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## C-Reactive Protein

### Potential Significance of Quantitation in Patients with Chronic Diseases\*

Hajime Hayashi, Ph.D.\*\* and Gerald A. LoGrippo, M.D.\*\*

**Serum C-reactive protein (CRP) levels in 351 patients with certain chronic diseases were assayed by a micro-double immunodiffusion technique developed and used in this hospital. Elevation of CRP values and severity of disease were evident in the following clinical entities: 31 of 54 patients (57%) with liver cirrhosis; 122 of 204 (60%) hepatitis patients; 34 of 52 (65%) patients with gastro-intestinal surgery; 8 of 21 (38%) uremic patients; and all of 20 patients with renal transplantation. There was good correlation between markedly elevated serum CRP values and degree of inflammation and/or physiologic stress during clinical course and recovery.**

Serum C-reactive protein (CRP) offers an important index in evaluating patients with a wide variety of diseases, especially acute and chronic inflammatory conditions. Although the biologic nature of CRP in clinical disease is incompletely known, numerous investigators have emphasized its significance as an index to persistent inflammation and physiologic stress when

other tests for residual inflammation return to normal.<sup>1-8</sup>

A quantitative method for assaying CRP levels in serum (on a mg per cent basis) was developed in our laboratory.<sup>9</sup> Our micro-double immunodiffusion technique was applied to serum specimens from patients with varied pathological conditions. It offers another parameter in the battery of tests for evaluating the immunologic status of patients with chronic diseases.<sup>10-13</sup> Other tests employed for immunologic status of the individual are serum immunoglobulins (IgG, IgA, IgM and IgE) complement (CH<sub>50</sub> and Beta-<sub>1C/1A</sub> globulin); and antibody responses to common micropathogens

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TABLE I

SERUM C-REACTIVE PROTEIN LEVELS  
IN VARIOUS CLINICAL ENTITIES

Clinical Entity	Total Tested	Percent of Patients with:	
		1 - 10 mg%	> 10 mg%
Normal*	750*	5.5 %	0 %
Liver Cirrhosis	54	41	17
Virus Hepatitis	204	40	20
Gastro-intestinal Surgery	52	23	42
Uremia	21	33	5
Kidney Transplant.	20	25	75

\*95 percentile of normal showed less than 1 mg %

(10 enteric and several upper respiratory viruses, 3 gram-negative enteric bacteria, staphylococci and two toxoids).<sup>14,15</sup>

The purpose of this presentation is to discuss the potential significance of the quantitation of CRP in certain particular chronic diseases.

#### Materials and Methods

Serum specimens were obtained from 351 patients with a variety of chronic conditions, and kept sterile during collection and storage until quantitation of C-reactive protein was performed using our technique. For controls, we used 750 blood bank

donors to represent a supposedly healthy population.

Elevation of serum CRP levels greater than one mg per cent was considered to have clinical significance since only 5.5% of the 750 blood bank donors fell into this range of serum values.

#### Results

The 351 patients studied included 54 with liver cirrhosis; 204 with viral hepatitis; 52 undergoing gastro-intestinal surgery; 21 uremic patients; and 20 who had received kidney transplantation. The clinical conditions reported here comprised those disease entities which warranted serial serum

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studies and offered an adequate follow-up of serum specimens for this evaluation. The data, as summarized in Table I, are divided into two columns (1-10 mg per cent and greater than 10 mg per cent) to emphasize the degree and variation of CRP levels found among the respective clinical entities.

In cirrhosis of the liver, 41% of patients had 1 to 10 mg per cent serum values of CRP; whereas 17% showed 10 mg per cent or greater values, making a total of 58% who had CRP values above the normal controls. Among 204 patients with viral hepatitis, we found a range of CRP values similar to those with cirrhosis. Among patients with gastro-intestinal surgery, 42% showed elevations above 10 mg per cent with frequent rises above 100 mg per cent. Only 5% of the uremic patients had elevated CRP values above 10 mg per cent whereas 75% of those having kidney transplantation had CRP values above 10 mg per cent.

The data indicated that the severity of the clinical condition usually correlates well with fluctuations and marked elevations of serum CRP levels. This is exemplified in Figure 1 which lists CRP levels in uremic patients measured (a) during uremia, (b) after nephrectomy and chronic dialysis, and (c) after renal transplantation. Six examples among 20 patients are plotted to show two extreme trends. The sera of three patients (KT-1, KT-3 and KT-4) revealed relatively low or undetectable CRP levels in the routine assays over a 3-year period of study. Although elevations of CRP were seen on occasion, such as after surgery, the levels returned to normal during the usual recovery period. This seemed

to correlate well with the uncomplicated course of recovery. Three other patients (KT-2, KT-9 and KT-13) had persistent elevated serum CRP levels. In two of these, the serum values increased to 70 mg per cent or greater, (KT-9 and KT-13) and these high CRP levels persisted until death.

