Experimental Investigation of Immuno Suppression and Exolitonic Dynamics in Thermal Burns Afflicted with Pseudomonas Aeruginosa and Klebsiella

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Summary

In a systematic analysis of serum immunoglobulin levels in 50 burned patients and 20 normals, we have studied the time dependence of IgG, IgM & IgA for different values of burned surface area. Variation of these immunoglobulins is also studied as a function of the burned surface area (A_b) within the first 24 hours after the burn injury. Several terminal cases are also included in the present study. Immunosuppression process is found to be neither linear nor exponential. Dynamics of exolitons appears to be most pronounced within the domain $40 \leqq A_b \leqq 70$.

Introduction

Alterations in the host immune system due to thermal burn injury were reported earlier by Keeling et al. (1979). It has been seen that thermal injury leads to tissue damage, impairement of integument barriers inflammatory reactions, depression of neutrophils and the action of exogeneous antigen. Host immune response is influenced by a series of factors such as extent of burns, depth, age, presence and absence of infections, type of treatment etc. (Antia et al. 1977). The susceptibility of the burned patient is increased by many factors

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like, open wound, increased metabolic requirements, decreased nutritional intake, loss of plasma protein and suppressed immune defence mechanism (Leguit et al., 1973). Still infection continues to be a leading cause of death. It was reported that 75% of all burn mortality is due to infection (Polk, 1979). The normal response is reflected in terms of gammaglobulins (Munster et al., 1970). Miller (1979) studied the impact of thermal burn injury elevated by suppressor cell activity associated with impaired host defenses in many critical situations involving intracellular parasites. Some globulins levels of IgG, IgA and IgM have signficant antibody activity against microorganisms (Fried et al., 1975). Arturson et al. (1969) reported that the changes of values of all immunoglobulins decrease after burn, but return to normal level during first and second week. Kohn and Cort (1969) published similar observations regarding these changes with the extent of burn injury. Munster (1970) reported that levels of IgM and IgA remained relatively unaltered. Efforts to correlete changes in gammaglobulin levels with wound infection or severity of trauma have given contradictory results (Arturson, 1969, Ninnemann et al., 1979, Heideman et al., 1979). Munster (1970) reported the elevation of the IgM level in the patients with fungal infections following burn injury. To obtain more detailed information regarding immunological alternations we have measured changes in 50 burn cases, including 20 healthy individuals and 30 patients with partial thickness burns. The normal value of IgG lies in the range of 1060–1370 mg/dl. whereas normal values for IgM and IgA were found to be in the range between 90–150 mg/dl and 120 – 300 mg/dl respectively. The object of our work was to investigate the changes due to Gram–negative bacterial infection with the extent of burn, time elapsed after the burn injury and to investigate the dynamics of exolitons at higher burned surface areas.

Materials and Methods

Fifty burned patients admitted to the Department of Burns of Safdarjung Hospital were studied. All the patients were given antibiotic treatment and electrolytes along with topical therapy. There were sixteen females and thirty four males in the series within the age group of 5–50 years. The extent of burns surface area (A_b) varied from 20 to 90%. Blood samples were drawn on admission day and at 3rd, 5th, 7th, 9th, 11th, 13th and 15th day of post burn injury. Samples were immediately centrifused and studies were carried out with serum. Determination of the concentration of IgG, IgM and IgA were carried out using radial immunodiffusion Tripartigen plates. Each of these plates was checked by comparing the immunoglobulin levels using plates obtained from different sources.

Normal samples were collected from twenty non burned plastic surgical patients undergoing operations. Attempts were made to separate results on the basis of age groups and infections.

Results and Discussion

The profiles of the immunoglobulins changes are depicted in Fig. 1 and Fig. 2. Fig. 1 shows variation of IgG with the number of days after burn injury. It can be observed that A_b plays significant role on these variations of Immunoglobulin. We see that IgG level falls abruptly on the 1st day to the level ranging from 200 to 600 mg/dl as A_b varies between 30 to 90%. In all the cases IgG decreaes till the 3rd day. Two fatalities occured on the 3rd day as level fell down to range between 100 and 150 mg/dl which is about 10% of the normal value. Our results are in line with those reported by Zeliner et al. (1977) about the patient with fatal outcome. Generally we noticed a gradual fall till fifth day. In the cases infected with Gram-negative bacteria such as Pseudomonas aeruginosa and Klebsiella having $30 < A_b < 45$, IgG starts increasing gradually. It may be the positive indications of the immune response of the patients. In the first week we again observed death of a patient with IgG value equal to 250 mg/dl. In the case of surviving patients we see shooting up pattern on 1st and 2nd week till the level reaches the normal range which starts from the first week. Fig. 1(a), shows the consistency in the values of IgG of patient who eventually died when compared with those of the survivers. We found a dangerous zone for the infected patients with $A_b > 60$ lying between 100-300 mg/dl.

