



## Dietary approaches to managing nonalcoholic fatty liver disease

*Abstract: Nonalcoholic fatty liver disease (NAFLD), a multisystem, prevalent liver disease, can be managed with lifestyle interventions, including diet, given the lack of well-established pharmacologic therapies. This review explores the different dietary approaches that have been found effective in the management of NAFLD, offering a unique resource to healthcare professionals.*

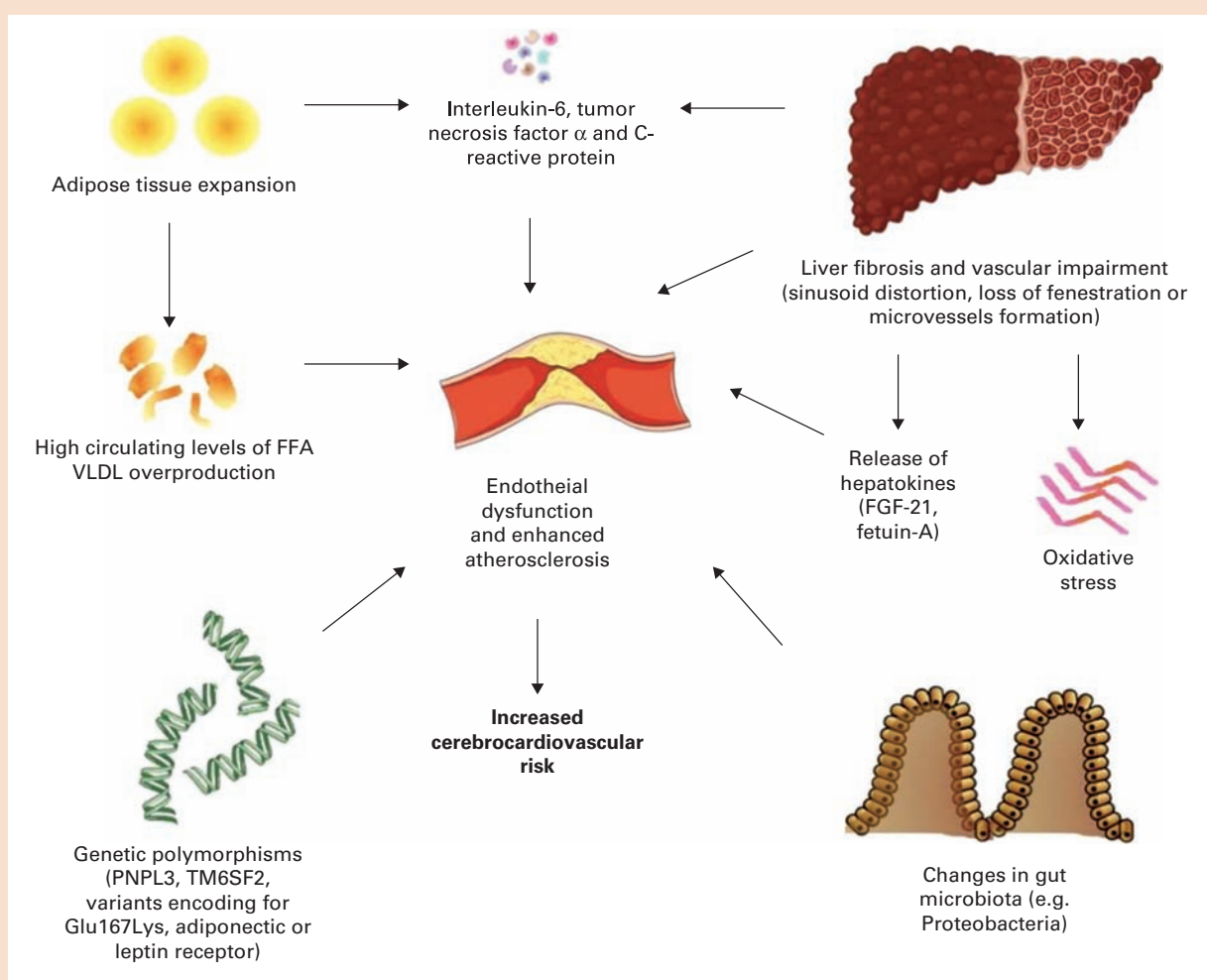
By Dalia El Khoury, PhD, RD; Rosemary J. Pauley, APRN; and Carol Lynn Berseth, MD

