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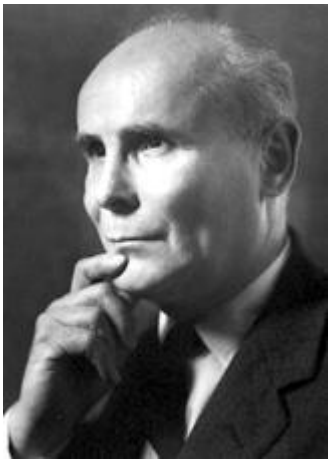
Nobel Prize in Medicines 1956


André Frédéric Cournand


Werner Forssmann


Dickinson W. Richards

The Nobel Prize in Physiology or Medicine 1956 was awarded jointly to André Frédéric Cournand, Werner Forssmann and Dickinson W. Richards "for their discoveries concerning heart catheterization and pathological changes in the circulatory system".

The heart is the sun of the microcosm formed by the human body, as stated already by William Harvey in his monumental treatise on the circulation of the blood. Its central role in both healthy and pathologic states is well known and is illustrated, for example, by the fact that cardiovascular diseases are at present responsible for more deaths than any other group of diseases. It is for essentially new contributions in this important field that the Nobel Prize for Physiology or Medicine has been awarded this year.

Two factors are decisive for the work of the heart. One is the pressure conditions in its various chambers. The other is the quantity of blood forced by its right side through the pulmonary vessels to its left side which, in turn, transmits the blood to all the parts of the body, to be returned once more to the right atrium. Exact data regarding these two factors have long been available through animal experiments. It has been possible to measure the

pressure, after introduction of catheters connected to suitable recording instruments. The minute volume, i.e. the blood flow per time unit, has been determined by measuring both the oxygen uptake of the lungs, and the difference between the oxygen content of the blood just leaving the lungs and that of the oxygen-poorer blood flowing to them from the right side of the heart.

As far as man is concerned, these methods were for a long time only partly applicable. Thus, it was possible to record the pressure in the peripheral arteries - and this is what is usually meant when we speak of the blood pressure - as well as in the superficial veins. These values reflect to some extent the conditions in the left ventricle and the right atrium. But measurements of the right ventricular pressure, which is of essential importance for the work of the right side of the heart, was impracticable. Similarly, it was possible, for determination of the oxygen content, to take samples of the arterial blood, but not of the mixed venous blood in the right side of the heart, which gives the average value for the body as a whole. It was, in fact, necessary to resort to indirect methods. These have yielded valuable results, although they have somewhat undeservedly - as is often the case - been overshadowed by the subsequent conquests. One of the factors limiting the applicability of these indirect methods was, however, that they required the active cooperation of the experimental subject or patient, and this was at times associated with difficulties or was altogether unfeasible.

As late as 1928, there were good reasons for the statement in a textbook that in man, one was «naturally» confined to the use of the indirect methods. Consequently, it was highly surprising when, already in the following year, Werner Forssmann at the surgical clinic in Eberswalde was able to show - by making, with the intrepidity of youth, by no means harmless experiments on himself - that a narrow catheter could be advanced from a cubital vein into the right atrium itself, a distance of almost two-thirds of a metre. Obviously, this constituted a remarkable advance. It was thereby demonstrated that, on principle, the methods well known from animal experiments could also be adapted for studies in man.

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This was naturally of paramount importance for a study of pathologic changes in the circulatory system, which could be reproduced with difficulty, or not at all, in animal experiments. It also opened up better opportunities for röntgenologic examination of the right side of the heart and the pulmonary vessels, after injection of contrast medium directly into these organs. For this purpose as well, Forssmann made experiments on himself. It must have required firm conviction of the value of the method to induce self-experimentation of the kind carried out by Forssmann. His later disappointment must have been all the more bitter. It is true that the method was adopted in a few places - in Prague and in Lisbon - but on the whole Forssmann was not given the necessary support; he was, on the contrary, subjected to criticism of such exaggerated severity that it robbed him of any inclination to continue. This criticism was based on an unsubstantiated belief in the danger of the intervention, thus affording proof that - even in our enlightened times - a valuable suggestion may remain unexploited on the grounds of a preconceived opinion. A contributory cause in this substance was presumably that Forssmann was working in a milieu that did not clearly grasp the great value of his idea.

