Anti-B-Cell Monoclonal Antibody-Purged Autologous Bone Marrow Transplantation for B-Cell Non-Hodgkin’s Lymphoma: Phenotypic Reconstitution and B-Cell Function


In the present report we have attempted to examine immunologic reconstitution following high-dose chemoradiotherapy and anti-B-cell monoclonal antibody (MoAb)-purged autologous bone marrow transplantation (ABMT). By cell-surface phenotypic analysis, the majority of patients had normal percentage of natural killer cells (NK), monocytes, and CD8+ T cells at one month post-ABMT. In contrast, the percentage of CD4+ T cells was reduced for at least 3 years, and the CD4:CD8 ratio reflected this imbalance. B-cell reconstitution was slightly prolonged, with normal percentage and absolute numbers of CD20+ B cells evident by 3 months. Although B cells returned by 3 months, in vitro assessment of B-cell function demonstrated impairment of proliferative responses to either anti-immunoglobulins bound to beads (anti-Ig), Epstein-Barr virus (EBV), or interleukin-2 (IL-2) for approximately 1 year and low molecular B-cell growth factor (BCGF) for approximately 2 or more years. Moreover, in vivo B-cell reconstitution demonstrated a more selective defect, with normal levels of immunoglobulin IgM returning at 6 months, IgG at 12 months, and IgA after 2 years. Despite normal numbers of B cells and relative normal levels of Ig early following ABMT, our in vitro data suggest an intrinsic defect in B-cell responsiveness. Moreover, these defects are similar to those observed following nonpurged autologous and allogeneic BMT, although the interval of immune impairment appears more prolonged.

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described. Of the 99 patients transplanted, cells were available in 79 patients. In 377 blood samples from these 79 patients, we studied the median time to recover normal percentages of B cells by expression of the CD20 antigen (Ag); of T cells by analysis of the CD3, CD4, and CD8 Ag; of natural killer cells (NK) by NKH1; and of monocytes by CD14 Ag. For these Ags and for the CD4/CD8 ratio, the time was calculated from bone marrow reinfusion to the first achievement of the lower bound of normal or the last recorded value below the normal. Normal values are between 5% to 10% for the CD3 Ag; 15% to 30% for the CD8 Ag; 10% to 20% for NKH1; and 15% to 30% for CD14 Ag. We also studied the percentage of expression of these Ags over time. The median percentage at different times after ABMT has been calculated by pooling all patients with phenotypic data available at the corresponding period.

The absolute numbers of B cells have been calculated. Normal values for white blood cells (WBC) are 4,800 to 10,800 cells/μL, of which 20% to 40% are lymphocytes, and of these, 5% to 10% are B cells. Therefore we considered normal an absolute number of B cells between 60 to 400 cells/μL, which is a lower value than others used.

**B-cell proliferation assays.** B-cell function studies were carried out in 66 patients without signs of infection or relapse. PBMC were isolated freshly and on the majority of patients seen in the follow-up from January through July 1988 (106 samples). In addition to these, 50 cryopreserved specimens of PBMC were analyzed. In 21 samples from 13 healthy volunteers we did not find significant differences in the stimulation of fresh or frozen cells, and therefore the results obtained with 50 frozen samples are analyzed together with the 106 samples of fresh cells. For studying function over time, the following groups have been considered: 17 samples of 17 patients before ABMT, 32 samples of 26 patients at 1 to 3 months after ABMT, 17 samples of 15 patients at 4 to 6 months, 25 samples of 23 patients at 7 to 12 months, 25 samples of 21 patients at 13 to 18 months, 18 samples of 16 patients at 19 to 24 months, 10 samples of 9 patients at 25 to 36 months, and 12 samples of 9 patients later for a total of 156 samples. Most of the patients were studied one or two times, 7 patients were studied more than five times. PBMC, 1 × 10^6, were cultured per well as previously described. Results are presented as stimulation indices (SI; i.e., the ratio obtained by dividing the median cpm of the stimulated triplicates by the unstimulated). All lymphokines, including interleukin-2 (IL-2; gift of Biogen, Cambridge, MA) and B-cell growth factor (BCGF; Cellular Products, Buffalo, NY) were added at the minimal concentration needed to obtain nearly maximal proliferation in controls. B cells were activated with antihuman Ig bound to beads (anti-Ig) as previously described. To evaluate the synergistic effect of these lymphokines on the B-cell population only, the SI obtained with IL-2 or BCGF alone has been subtracted from that achieved with the combination of these lymphokines with anti-Ig (anti-Ig + IL-2 or anti-Ig + BCGF). Therefore the SI we calculated is B-cell specific and can be considered synergistic.