**N**onalcoholic fatty liver disease (NAFLD) is the most prevalent liver disease worldwide, affecting 24% of the adult population.<sup>1,2</sup> NAFLD is defined by the presence of more than 5% fat in the liver not caused by excess use of alcohol, viruses such as hepatitis B or C, autoimmune hepatitis, use of hepatotoxic drugs,

or rare genetic forms.<sup>3</sup> When this progresses to non-alcoholic steatohepatitis (NASH), it is characterized by inflammation of the liver, which in turn can progress to cirrhosis and liver failure.<sup>4</sup> The presence of fat in the liver is often unrecognized until it is identified incidentally or has progressed to NASH and/or cirrhosis.

**Keywords:** diet, healthcare professionals, management, nonalcoholic fatty liver disease (NAFLD), personalized counseling, toolbox

**NAFLD and increased cardiovascular disease risk<sup>5</sup>**



FFA, free fatty acids; VLDL, very low-density lipoprotein

There is growing evidence that NAFLD is a multi-system disease, with multiple mechanisms underlying its link to increased risk of developing cardiovascular diseases and type 2 diabetes mellitus (see *NAFLD and increased cardiovascular disease risk*).<sup>3,5</sup> In particular, an interplay between fat accumulation in the liver, hepatic insulin resistance, and impaired beta-cell function (leading to type 2 diabetes mellitus), known as the twin cycle hypothesis, has been described (see *Interrelation between liver and pancreatic diseases*).<sup>6</sup> This hypothesis postulates that the liver and pancreas cycles are linked by elevated insulin levels, which drive increased *de novo* lipogenesis and the export of hepatic fat metabolites.<sup>6</sup> The increased exposure of pancreatic beta cells to these fat metabolites eventually leads to beta cell failure.

**■ Dietary tools to manage NAFLD**

Patients generally assume that NAFLD is linked to overindulgence of fats; however, it is mainly the result of increased intake of carbohydrates.<sup>8</sup> Furthermore, because there is a higher incidence of NAFLD among those with type 2 diabetes mellitus, it is prudent to consider screening those patients for the presence of NAFLD given the absence of reliable screening tools for NAFLD.

There is no FDA-approved pharmaceutical treatment for NAFLD. Antidiabetic drugs and lipid-lowering agents have been studied, but current evidence is insufficient to support their standard use.<sup>8</sup> Effective lifestyle interventions including a variety of dietary approaches are currently the therapeutic

strategies of choice for NAFLD.<sup>9,10</sup> Several chronic diseases are treated with nutritional changes, given the general lack of adverse reactions with this approach. This review summarizes the different dietary tools suggested for the management of NAFLD and focuses on their effectiveness as well as the challenges patients face for long-term adherence. This information can serve as a valuable resource to healthcare professionals (HCPs) when providing personalized, patient-centered nutritional care to patients with NAFLD. It is worth noting that, in addition to the dietary approaches discussed in this review, alcohol avoidance and exercise (irrespective of weight loss) have been established as effective strategies for the management of NAFLD.<sup>11,12</sup>

