

Rundle and His Curve

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It's time to set the record straight on Rundle's curve. For many years, the term *Rundle's curve* has been used as shorthand in the lexicon of Graves ophthalmopathy as a descriptor of the disease's putative natural history. As depicted in **Figure 1**, the disorder's signs and symptoms are thought to worsen rapidly during a dynamic phase, reach a point of maximum severity, and then abate to a static plateau that is improved but not resolved to the baseline condition. The curve's sinuous shape is probably applicable to many other diseases, such as rheumatoid arthritis, as well as to numerous nonmedical phenomena, such as the sales of Beatles' recordings since 1964 or the waistline of the average American between Thanksgiving and Valentine's Day.

Rundle's curve is so widely recognized that it frequently is named without citation.^{2,3} When a reference to F. F. Rundle's work is provided,¹ it almost always is to a publication he coauthored with C. W. Wilson in 1945.⁴ Occasionally,⁵ the origin of the curve is traced to an article that Rundle wrote with I. B. Hales in 1960.⁶ A review of the Hales and Rundle article, however, finds neither the familiar figure nor a description of Graves ophthalmopathy's untreated chronologic course. In some articles, such as a thoughtful review by Wiersinga,⁷ both the 1945 and 1960 studies are referenced, but, in that particular article, Rundle's curve is depicted as an inverse of what is commonly recognized today (**Figure 2**). So what is Rundle's curve, and where did it originate?

The oft-cited 1945 article by Rundle and Wilson⁴ contains several graphs, one of which—their Figure 2—could be construed as a forerunner of Rundle's curve (**Figure 3**). In 1 panel of that figure, “ocular prominence” (ie, exophthalmometry measurements) is plotted for 2 patients, identified as cases 7 and 8, over an interval of 30 months. But the fine print in the figure's legend is important as regards the applicability of the curves to the natural

history of Graves ophthalmopathy. First, the time frame starts with the date of first examination, not the date of onset of signs or symptoms or the date of diagnosis of thyroid dysfunction. Second, neither case purely evinces natural history. One patient (case 7) had euthyroid Graves ophthalmopathy (ie, characteristic eye findings with normal thyroid function as determined by the laboratory tests available at the time), but the patient became pregnant 17 months after the initial examination. The other patient (case 8) had full-blown Graves disease with thyrotoxicosis but underwent thyroidectomy 1 week after the first examination. Both pregnancy and thyroidectomy have biochemical and immunologic sequelae that may be clinically relevant to the course of Graves ophthalmopathy.

If we cannot firmly anchor Rundle's curve in Rundle and Wilson's 1945 article, then is the publication of little value to us today? By no means: in fact, the article is a tour de force. First, the article leads us to Rundle's previous work.⁸⁻¹³ He was an assiduous examiner who developed several instruments to measure the clinical features of thyroid eye disease to an admirable level of accuracy. His observations demonstrate extraordinary insight by a nonophthalmologist into an ophthalmic disease that, even decades later, re-

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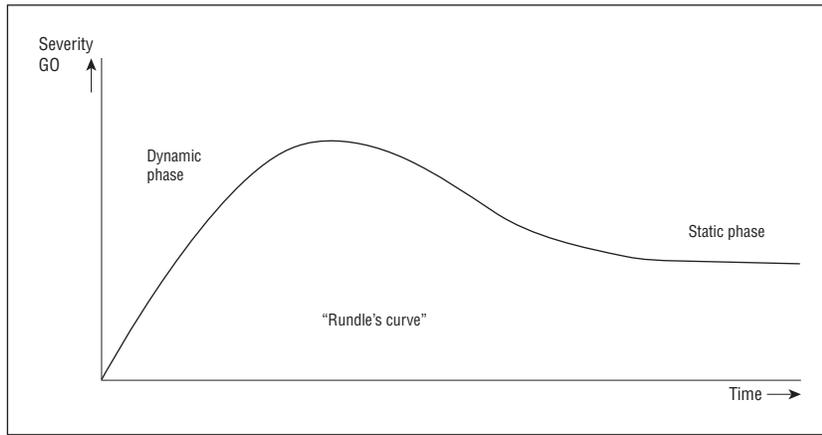


Figure 1. Rundle's curve from Kalmann and Mourits.¹ GO indicates Graves ophthalmopathy. Adapted from Kalmann and Mourits¹ with permission from Elsevier.