It was no mere coincidence that it was in New York that Forssmann's contribution was once more brought to light. There, André Cournand and Dickinson Richards had, with various co-workers, made a thorough study of the circulation in different pathologic conditions. Since their own experience had made them familiar with the limitations of the current methods, they realized the great desirability of being able to make direct analyses of the conditions in the right side of the heart. It is, however, characteristic that it was not until after several year's preparations and much hesitation that the New York school was able, in 1941, to publish a report of cardiac catheterization in man. A few minor improvements were introduced, but the main point was that a well-known research group at a distinguished clinic had set their seal of approval on the method, which then made its triumphant entry into the world of clinical medicine.

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Scientific progress often takes place by leaps and bounds, not infrequently due to improvements in the technique which, in the hands of skilful workers, may allow new fields of applicability. Nor was success slow to occur in this case.

During World War II, as well as on earlier similar occasions, secondary wound shock constituted a serious problem. This is a state of circulatory failure which may appear several hours after a severe injury. Cournand, Richards, and co-workers showed that, although the causative mechanism varies, the essential feature is a considerable decrease in the minute volume, due to a diminished return of blood to the heart. This may, in turn, be a result of blood loss, or it may also be due to insufficient contraction of the smooth muscles in the blood vessel walls. A study of the improvement brought about by blood transfusion could be made by means of cardiac catheterization.

The turn then came to the acquired heart diseases, in which the minute volume and the pressure conditions at rest and at work were found to vary with the art and severity of the illness. The observations illustrated the influence of the left side of the heart on the right. They also provided a basis for evaluation of the mutual role of changes in the heart muscle itself and in the valvular apparatus. Although congenital heart disease occupies a relatively modest place in the large complex of cardiac disorders, it is by no means a rarity. It is generally a question of developmental anomalies of widely divergent nature, such as constriction or dilation of the great vessels given off from the heart, of persisting patent communications between them, or of defects in the ventricular or atrial septum. By taking blood samples from different chambers of the heart and the great vessels, by measuring the pressure at various sites and by the refined röntgenological analysis, it has been possible to make considerable diagnostic improvements and to obtain a better conception of the conditions than that provided by earlier techniques. It is, for example, possible to calculate the minute volume in the systemic and the pulmonary circulations separately, and thus to determine the quantity that is short-circuited from one side of the heart to the other, usually from the left side to the right. These investigations have, to an appreciable degree,

been instrumental in promoting the remarkable advances in heart surgery made in recent time.

Respiration and circulation serve the common purpose of assuring the gas exchange in the cells that is a prerequisite for the maintenance of life. It is therefore entirely natural for an intimate association to exist between them. Thus, a diminution in the blood flow may produce increased respiration, and pathologic changes in the respiratory apparatus may have an effect on the heart. An example is the enlargement and, at times, failure of the right ventricle which may appear in certain chronic pulmonary diseases, among them silicosis, which is a threat in certain occupations, and emphysema.

Cournand, Richards, and their group have shown that pulmonary changes can, during slight work or even at rest, produce raised pressure in the pulmonary artery, with increased demands on the right ventricle as a result. They have also thoroughly studied and elucidated the various factors responsible for these disturbances, such as a reduction in the cross section of the vascular bed, and decreased oxygen saturation of the arterial blood owing to inadequate respiration, as well as impairment of the actual membrane through which the oxygen must pass into the blood.

These results, of which brief mention has been made, have been the fruit of extensive investigations, implying the cooperation of a large number of highly skilled research workers. Cournand and Richards have, however, consistently been the pioneers and the leaders. Moreover, the contributions made by the New York school have been a source of inspiration in other parts of the world and have, there as well, led to successful study of countless problems.

Professors Cournand, Forssmann, and Richards. The Caroline Institute has decided to award this year's Nobel Prize in Physiology or Medicine to you jointly for your discoveries concerning cardiac catheterization and pathologic changes in the circulatory system. Your investigations have been performed at different times and in far distant parts of the world. Together, they signify the initiation and development of a new and important approach to our understanding of heart disease.

Professor Forssmann. As a young doctor you have had the courage to submit yourself to heart catheterization. As a result of this, a new method was born which since that time has proved to be of very great value. It has not only opened up new roads for the study of the physiology and the pathology of the heart and the lungs, it has also given the impetus for important researches on other organs. We are glad to be able to welcome you in this country where once your ancestors worked.

Professor Cournand and Professor Richards. The practical value of cardiac catheterization has been definitely proved by you and your co-workers. This method, combined with those already available before, has in your hands led to many important new observations, to diagnostic as well as therapeutic advances. The field is still in the process of exploration, and there is good reason to believe that rich harvests will also be reaped in the future. It is our hope that you will have the opportunity of continuing to take an active part in this development for many years to come.

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