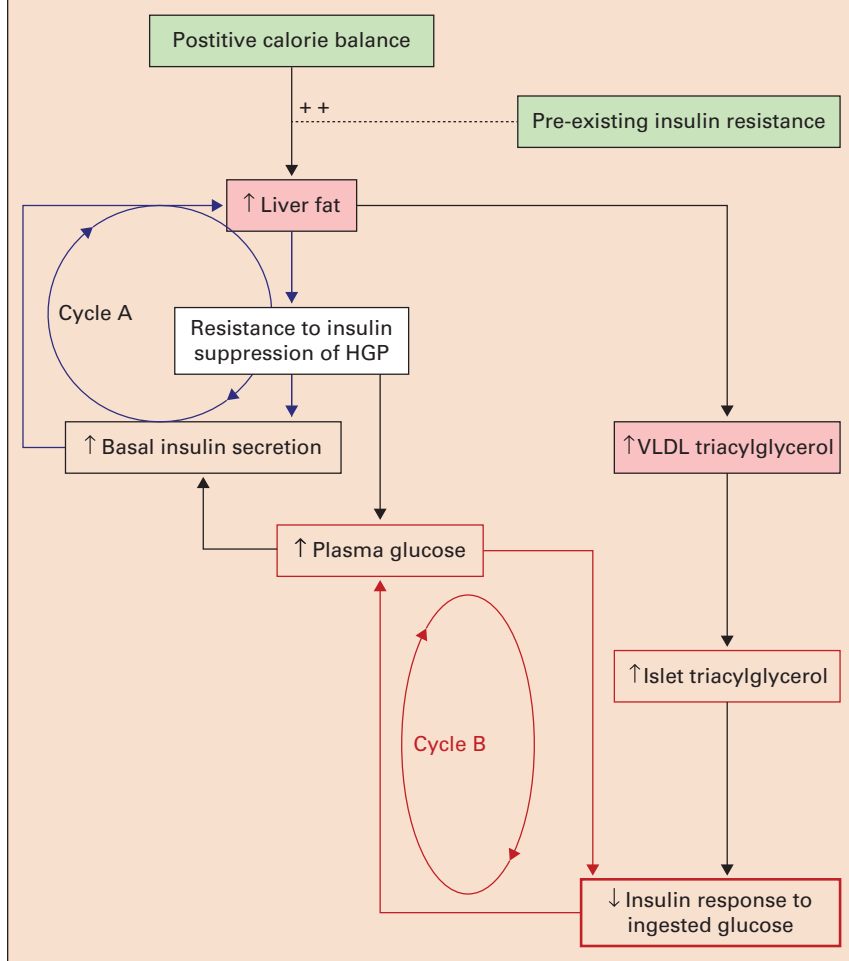
**Weight loss.** Weight reduction in response to low-calorie and very-low-calorie diets, independent of diet composition, has been the mainstay treatment strategy for NAFLD. Weight loss of 7% to 10% is typically recommended. Studies have demonstrated that weight loss leads to normalization of metabolic disturbances and improvement in liver health.<sup>13,14</sup> These findings were supported by a recent meta-analysis by Koutoukidis and colleagues, which evaluated the effect of weight loss on NAFLD-related biomarkers from 22 clinical trials.<sup>15</sup>

However, in one study, individuals with obesity and NAFLD were found to be less likely to achieve 5% loss of body weight compared with individuals with obesity but without NAFLD after 3 months on a very-low-energy diet.<sup>16</sup> These findings suggest that individuals with NAFLD may face greater metabolic challenges to achieve clinically significant weight loss. In addition, a number of factors were reported to impact long-term adherence to weight management programs (see *A dietary toolbox for HCPs for the management of NAFLD* and *Factors affecting long-term*

*adherence to weight management programs*). Hence, many patients with NAFLD are likely to require a greater level of support to adhere to weight loss diets.<sup>17</sup> Unfortunately, sustainability of weight loss is difficult with more than 50% of the weight lost regained within 2 years and nearly 80% regained in 5 years.<sup>18</sup> Weight loss may not be an absolute requirement for metabolic improvement in patients with NAFLD, as a number of dietary patterns were also found to be effective irrespective of weight loss.

**Diets of varied composition.** Given the multifactorial origin of NAFLD, whole food-based dietary approaches have been proposed for the management of its risk factors.<sup>7,20</sup> However, adherence to these dietary patterns can be challenging. Nonadherence of as high as 70% has been reported when regimens require lifestyle changes and the modification of existing habits.<sup>21</sup>

### Interrelation between liver and pancreatic diseases<sup>7</sup>





**A dietary toolbox for HCPs for the management of NAFLD**

Dietary approach	Advantages	Challenges
<b>Weight loss</b>	Less costly Weight loss effective	Adherence difficult —social, cultural, and psychological stressors —nutritional, economic, and lifestyle disruption
<b>Use of specific diets such as Mediterranean, DASH, low-fructose, or high-fiber diet</b>	These specific diets may be effective if maintained	—family support needed —hard to sustain —high incidence of rebound weight gain  Palatability and gastrointestinal issues
<b>Dietary supplements</b>	Potentially effective when used Adherence easy	Evidence still inconclusive  Costly  Inconsistency in supplement products  Ingredients not fully displayed on the label  Potential contamination  Low adherence to recommendations
<b>Functional or plussed foods</b>	Potentially effective when used Adherence easy	Evidence still inconclusive  Modestly costly  Accessibility issues  Appropriate selection of food products with minimal changes in taste and characteristics

