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This Week's Citation Classic

Hatch F T & Lees R S. Practical methods for plasma lipoprotein analysis. *Advan. Lipid Res.* **6**:1-68, 1968.
[Bio-Medical Div., Lawrence Radiation Lab., Univ. Calif., Livermore, CA and Rockefeller Univ., New York, NY]

In this review we presented full details for using some relatively simple and only moderately expensive procedures of lipoprotein analysis. Because the review was intended to be every 'person's' lipoprotein manual, we included comparisons of results obtained with older or more complex methods, so that an appropriate selection of methods could be made by the readers. [The *SCI*® indicates that this paper has been cited over 315 times since 1968.]

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"In 1960 I organized a new Arteriosclerosis Unit at the Massachusetts General Hospital. This unit was to do both basic biochemical and clinical research on atherosclerosis and coronary heart disease, with emphasis on lipoprotein metabolism. During the 1950s the work of John Gofman and associates at the Donner Laboratory in Berkeley established that the plasma lipids are transported in the form of a series of macromolecular complexes of lipids and proteins, the lipoproteins.[1] They also found that patients with certain hereditary disorders exhibited striking abnormalities of the lipoprotein spectrum. The foregoing work utilized new and complex techniques of ultracentrifugation that were available in only a handful of laboratories in the world.

"One of our earliest objectives was to adapt or develop a suite of relatively simple methods that would enable quantitative or semiquantitative measurements of lipoprotein patterns in animals and humans to be performed in our laboratory and other biophysically unsophisticated laboratories. Methods involving zone electrophoresis in paper and other media soon took on a major role in this suite of methods. N. Zöllner of Munich suggested that we add albumin during electrophoresis, since this had previously been used to improve the resolution of radioactively labeled insulin. Robert Lees and I indeed found that adding one percent serum albumin to the buffer for paper electrophoresis greatly improved the resolution of lipoprotein fractions, and we showed that these corresponded to the fractions separated with the ultracentrifuge.[2] Our method contributed heavily to the development of a typing system for the hereditary lipoprotein disorders, which is still widely used today.[3] Subsequently, there was an explosive growth of clinical research on lipoprotein disorders and of interest in the metabolic and other risk factors for coronary heart disease. Our electrophoretic method became a widely used standard, later to be replaced by superior agarose gel methods. This is undoubtedly responsible for the frequent citation of the review 'handbook' on methods that Lees and I wrote, together with the fact that we aimed it at clinical researchers. With various other collaborators I later made the paper and agarose gel electrophoretic techniques as quantitative and standardized as was feasible. The current state of this art was published by Frank Lindgren and a Donner Laboratory group.[4]

"Although I have now reoriented my research toward chromatin biochemistry and genetic toxicology, it is very gratifying to have participated for a long time in the assault on heart disease, which recently is showing clear signs of success. Lees remains active in the clinical investigation and treatment of patients with atherosclerosis."

1. **Gofman J W, Glazier F, Tamplin A, Strisower B & de Lalla O.** Lipoproteins. coronary heart disease. and atherosclerosis. *Physiol. Rev.* **34**:589-607, 1954.
2. **Lees R S & Hatch F T.** Sharper separation of lipoprotein species by paper electrophoresis in albumin-containing buffer. *J. Lab. Clin. Med.* **61**:518-28, 1963.
3. **Fredrickson D S, Levy R I & Lees R S.** Fat transport in lipoproteins: an integrated approach to mechanisms and disorders. *N. Eng. J Med.* **276**:32-44, 94-103, 148-56, 215-26, 273-81, 1967.
4. **Wong R A, Banchero R G, Jensen L C, Pan S S, Adamson G A & Lindgren F T.** Automated microden sitometry and quantification of lipoproteins by agarose gel electrophoresis. *J. Lab. Clin. Med.* **89**:1341-8, 1977.