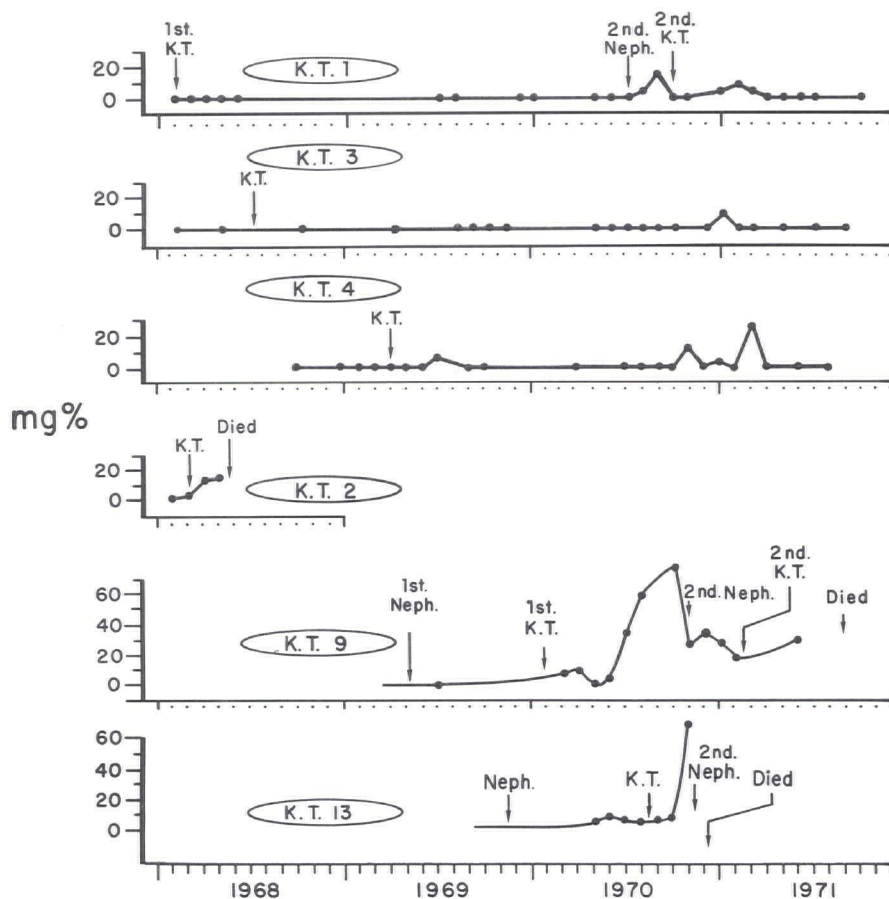
### Discussion

As emphasized in our previous publication,<sup>9</sup> the micro-double immunodiffusion technique has the following advantages over the capillary tube method for CRP determinations: (1) differentiation and identification of the specific, precipitable reactant (CRP) from non-specific precipitable reactants which are inclusive in the values obtained with the tube method; (2) increased sensitivity; and (3) quantitative values expressed in mg per cent for a specific protein (CRP) in lieu of total precipitation expressed in millimeters by the capillary tube method.

The advantages in the improved method should reassure the clinician of the value of these measurements for CRP in chronic diseases. The tube method frequently gives false positive values and has the disadvantage of limited quantitation (a maximum of 6 plus in total tube precipitation). The degrees and variations of serum CRP values in mg per cent appear to reflect the degree of inflammatory stress upon the host in certain disease states, as well as revealing unresolved inflammation when other tests return to normal. Moreover, unusually high and persistent elevations of CRP (values above 70 mg per cent) suggest a critical state of inflammation or physiological stress. Good correlation was found between



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**Figure 1**

serum CRP values and inflammatory stress during the clinical course and recovery period of the diseases evaluated.

**Conclusion**

Serum levels of CRP in various clinical pathologic settings were studied. Quantitation of these values seems to have an additional advantage over the tube precipitation method in general

use. We found particularly interesting the markedly elevated serum levels of CRP in patients experiencing failure of kidney transplants. Multiple parameters<sup>14,15</sup> are used in an attempt to evaluate rejection crisis in these patients, and the CRP may well be a worthwhile test to add to the battery of tests presently used to evaluate this problem.

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