Stimulation with Epstein-Barr virus (EBV) was carried out on enriched B cells of 41 patients and 9 controls after T-cell depletion by sheep red blood cell (RBC) rosetting to eliminate the suppressive effect that CD8+ cells exert on EBV-infected B cells. Serum immunoglobulins. Determination of immunoglobulin (Ig) G, M, and A levels have been possible for the 98 samples in which concomitant in vitro studies were performed: 11 before ABMT, 22 at 1 to 3 months, 11 at 4 to 6 months, 19 at 7 to 12 months, 15 at 13 to 18 months, 8 at 19 to 24 months, 4 at 24 to 36 months, and 8 after 3 years. Values between 800 and 1,800 mg/dL for IgG; 90 and 450 mg/dL for IgA; and 60 and 280 mg/dL for IgM are considered normal.

**Statistical analysis.** Considering the number of tests and the fact that many of the tests are not independent, the P value for significance was reduced with a Bonferroni adjustment to reduce the chance of type I error (false positive). Differences between controls and patients have been evaluated by the Wilcoxon Rank Sum procedure with an α-level for significance of 0.06. Plots of recovery and median times to recovery were estimated by the method of Kaplan and Meier. Proliferation studies similar to ours considered results below one third of the control value to be abnormal. We have indicated this cut-off on the scattergrams of the results of these studies. Along with median values, the tables of the results of the proliferation studies give the interquartile range (QR); these are the values that mark 25% and 75% of the observed data (remembering that the median is the 50% point) and are an indicator of the dispersion useful and appropriate when data do not have a symmetrical (“normal”) distribution.

**RESULTS**

**Phenotypic analysis of reconstituting peripheral blood mononuclear cells.** As seen in Fig 1a, approximately 50% of patients recovered normal percentages of NK cells and monocytes within 1 month following ABMT. By 3 months, 75% of these patients have reconstituted normal percentages of NK cells and monocytes. T-cell repopulation was severely delayed. Although 25% of the patients achieved normal percentage of CD3+ cells by 1 month, only 50% reconstituted CD3+ cells at 3 months, which did not markedly increase at 9 months (Fig 1a). From 1 month to 23 months the median percentage of NKH1+ cells and CD14+ cells was within normal limits, whereas the percentage of CD3+ cells remained low (Fig 1b).

Figure 1c and d examines the recovery of CD4+ and CD8+ cells. Nearly 70% of patients recovered CD8+ cells by 1 month, and 90% achieved normal percentages at 3 months (Fig 1c). In contrast, only 14 of 79 patients recovered more than 40% of CD4+ cells at a median follow-up of 24 months. The median time to recover a normal percentage of CD4+ cells is estimated to be at least 3 to 4 years. The CD4/CD8 ratio was therefore reversed for the same period of time. Figure 1d demonstrates that during the first year this reversed CD4/CD8 ratio was a consequence of both the low percentage of CD4+ cells and the high percentage of CD8+ cells. CD4+ cells began to recover after 6 months following ABMT but remained lower than normal for more than 2 years. In contrast, the percentage of CD8+ cells began to decrease by 1 month and was normal by 12 to 18 months.

Figure 1e examines the recovery of B cells. The first CD20+ cells were detected by 1 month, whereas 50% of patients recover normal percentage of B cells at 3 months (Fig 1e). By 9 months 63 of 79 patients had normal percentage of CD20+ cells, and this figure remained constant over 2 years following transplantation. Only one third of the patients had abnormally low or high percentage of B cells from 6 to 24 months post-ABMT (Fig 1f). As shown in Fig 2, only 5 of 14 patients had more than 60 cells/μL prior to ABMT. There were 7 of 26 patients at 1 to 3 months post-ABMT, and 8 of 12 patients had normal numbers of B cells at 4 to 6 months. After 6 months 47 of 62 samples...
RECONSTITUTION AFTER AUTOLOGOUS BMT IN NHL

Fig 1. Phenotypic reconstitution of PBMC following ABMT. (a) The probability of recovering normal percentage of CD3⁺, NKH1⁺, and CD14⁺ cells during the first 9 months following ABMT. (b) The median percentage of CD3⁺, NKH1⁺, and CD14⁺ cells from 1 to 23 months post-ABMT. (c) The probability of recovering normal percentage of CD4⁺ cells and CD8⁺ cells and the CD4:CD8 ratio during the first 9 months following ABMT. (d) The median percentage of CD4⁺ and CD8⁺ cells from 1 to 23 months post-ABMT. (e) The probability of recovering normal percentage of CD20⁺ cells during the first 9 months after ABMT. (f) The median percentage of CD20⁺ cells from 1 to 23 months post-ABMT.