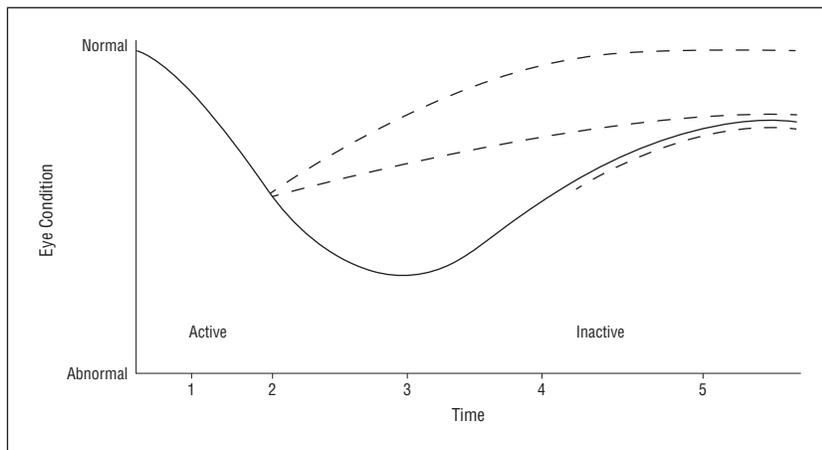


Figure 2. Rundle's curve, from Wiersinga.⁷ The solid line depicts the natural history of the "eye condition" becoming more abnormal during the "active" phase of Graves ophthalmopathy, reaching a nadir, and then improving and stabilizing over a numerically unspecified time course. Adapted from Wiersinga⁷ with permission from Mary Ann Liebert Inc publishers.

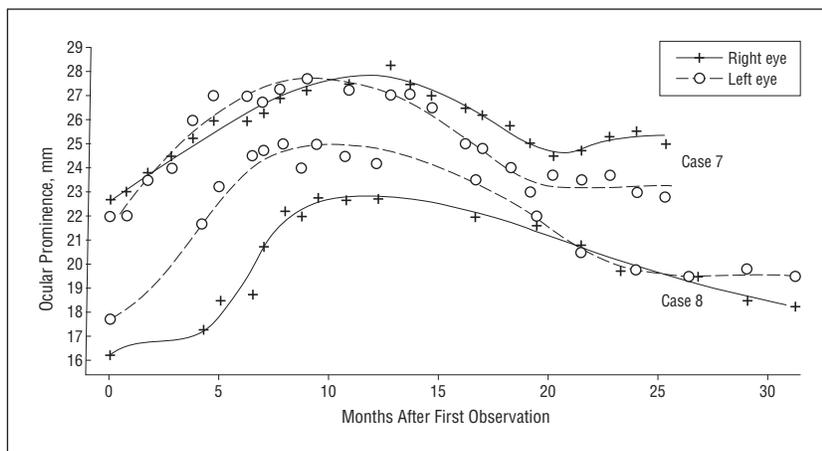


Figure 3. Figure 2 from Rundle and Wilson⁴ depicts the exophthalmometry measurements of 2 patients during the 30 months after their initial examinations. Adapted from Rundle and Wilson⁴ with permission from the Biochemical Society (<http://www.clinsci.org>).

mains poorly understood. Second, Rundle was a cutting-edge investigator: buried in the legend to 1 of the tables is a *P* value (!)—a statistical sighting rare in the medical lit-

erature of the mid-1940s. And third, Rundle's writing style is elegant and enjoyable, with phrases such as "correlative changes in the degree of lid protrusion occur *pari passu* [with or-

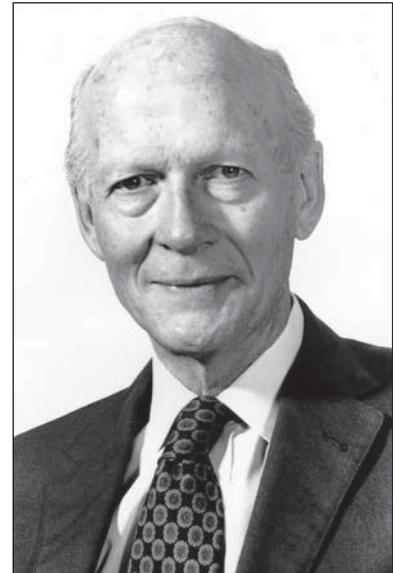


Figure 4. Francis Felix Rundle, 1910-1993. Courtesy of Patrick and Julian Rundle. Used with permission.

bital tissue bulk]" and "the increment [of exophthalmos change] is not characteristic of thyroidectomy, qua thyroidectomy" used effectively and without affectation. Which brings us to the man himself: who was F. F. Rundle?