Among the most studied dietary patterns is the Mediterranean diet for the treatment of NAFLD irrespective of weight loss.<sup>8,22,23</sup> Its success is mainly attributed to the diet’s beneficial fatty acid profile with a rich content of fiber and antioxidants.<sup>22</sup> However, a number of barriers were described including psychological, behavioral, and practical factors impacting the process of dietary behavior change and readiness and ability to adapt to the new dietary patterns.<sup>24</sup>

The Dietary Approaches to Stop Hypertension (DASH) diet was initially developed to treat hypertension.<sup>25</sup> Emerging studies have also shown a role for this diet in managing NAFLD, with greater adherence to the DASH diet resulting in less NAFLD risk and improved NAFLD-related metabolic status in patients with NAFLD.<sup>26,27</sup> As noted with the Mediterranean diet and as with any prescribed plan, long-term adherence to the DASH diet can be difficult.

Data from animal and human studies have implicated added sugars, particularly fructose, in the development of NAFLD. Dietary fructose reduction was found to improve markers of cardiovascular disease risk in adolescents with NAFLD, even in the absence of effects on hepatic steatosis.<sup>28</sup> Individuals’ preferences to the palatability of fructose may partly explain

difficulties in adhering to a low-fructose or fructose-free diet.<sup>29</sup>

Diets with higher fiber content have been proposed for protection against NAFLD; however, studies are still limited.<sup>30</sup> Several clinical trials reported improved liver health and metabolic parameters with increased fiber intake under energy restriction conditions.<sup>31,32</sup> One of the proposed mechanisms is the enrichment of gut microbiota generally seen with increased fiber consumption.<sup>33</sup> Industrialized populations appear to be intolerant to high amounts of fiber due to its gastrointestinal adverse reactions; however, tolerability seems to improve over time as gut microbiota adapts to a higher fiber intake.<sup>34</sup>

**■ Is there a role for dietary supplements against NAFLD?**

A number of dietary supplements were investigated for the management of NAFLD, and promising findings were reported, although studies in humans are still inconclusive. These supplements appear to provide anti-inflammatory benefits rather than exerting direct effects on the fatty infiltration of the liver.<sup>35</sup> To date, there are no dietary supplements with strong scientifically proven benefits for NAFLD.

Vitamin D, a critical factor in lipid and glucose metabolism and inflammation, negatively correlates with histologic severity of steatosis, necroinflammation, and fibrosis in patients with NAFLD who are deficient in vitamin D.<sup>36</sup> Despite these findings, supplementation studies have not all been promising, with few reporting improved hepatic steatosis.<sup>37,38</sup> Vitamin E supplementation improves levels of liver enzymes as well as histologic markers and resolution of steatohepatitis in patients with NAFLD, including those with NASH, via its suspected antioxidant properties, although effects on liver fibrosis are mixed.<sup>7,39</sup> Unsaturated fatty acids have shown effectiveness in the management of NAFLD biomarkers associated with hyperlipidemia.<sup>39</sup> Among unsaturated fatty acids, supplementation with omega-3 has shown the greatest benefits in children and adults with NAFLD, including those with NASH.<sup>40,41</sup>

