hypertension was the result of a pressor vasoactive substance released by the ischemic kidney [15].

Soon after, using the same methodology, I was able to prove that also the increase in blood pressure which follows the re-establishment of circulation in kidneys, previously discontinued, was produced by the release of the same vasopressor vasoactive substance [16]. Subsequently Fasciolo and Braun Menéndez [17] perfusing an isolated kidney, by a heart lung preparation, were able to show that the kidney must only be ischemic during a short time to release the vasoactive substance.

At this stage, 1938, Houssay delegated the problem to a team formed by Braun Menéndez, Fasciolo, Leloir (Nobel Prize 1970), Muñoz and myself.

The first significant result was attained in 1939, at the time I was in the United States working as research fellow at Harvard University. Braun Menéndez, Fasciolo, Leloir and Muñoz [1] extracted a pressor substance from the plasma of venous blood of acute ischemic kidneys dializable, thermostable and with a short pressor effect which they called hypertensin. Shortly after, they proved that it was the result of an enzymatic reaction in which renin was the enzyme and plasma the substrate [2].

**Fig. 1**



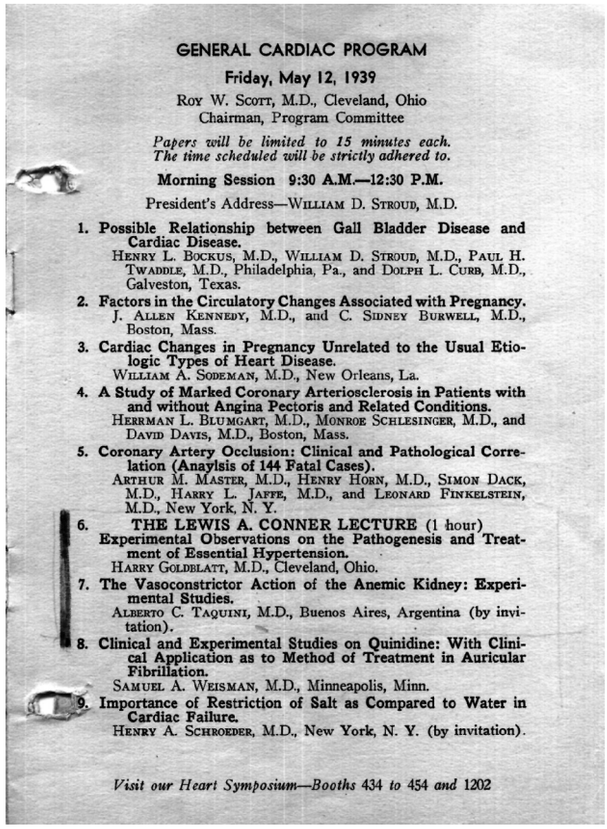
PROGRAM
of
FIFTEENTH SCIENTIFIC SESSIONS
of the
AMERICAN HEART ASSOCIATION

May 12 and 13, 1939

HOTEL JEFFERSON
St. Louis, Missouri

Original program of the XVth Scientific Sessions of the American Heart Association found carefully archived in Taquini's desk.

**Fig. 2**



GENERAL CARDIAC PROGRAM

Friday, May 12, 1939

Roy W. Scott, M.D., Cleveland, Ohio
Chairman, Program Committee

*Papers will be limited to 15 minutes each.*
*The time scheduled will be strictly adhered to.*

**Morning Session 9:30 A.M.—12:30 P.M.**

President's Address—William D. Stroud, M.D.

1. **Possible Relationship between Gall Bladder Disease and Cardiac Disease.**
   Henry L. Bockus, M.D., William D. Stroud, M.D., Paul H. Twaddle, M.D., Philadelphia, Pa., and Dolph L. Curb, M.D., Galveston, Texas.
2. **Factors in the Circulatory Changes Associated with Pregnancy.**
   J. Allen Kennedy, M.D., and C. Sidney Burwell, M.D., Boston, Mass.
3. **Cardiac Changes in Pregnancy Unrelated to the Usual Etiologic Types of Heart Disease.**
   William A. Sodeman, M.D., New Orleans, La.
4. **A Study of Marked Coronary Arteriosclerosis in Patients with and without Angina Pectoris and Related Conditions.**
   Herrman L. Blumgart, M.D., Monroe Schlesinger, M.D., and David Davis, M.D., Boston, Mass.
5. **Coronary Artery Occlusion: Clinical and Pathological Correlation (Anaylsis of 144 Fatal Cases).**
   Arthur M. Master, M.D., Henry Horn, M.D., Simon Dack, M.D., Harry L. Jaffe, M.D., and Leonard Finkelstein, M.D., New York, N. Y.
6. **THE LEWIS A. CONNER LECTURE** (1 hour)
   **Experimental Observations on the Pathogenesis and Treatment of Essential Hypertension.**
   Harry Goldblatt, M.D., Cleveland, Ohio.
7. **The Vasoconstrictor Action of the Anemic Kidney: Experimental Studies.**
   Alberto C. Taquini, M.D., Buenos Aires, Argentina (by invitation).
8. **Clinical and Experimental Studies on Quinidine: With Clinical Application as to Method of Treatment in Auricular Fibrillation.**
   Samuel A. Weisman, M.D., Minneapolis, Minn.
9. **Importance of Restriction of Salt as Compared to Water in Cardiac Failure.**
   Henry A. Schroeder, M.D., New York, N. Y. (by invitation).

