One of the main rationales for the development of COSAS was that it would be a management tool in national or regional vaccination programmes. Its use will result in greater uniformity in the way that data are presented and will make it possible for surveys conducted in different places and at different times to be compared. The use and adaptation of HIPI technology, such as COSAS, could serve as a focus for the development of a co-ordinated national strategy for the control of vaccine-preventable diseases in South Africa.

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Copies of COSAS are available from the HIPI, WHO, 1211 Geneva 27, Switzerland.

REFERENCES

Greek says, until an excess of sugar became available, that diabetes mellitus manifested frequently enough to attract the attention of ancient physicians, including Galen and the encyclopaedist, Celsius. From this information it is fair to infer that diabetes mellitus is a preventable illness; but, through prevention is possible, it would not be popular. For treatment, however, control is vital and insulin essential.

Biographical note
Nicolas-Constantine Paulesco (or Paulescu, the Romanian spelling of his family name) was born in Bucharest in 1869. He was the medical scientist who originated the best method for the proper treatment of diabetes mellitus with insulin, as we know it today, which he isolated but named pancreas. Paulesco went to Paris for his medical education. While he was still a student he attracted the notice of Ennemi Lancereaux, the President of the French Academy of Medicine and physician-in-chief at the Hôpital de Notre-Dame du Perpênal Secours. In 1877 Lancereaux postulated an aetiological relationship between an organic change from normal in the pancreas and diabetes mellitus, and 3 years later he described the condition of the pancreas as it appeared in a case of diabetes mellitus and the clinical state of the patient who was "a thin diabetic." (Aristotle appears as the first writer to have used the name pancreas for the organ in vertebrates, although it was a designation in common usage. He gives no reason for its obvious etymology.)

FIG. 1.
Nicolas Constantine Paulesco, 1869 - 1931.

Thus it came to pass that Paulesco, under the clinical and experimental guidance of Lancereaux, became inclined towards research, at first clinical and later experimental. There were other investigators in the same field in Europe who constituted stimulating rivalry. Oscar Minkowski on 17 May 1889 reported to the Strasbourg Society of Scientists and Physicians: "I have just finished, with the assistance of von Meiring, some experiments on total pancreatectomy of dogs, rabbits, and pigs. In all these animals it has been proved that pancreatectomy produces diabetes in animals." Twelve years later (1901), when Paulesco was back in Bucharest, Minkowski could add in an address to an assembly of scientists in Cologne, that "a lack of a substance in the pancreas, different from its external secretion, is responsible for experimental diabetes."

After qualifying in medicine, Paulesco was appointed to the staff of Lancereaux's hospital, where he was able to complete a thesis on the micro-anatomy and physiology of the spleen. The thesis obtained for Paulesco a doctorate with the commendation "excellent bien!"

At the Sorbonne, not noted in its history for scientific advances so much as theological revelations, Paulesco acquired a second scientific doctorate. Nevertheless, with his medical and scientific accomplishments, Paulesco continued his professional association with his patron, Lancereaux, and at Lancereaux's hospital he combined his clinical and laboratory research into endocrinology. Several of his publications appeared in the French medical literature. A pointer to the esteem in which his professional skill was held is Harvey Cushing's observation in the USA that Paulesco's surgical approach for the extirpation of the pituitary gland was "by far the most important contribution to the subject." The two men became warm friends. Before Paulesco returned to Bucharest in 1900, he completed a Tracté de Médecine in 4 volumes. He had begun this major literary work with Lancereaux, but Lancereaux died soon after the completion of the first volume.

In Bucharest Paulesco was appointed assistant to the professor of physiology at the medical school and, 4 years later, to the Chair itself. Here he pursued his endocrinological research. In Europe at this time Zuelzer had had some success with an extract of the pancreas administered to diabetic patients and Mayer's published research done with pancreatic extract to determine its effects on different organs of the body, but particularly on renal function. Scott also, in North America, had experimented with an extract of pancreas injected intravenously into animals rendered diabetic.