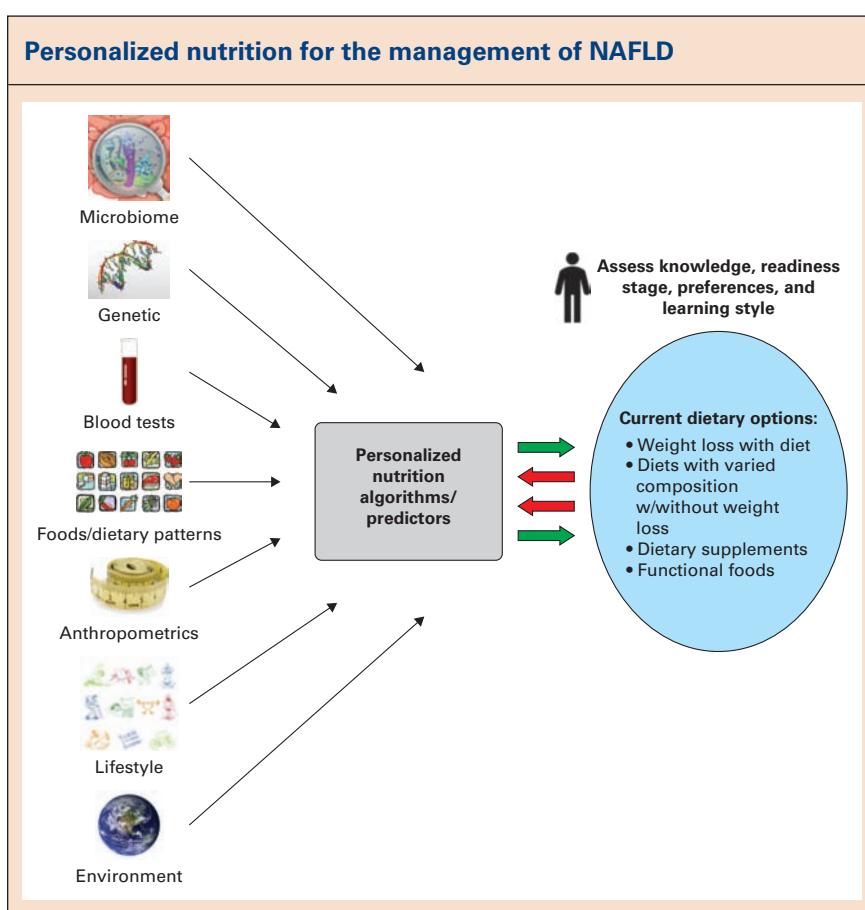
Consumers are generally drawn to dietary supplements because of their convenience and presumption of safety and efficacy (compared with pharmaceutical drugs).<sup>42</sup> However, dietary supplements are not as well regulated as foods and drugs.<sup>43</sup> Quality control standards for supplements vary by manufacturers, leading to inconsistencies in composition and purity.<sup>42</sup> Discrepancies between factual and claimed statements, claims not supported with scientific evidence, and cases of contamination are commonly reported.<sup>44,45</sup> Third-party organizations such as the American Botanical Council are doing extensive work on standards for confirming the active components of botanicals and supplements.

The bioavailability of nutrients is another key determinant of the effectiveness of dietary supplements, with larger doses of these nutrients possibly having negative effects on the absorption and metabolism of other nutrients and resulting in unpleasant adverse

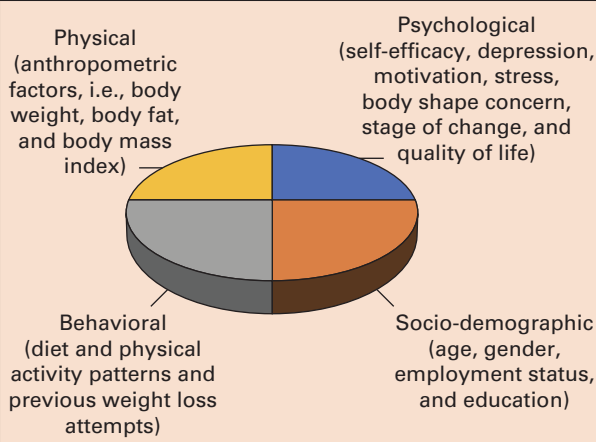
reactions.<sup>46</sup> Low compliance to long-term use of supplements has also been reported, partly due to misunderstanding of instructions, adverse reactions, and frustration about the frequency and number of pills to be taken.<sup>47</sup> Some supplement users may even have the fear of being labeled as sick.