*Visit our Heart Symposium—Booths 434 to 454 and 1202*

A page of the original program showed in figure 1, marked by Taquini.

Simultaneously with the studies of our group Page and coworkers, at the Meeting of the American Heart Association, held in May 1939 (Fig. 1), presented their paper 'Activation of renin and its vasoconstrictor properties' in which they postulated that renin activated by plasma becomes vasoactive [18]. I was present at that meeting, to which I had been invited to present my experience with totally ischemic kidneys (Fig. 2).

Well informed that the properties of the substance isolated by my peers clearly showed that it was not renin, I objected to Page's and coworkers interpretation. Goldblatt who was also present, apparently, was the only one to take my comments into consideration. At the end of the sessions he invited me to stop at his laboratory on my way back to Boston in order to analyze the problem more extensively...

Dr Taquini immediately sent his presentation to the *American Heart Journal* and it was published in the issue of May 1940 [19].

In this paper, dogs were employed to investigate total renal ischemia, with several aims:

(1) to see whether the totally ischemic kidney produces vasoconstrictive substances as Volhard affirms but many dispute; (2) to learn whether the pressor substances from totally and partially ischemic kidneys are similar; (3) to employ a technique which should permit one to obtain the pressor substance more easily, quickly, and safely, facilitating chemical and pharmacologic study.

Dr Taquini concluded that [19]: (1) the re-establishment of the circulation to a previously totally ischemic kidney causes a rise in the arterial pressure; (2) this rise is caused by the liberation of a pressor substance formed during the total renal ischemia; (3) this substance acts directly upon the peripheral vessels and produces marked vasoconstriction and consequent hypertension.

Therefore, the description of renin as an enzyme acting on a plasma protein to form hypertensin (angiotensin) was

defended by Dr Taquini in the presence of the others 'fathers of hypertension' on 12 May 1939. Then, with the passing of time, the 'adventure' of the discovery of angiotensin was supported by a body of evidence that made it reality.

Many years after, Dr Taquini narrated the following:

> I believe not to be mistaken when thinking that, to a certain extent, my belief in the existence of a hypothetic vasoactive substance linearly oriented all the projects that culminated with the discovery of hypertensin; this is also suggested by Irvine Page in his book 'Hypertension Research: A Memoire 1920–1960', when talking about the publication of this last finding, in which I do not appear, says: '... Remarkably, the name of Taquini does not appear..' [20]. The fact is that by the end of 1938, a little after Leloir and Muñoz joined the group by suggestion of Houssay, in order to collaborate with me in the identification of the vasoactive substance, already detected [16,21,22], I moved to the United States, and Braun Menéndez, already returned from Cambridge, took my place. 'Mistaken in time', as Borges would say, when they succeeded to identify the substance [1,2], I was at Harvard.

Braun Menéndez, Taquini, Fasciolo, Leloir and Muñoz worked together until 1943, each one contributing to his full capacity to elucidate the problem of hypertension. At the end of 1943, and because of the political persecution against Houssay, the group was dissolved.

Dr Taquini founded the Instituto de Investigaciones Cardiológicas in 1944 and directed it for more than 54 years, until his death in 1998. This institute belongs to the Faculty of Medicine of the University of Buenos Aires. The Institute is dedicated to research in connection with CONICET (National Research Council), where a significant number of outstanding researchers have been trained, most of them having made important contributions to the American Heart Association, Inter-American Society of Hypertension, European Society of Hypertension and International Society of Hypertension.

From the very beginning, research has been centered on hypertension, hypoxia and hemodynamic adaptations, renal physiology and electrolytes, arterial wall, cardiac metabolism, myocardial pharmacology and regulation of the circulation by the central nervous system.

During his long and fruitful life, Dr Taquini was President and Honorary Member of many international scientific societies, he was co-founder of the Argentine Society of Cardiology, received more than 100 national and international awards and published more than 350 papers in high-level journals [23].

Dr Taquini also played an important role in promoting science at the national level, and formed a legion of disciples, some of whom now provide continuity to the scientific tradition he established so strongly.

He believed that 'scientific research is something more than planning and producing, that it also involves creating knowledge'.

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