Fig. 1(b) shows the pattern adopted by immunoglobin M. No significant difference in results was odserved on the first day when comparison was made with the range of normal Indian helthly subjects. Profound and steep drop in concentration down to level of 67-77 mg/dl was observed in the cases with fatal outcome on 3rd day. In the other cases with $60 < A_b > 30$, we observed a gradual rise in the IgM. level. This considerable rise may be due to endotoxin response of the Gram-negative infection as reported by Rapport et al. (1976). A significant feature observed by us was the sudden drop in the IgM level of the patient with fatal outcome which is the clear contradiction of the previous work done by Ninnemann (1978). No predicted elevation in serum IgM level was observed in the patients with large injury. Fig. 3 shows the behaviour of IgA, again we see slight decrement in the level on the 3rd day, we report here the dangerous zone for IgA ranging between 110-166 mg/dl. No significant difference was observed in the serum IgA concentration of non-infected patients. In the case of

patients with A_b lying between 40 to 45%, IgA values fall gradually till the first week after which pattern reverses with the gradual increase till 2nd week. Arturson (1969) reported previously that the fall of immunoglobulin level is maximum on the 2nd day post burn, but we observed the maximum fall in the levels on the 3rd day with the proliferation of infection caused by the growth of Gram-negative species particularly Pseudomonas aeruginosa and Klebsiella in our studies. The fatalities occured on the third day may well be connected with the depressed immune response of the patient leading to splitting of the IgG molecules as observed by Grzybowski (1977) and due to the mechanical leakage from the burn wound. It was noticed that greater the area affected more pronounced is the decrease of gammaglobulins. No significant changes were observed in the IgM and IgA concentration in case of patients with A_b lying between 30-45% when compared with those of normal subjects. It shows that in the infected burned patients IgA and IgM antibodies respond poorly. Our report of low serum concentrations of IgG agrees with the findings of (Fedonov 1978) which may be due to the collapse of the immune response of the patient leading to death. The behaviour of gammaglobulin when studied with Gram-negative bacterial infection shows its relation with the dynamics of immunoglobulin synthesis and its break down. The active participation in the synthesis leads to the healing of the wound as noticed clinically in cases which are significantly away from post-dangerous zone.

Conclusion

From the foregoing it follows that humoral immunity in the host against infection collapses and produced B lymphocytes and their plasma cell progeny specific antibodies directed towards bacteria and their product fails to set right the immune response of the patient. The present work shows the significant role of Gram-negative bacteria on the host defence mechanism compared to the results of earlier works. We were able to identify the dangerous zone for each of the immunoglobulin which is found to be lying in the range 90-310 mg/dl for IgG, 110-140 mg/dl for IgA and 67-85 mg/dl for IgM with $60 \geqq Ab \geqq 90$ Severity of the burn is found to be related with the decrease in the values of immunoglobulins (Scandov, 1978). We find very interesting features in our study on the variation of IgG, IgM and IgA with A_b Fig. 2 (a, b, c). To our great surprise we found that the immunoglobulin levels fall with A_b neither linearly nor exponentially. We would like to stress that the points shown in Fig. 2(a) - (c) are averages of all the identical cases studied by us. The region $40 \leqq A_b \leqq 70$ is a representative of the mechanism involving the role of immunoglobulins in perturbed situations. Our earlier work has shown that around 40% value

of A_b electrical properties of burned tissues change. It appears that within this domain the perturbation energy imparted by causative factors is capable to affect the dynamism of Davidov solitons. In addition it is also possible that we may have a short-lived exoliton in this region. Exolitons seem to vanish when the burned surface area becomes greater than 70%. Our conclusions are strongly supported by our ESR, dielectric, conductivity and loss factor measurements. (Aryal, et al. 1984).