His achievement
Paulesco knew of Zuelzer's work, which was made known to the Berlin Medical Society on 15 June 1908, when 8 years later in 1916 he showed that an aqueous extract of the pancreas injected into a diabetic dog produced an immediate though temporary amelioration of symptoms, but World War I interrupted his research. Nor until 1920, 2 years after the Armistice, was Paulesco able to resume his experimental work, which confirmed his earlier conclusion. His scrupulous accuracy and diligence and the results he achieved are apparent in his publication of Augus 1921. Paulesco proved without any doubt that he had succeeded in the isolation, if not the purification, of the "anti-diabetie factor," which he named pancreas. The function of pancreas Paulesco demonstrated not only on diabetic dogs but, significantly, also on normal animals. He improved upon his raw extract by obtaining a soluble powder suited to subcutaneous injection, but the quantity was small. Because of the extreme restriction on the availability of equipment in Romania, Paulesco was not able to increase the quantity of pancreas and this meant the treatment of human diabetics was also severely limited. In Romania there was no pharmaceutical corporation, such as Eli Lilly, waiting impatiently in the wings to enter upon the stage to purify and commercialise for wide consumption the pancreas he had isolated.
Paulesco opened his article with the statement that it was Claude Bernard who showed that the pancreas has a physiological digestive role, and that Lancereaux had confirmed this discovery. He then stated, modestly, that with other workers in the direction indicated by Lancereaux, he had arrived at a stage where he could make a worthy contribution. He proposed to begin with an account of his experiences with the action of a pancreatic extract injected into the bloodstream and then to continue with a description of a method of treatment of diabetes, which he had developed from his observations and the results of his experiments. He concluded with his own theory of the pathogenesis of diabetes mellitus and of the part the pancreas plays in the digestion of food and its assimilation into the substance of the body.

In the first part, Paulesco described the action of ‘pancréase’ in the bloodstream of a diabetic dog, with a comment on his method of ablating the whole pancreas from the animal — explicit, with detailed results. From this, he drew unequivocal conclusions. By intravenous injection of ‘pancréase’ into the jugular vein he was able to lessen or even remove the hyperglycaemia and replace it by a hypoglycaemia. At the same time, he could lessen or remove glycosuria and considerably reduce the blood and urinary urea. There was an associated remarkable diminution of acetonaemia and acetonuria. He showed that the effect of the extract on glycaemia and glycosuria varied with the lapse of time from the injection; that the effect began immediately after the injection, reached a maximum after 2 hours and persisted for about 12 hours. It also varied with the quantity of pancreas used in preparing the extract. A most significant finding was that a normal animal used as a control, responded in the same way.

Injection intravenously of physiological serum or an extract of any other organ than the pancreas had no similar action; nor did an intrathecal injection of a solution of nuclease of soda, which provoked fever.

Romans 13:7

The foregoing is a very brief summary of Paulesco’s article, not published in Romania but in the French language in France. It was received and accepted by the editor of Archives Internationales de Physiologie on 22 June 1921 and published in August of that year. It was titled: Recherche sur le Rôle du Pancreas dans l’Assimilation Nutritive.

In 1923 the Nobel Prize Committee awarded the Prize in Medicine to the authors13,14 of a paper describing the isolation of the pancreatic hormone which they named ‘insulin’, for the therapeutic control of diabetes mellitus, published in the Journal of Laboratory and Clinical Medicine (1922; 7: 266). Paulesco had not been nominated.

That Paulesco’s work and achievement was known to researchers in North America is established by the misquotation in English translation by the aforementioned authors, of a statement by Paulesco which appeared in his French publication, to give a directly contrary meaning. This misquotation reads: ‘Injections into peripheral veins produce no effect and his [Paulesco’s] experiments show that second injections do not produce such a marked effect as the first.’ Was ever such an absurd solecism seen in so famous a scientific article. This astonishing fact was admitted openly after many years at the Jubilee Celebration of the Discovery of insulin in 1971, in Israel.1 Although Paulesco’s lamp had been obscured in Bucharest, he had delivered some lectures to the Société de Biologie in Europe on ‘pancréase’ after having completed his research and months before the publication of his paper in August 1921. In 1924 Paulesco did publicly, but in Romania, declare his priority in the isolation of the pancreatic hormone, in the Comptes Rendus of the Romanian Biological Society.

It is fitting to repeat a thought of Wilfred Trotter which he expressed at his Hunterian Oration of 1932, which happened to be 1 year after Paulesco’s death: ‘With the process of time it will become increasingly difficult to separate the commemoration of the dead from the responsibility for their treatment during life, or to believe that posthumous honour is in any real sense a reparation for the dead, or a discharge of the liability of the living.’

REFERENCES