Francis Felix Rundle was born on April 13, 1910, in Newcastle, Australia. He graduated from Sydney University Medical School in 1932 and then headed to London, England, for his postgraduate training. While in England he developed an interest in thyroid disease, leading to a thesis that won the prestigious Jacksonian Prize from the Royal College of Surgeons. After World War II, Rundle spent a year in the United States at Harvard, Johns Hopkins, and Stanford as a Rockefeller Traveling Fellow. He was favorably impressed with the role of clinical research in these academic medical centers and sought to replicate such an environment when he returned to Australia in 1950, accepting a post as Director of Clinical Investigation at Sydney's new Royal North Shore Hospital. Rundle advanced to the role of Foundation Professor of Surgery in 1959 and the following year was named dean of the newly established medical school at the University of New South Wales. He guided the school ably until his retirement in 1973. According to 1 of his sons, Julian, F. F. Rundle (**Figure 4**) was a polymath, facile in

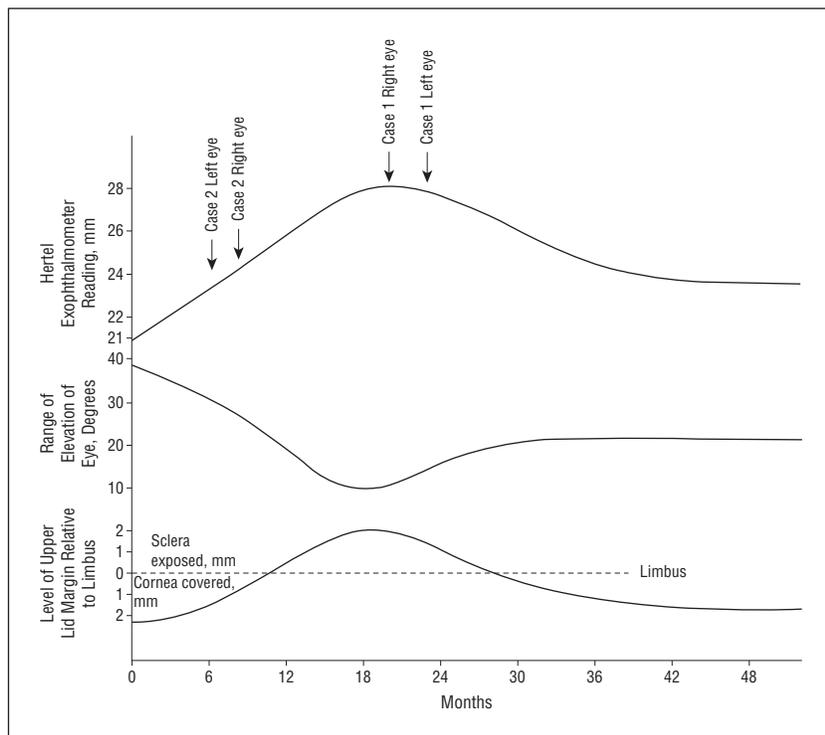


Figure 5. Rundle's "ideal and theoretical curves" indicate "the behavior of the principal ocular changes during the dynamic phase of protrusion and recession" of Graves ophthalmopathy. Adapted from Rundle.¹⁵ Used with permission.

the classics and a self-taught student of languages, learning them so that he could read research articles in the original. He passed away on December 17, 1993.¹⁴

But getting back to Rundle's curve . . . did Rundle ever describe it? Well, sort of. In an infrequently cited publication in 1957,¹⁵ Rundle plotted 3 curves on a single graph, with a timeline of 48 months on the x-axis (**Figure 5**). On the y-axis, he depicted exophthalmometry readings, the range of ocular elevation, and the position of the upper eyelid relative to the corneoscleral limbus. All 3 clinical features reach "in-gravescence" approximately 18 months from time 0 before becoming "static at a level of incomplete recovery." Rundle's commentary on the graphs is noteworthy:

[The figure] is an attempt to sketch diagrammatically the behavior of the principal ocular changes during the dynamic phase of protrusion and recession. They are ideal and theoretical curves in the sense that relatively few patients have been, or could be followed through the complete cycle.

Although "ideal and theoretical," Rundle's curve(s) has proved immensely valuable in providing a context to judge therapeutic interventions and a chronology to counsel individual patients. On the centennial of his birth, it is appropriate to honor F. F. Rundle for this and his many other contributions to ophthalmology, surgery, and medicine.

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