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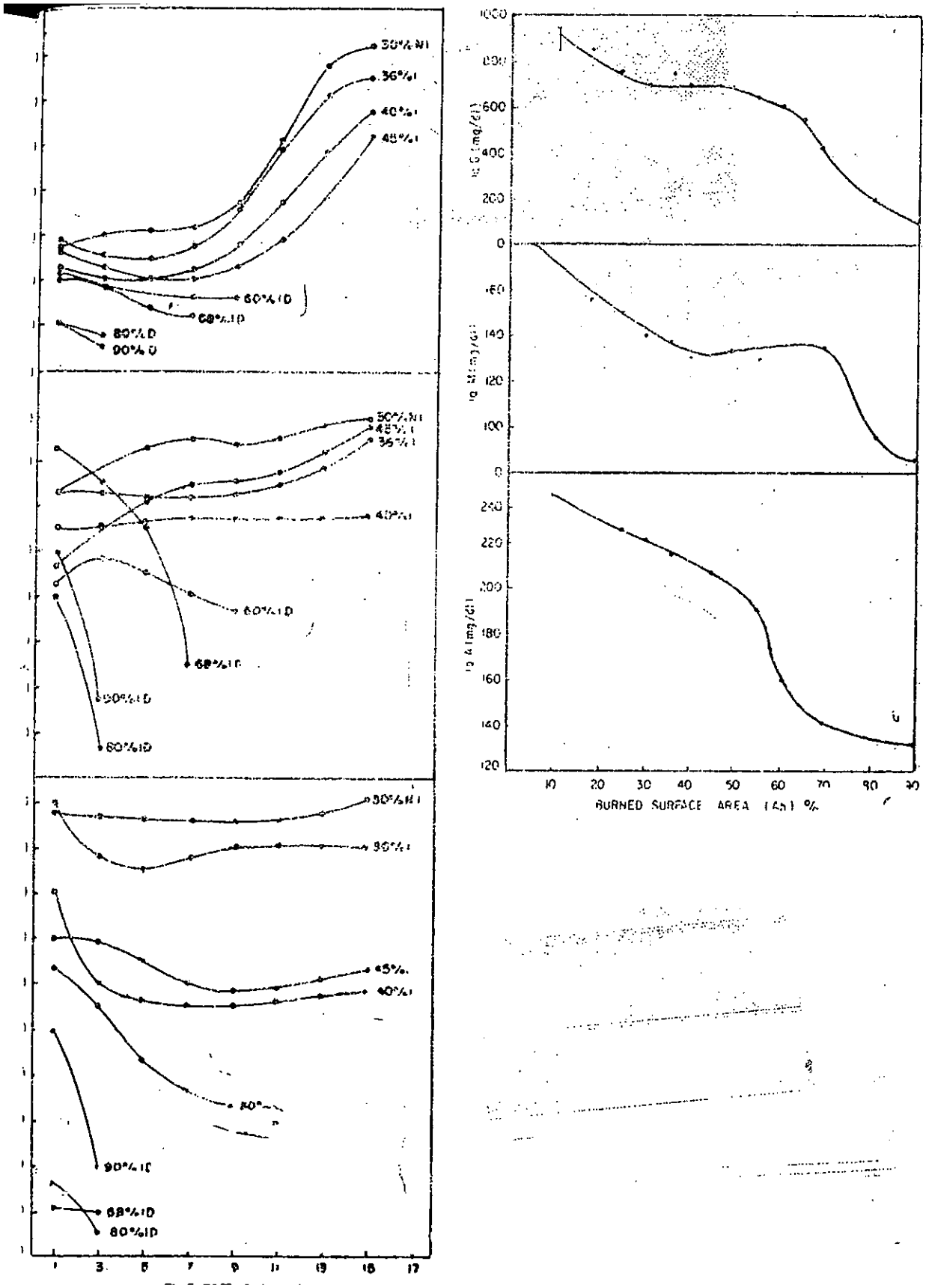
Figure Captions

Figure 1

Time dependence of (a) IgG (b) IgM & (c) IgA patients ($30 \lesssim A_b \lesssim 90$) having the well established infection due to Pseudomonas aeruginosa and Klebsiella. 'D' stands for 'died' and I. stands for 'infected'.

Figure 2

Variation of (a) IgG (b) IgM & (c) IgA with the burned surface area (A_b). Every point is the average of the data collected at that particular value of A_b.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