Adenocarcinoma of the colon and rectum is a disease of considerable proportions that affects more than 100,000 adults in the United States each year [1]. This incidence is second only to cancer of the skin, and its resultant mortality is second only to cancer of the lung [2]. Unfortunately, with the possible exception of Turnbull’s no-touch technique, there has been no real improvement in survival during the past three decades [3]. Surgical treatment has been suboptimal with about 80% of patients being resectable, but less than one half of this group are cured. Survival is related closely to stage of disease at time of therapy, and the only improvement has come from earlier detection and improved peri-operative care. The five year survival rates of patients based upon the Dukes’ classification of their disease generally range from 75 to 90% for Dukes’ A; from 45 to 65% for Dukes’ B and from 25 to 35% for Dukes’ C lesions; with those patients having distant metastases (Dukes’ D) rarely surviving 5 years [3]. Even these figures are optimistic since the gross survival of large mixed populations is somewhat less. Of 1687 patients with colon cancer at Charity Hospital in Louisiana, the determinate 5 year survival was only 23% and the gross survival only 17% [4].

The majority of these patients die from residual, recurrent or metastatic disease. In addition, the incidence of multiple or second colon primaries ranges from 0.2 to 12% [4, 5] and the incidence of multiple organ primaries ranges from 11 to 56% [4]. The postulated mechanisms for development of recurrence include: 1) development of a metachronous primary lesion; 2) presence of an overlooked synchronous lesion; 3) inadequate resection with continued growth and; 4) implantation at the site of the anastomosis [5]. Unfortunately, in patients with advanced disease, there exists no single or multidrug regimen which is capable of significant tumor regression with improvement in survival or quality of life [8].
Thus, when Gold and Freedman [9] identified an antigen (called carcinoembryonic antigen – CEA) in 1965 that appeared to be ‘tumor-specific’ for colon cancer, there was great enthusiasm that this would herald a new era of earlier diagnosis both of primary lesions and recurrent tumors. This was further heightened by the development of a radioimmunoassay [10] that could detect serum levels of circulating CEA. The criteria for clinical usefulness of such an antigen were described by Lawrence [1] and included: 1) the antigen or tumor product must pass from the tumor into body fluids; 2) the more tumor- or tissue-specific the antigen is, the more useful it will be; 3) serum levels of the antigen should bear some relationship to the amount of tumor present; and 4) the assay should be reproducible by routine techniques. Although the CEA has met these criteria at least in part, Goldenberg stated at the First International Conference on the Clinical Uses of CEA, that since its discovery, we have come to realize that no tumor antigens are truly tumor-specific but rather are tumor-associated. Further, despite all the activities and publications from research on CEA, many of the basic issues facing the practitioner regarding the interpretation of CEA results are still not resolved [1]. It is our goal to address these various issues regarding CEA, review the data in order to provide answers where they exist and, more importantly, to focus and direct further investigation in those areas where answers are unknown.

2. CEA-SUBSTANCE

Carcinoembryonic antigen (CEA) was first described by Gold and Freedman in 1965 [9] as a tumor-specific antigen contained in pooled tumor extracts but not present in normal colonic tissue. Its name was derived when it was also noted to be present in the gut and digestive organs of embryos and first and second trimester fetuses. Since that time, further studies have defined, categorized and quantified it in various organs, tumors and disease states [6, 9, 10, 12-17]. To summarize, CEA is a typical acid glycoprotein of molecular weight approximating 200,000 and is about 50% carbohydrate. It exhibits beta-globulin electrophoretic activity and has a sedimentation coefficient of 7.0–8.0 S. Using electron microscopy, it is of uniform size with a complex secondary structure, and even highly purified preparations of CEA manifest a degree of both intermolecular and intramolecular heterogeneity.

CEA is a peripheral membrane glycoprotein within the fluid mosaic of the cell membranes in which it is found. It is indigenous to the cancer cell and not simply absorbed or interiorized by these cells. From this site on the cell surface, it is easily released into surrounding body fluids. Once in circulation, it is rapidly catabolized and serum values fall to undetectable levels within 2–14 days postoperatively. All Animal studies suggest that the liver is the