### Emerging role of functional foods in the management of NAFLD

Functional foods, also known as plussed foods, have emerged as an easier-to-implement approach for the management of NAFLD. Functional foods are defined as “whole foods along with fortified, enriched, or enhanced foods that have a potentially beneficial effect on health when consumed as part of a varied diet on a regular basis at effective levels.”<sup>39,48</sup> Although often used interchangeably, functional foods are different from medical foods, which are formulated for the management of a disease and prescribed by physicians.<sup>49</sup> Functional foods are a dynamically developing segment of the food industry given consumers’ increased interest in foods with health benefits as a means of taking



**Factors affecting long-term adherence to weight management programs<sup>19</sup>**



greater responsibility for their own well-being.<sup>48</sup> Two-thirds of US grocery shoppers have reported purchasing a food/beverage specifically to address a health concern.<sup>50</sup> Many functional foods can alter the gut microbiome, which in turn can increase natural anti-inflammatory substances in the body, potentially conferring beneficial effects on the liver.<sup>51</sup>

A number of functional ingredients were explored for the management of NAFLD, including antioxidants, anti-inflammatory agents, and probiotics. Polyphenols like curcumin, resveratrol, and quercetin were reported to exert beneficial effects on metabolic parameters in patients at risk for or with NAFLD.<sup>52-54</sup> Other plant-based foods such as milk thistle and black pepper (piperine) were also investigated.<sup>55,56</sup> Given the growing evidence linking NAFLD to gut microbiota, probiotics have been suggested as another treatment option for NAFLD and NASH.<sup>57</sup> In fact, dysbiosis has been reported in 60% of patients with NAFLD and is suggested to activate the release of inflammatory cytokines.<sup>58</sup> In clinical trials on patients with NAFLD, supplementation with probiotics improved liver enzymes and reduced hepatic fat infiltration.<sup>59,60</sup> Health claims on probiotics are not strictly regulated, however, leading to misunderstanding as mechanisms of action vary among different species and strains of microorganisms.<sup>61</sup>

Besides the cost, the complexity of product development, and the technologic and regulatory obstacles, consumers' acceptance of functional foods is essential for benefits to be realized.<sup>62</sup> Scientific research establishing the bioavailability and clinical efficacy of

functional ingredients at levels that are physiologically achievable under typical dietary patterns is needed.<sup>48</sup> The interactions between nutrients and nonnutrients within the food matrix may impact the bioavailability of the functional nutrients; thus, the selection of an appropriate product for delivery of functional ingredients is important.<sup>63</sup>

Overall, there is still no conclusive evidence on the effectiveness of dietary supplements and functional foods in the management of NAFLD especially over the longer term.

**Personalized nutrition for the management of NAFLD**

HCPs play a central role in the management of NAFLD. Adopting a number of teaching tools aimed at improving patients' understanding of the disease and its risks as well as the importance of following dietary advice and its role in disease regression is critical.<sup>64</sup> Healthier nutritional behavior among patients with NAFLD is associated with a better understanding of the disease, trust in the efficacy of dietary approaches, and higher self-efficacy.<sup>65</sup>


HCPs should engage in a patient-centered personalized nutrition counseling approach, involving family members when possible to gain support and avoid conflicts. General dietary recommendations should not be given as each person is unique and may react differently to the same foods.<sup>20</sup> We recommend designing personalized diets for patients with NAFLD based on their family history, physiology, lifestyle, diet, and environment, and assessing their learning styles and preferences before integrating them into specifically designed plans that can predict individual responses to different dietary approaches (see *Personalized nutrition for the management of NAFLD*).

**Conclusions and recommendations**

Dietary modifications can be a key factor in the management of NAFLD and prevention of progression to its more severe conditions like NASH, hepatic fibrosis, and cirrhosis. This review offers a unique dietary toolbox for HCPs to explore with patients for personalized and effective management of NAFLD.

While ensuring that the key elements of a patient-centered counseling approach are in place, our recommendations to HCPs are as follows (see *Recommendations to HCPs when managing patients with NAFLD*):

1. Educate on NAFLD pathophysiology, risks, and risk factors.

2. Review existing dietary options for treatment.
3. **SHARE** in decision-making (**Seek** the patient's participation, **Help** provide options, **Assess** patient values, preferences, and risk tolerances, **Reach** a decision with the patient, and **Evaluate** in an ongoing fashion).
4. Define **SMART** (specific, measurable, achievable, realistic, and timely) goals.
5. Plan follow-up sessions to ensure long-term sustainability. 

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Lippincott Professional Development will award 1.5 contact hours for this continuing nursing education activity. Lippincott Professional Development is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 1.5 contact hours. Lippincott Professional Development is also an approved provider of continuing nursing education by the District of Columbia, Georgia, and Florida, CE Broker #50-1223. Your certificate is valid in all states.

**Payment:** The registration fee for this test is \$17.95.