

This Week's Citation Classic

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Zieve L. Jaundice, hyperlipemia and hemolytic anemia: a heretofore unrecognized syndrome associated with alcoholic fatty liver and cirrhosis.

Ann. Intern. Med. 48:471-96, 1958.

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Twenty alcoholic patients were described with jaundice, hyperlipemia, and hemolytic anemia. The illness and chemical abnormalities improved rapidly once drinking stopped. Hemolysis was slight and short in duration. The liver biopsy showed fatty infiltration and minimal to moderate cirrhosis. [The *SCI*[®] indicates that this paper has been cited in over 260 publications since 1961.]

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"As a resident in internal medicine I observed a few jaundiced alcoholic patients who were sent to surgery for obstructive jaundice, but were found to have fatty livers instead. These patients had hyperlipemia, usually only documented as an elevated blood cholesterol concentration. I looked carefully at the hospital records of a series of such patients with lipemia and noted a pattern of abnormalities not previously recognized. The jaundiced patients had lipemia or at least hypercholesterolemia and evidence of hemolysis. Both the lipemia and hemolysis were usually of short duration. On liver biopsy all of the patients had fatty infiltration and some had mild to moderate cirrhosis. None ever had severe cirrhosis. The occurrence of lipemia in alcoholics was fairly well known; however, the simultaneous occurrence of hemolysis had not previously been recognized. One of the confusing factors was the rapid improvement that occurred in these alcoholics once they stopped drinking upon becoming sick. The lipemia and the hemolysis improved spontaneously, often within a week, and only partial evidence of what had occurred remained. This did not fit into a known pattern, and the findings were usually ignored as the patient improved without treatment. The cases with persistence of elevated se-

rum cholesterol and alkaline phosphatase for more than a week were suspected of having obstructive jaundice, and some were operated on for gallstone obstruction of the common bile duct, which wasn't found at surgery.

"To me, understanding that the coexistence of jaundice, hyperlipemia, and hemolysis in an alcoholic patient was an entity with a predictable rapid recovery rate was important because one could eliminate from consideration the possibilities of more serious and prolonged liver diseases, and one did not confuse these cases with those of extrahepatic common duct obstruction and thus avoided surgical exploration. I therefore assembled data on 20 patients and presented a paper at an American College of Physicians meeting.

"The response to my paper by hepatologists was one of indifference for about two years. However, I heard from residents in training and from recent graduates of specialty training programs who wanted to discuss similar cases. Four years after my paper, a report of six similar cases introduced the term 'Zieve's syndrome' and discussed my paper in great detail.¹ This seemed to generate some interest in the subject, and prompted somebody to ask a question on the American Board Examination in Internal Medicine about the entity. Wide-spread interest in this area developed promptly among trainees in internal medicine across the country. Case reports describing similar patients appeared in many parts of the world over the next decade. In 1966, I contrasted the two types of hemolysis occurring in liver diseases.² A few skeptics are unconvinced there is anything to the syndrome, and they speak of the 'so-called Zieve's syndrome.' Others have studied possible etiologic mechanisms and have added to our understanding of possible pathogenesis, though the final answer is not in.³⁻⁵

"This paper has been cited whenever the differential diagnosis of alcoholic liver disease or the occurrence of lipemia or hemolysis in liver disease is discussed."

1. Kessel L. Acute transient hyperlipemia due to hepatopancreatic damage in chronic alcoholics (Zieve's syndrome). *Amer. J. Med.* 32:747-57, 1962.
[The *SCI* indicates that this paper has been cited in over 50 publications since 1962.]
2. Zieve L. Hemolytic anemia in liver disease. *Medicine* 45:497-505, 1966.
3. Balcerzak S P, Westerman M P & Heinke E W. Mechanism of anemia in Zieve's syndrome. *Amer. J. Med. Sci.* 255:277-87, 1968.
4. Kunz F & Stammvoll L W. The significance of plasma phospholipids in Zieve syndrome. *Blut* 21:210-26, 1970.
5. Goebel K M, Goebel F D, Schnobtz R & Schneider J. Hemolytic implications of alcoholism in liver disease. *J. Lab. Clin. Med.* 94:123-32, 1979.