Fig 2. The absolute number of CD20⁺ cells for controls (C) and patients before (P) and after ABMT. The normal range of absolute numbers is depicted between the two horizontal lines (80 to 400 B cells/μL).
demonstrated normal absolute numbers of CD20+ B cells, and only few were below the normal range after 12 months.

**In vitro analysis of B-cell function.** Human B lymphocytes can be specifically activated via cross-linking of anti-Ig. As seen in Fig 3, the median anti-Ig–induced SI of mononuclear cells from normal control donors was 5.3 (QR 2.7 to 8.3). In contrast, prior to ablative treatment but following conventional induction therapy, the SI was severely depressed, with a median SI of 1.0 (QR 1 to 1.6). During the first 6 months following ABMT, the lack of proliferation in response to anti-Ig persisted (median SI 1.2 to 1.4). At 12 months the median SI increased to 2.1 (QR 1.4 to 5.6). By 18 months the SI approached low normal, and the majority of patients exhibited normal SI thereafter (Fig 3). The comparison of SI of controls and patients prior to and during the first 6 months post-ABMT was significant at a level of .006.

To ascertain if the low SI observed early after ABMT was due to the low number of B cells present in the peripheral blood or to an intrinsic defect in B-cell activation, we examined the SI of those patients who had normal numbers of B cells. During the first 3 months an SI greater than 3 was observed in only 2 of 7 patients with more than 60 B cells/μL. Between 3 and 6 months, 4 of 8 patients with normal numbers of B cells exhibited a normal SI. In fact, there was no correlation between total number of B cells and anti-Ig–induced SI when the entire population of controls and patients was examined (correlation coefficient = .121).

After activation with anti-Ig, B lymphocytes become responsive to cytokines, including low or high mol wt BCGF or IL-2, which amplify their proliferation. To examine this phenomenon, PBMC were activated with anti-Ig and cocultured simultaneously with either BCGF or IL-2. As seen in Fig 4, after culture of PBMC with anti-Ig and BCGF, the median SI from normal controls was 12.6 (QR 7.5 to 17.5). As was observed for anti-Ig alone, PBMC from patients prior to ABMT and during the first 6 months thereafter did not incorporate 3H-TdR (SI 1.0). Between 7 and 24 months, the median SI gradually increased. However, the SI for the majority of patients never returned to the lowest normal levels seen in controls (one third of the median SI). Except for the interval from 19 to 24 months, the SI of patients compared with controls was significantly reduced (P < .006). Following culture of PBMC with anti-Ig and IL-2, the median SI for controls was 6.9 (QR 3.4 to 20.4). Prior to ABMT and during the first 3 months thereafter, the median SI was approximately 1.0 (Fig 5). This value increased over the next 9 months but still remained significantly reduced compared with controls (P < .006). After 12 months the median SI for anti-Ig and IL-2 returned to normal levels (Fig 5).

In an attempt to confirm the intrinsic inability of B cells to be activated, we examined the response to a second B-cell mitogen. EBV interacts with B cells through the CD21 receptor and induces these cells to proliferate without the addition of cytokines. The recovery of expression of the CD21 Ag lagged 1 month behind that of the CD20 Ag as seen in Fig 1e (data not shown). Following culture of T-cell–depleted PBMC for 6 days, median SI for controls was 14 (QR 8 to 23). The SI obtained at different times prior to and following ABMT are shown in Fig 6. Despite the small number of samples analyzed before and during the first 6 months post-ABMT, the SI observed was significantly lower than normal (Fig 6).
reduced as compared with controls ($P < .006, \text{ before and at 3 months}, P < .008 \text{ at 6 months}$). Subsequently 50% of patients achieved a normal SI; however, $^{3}$H-TdR uptake was diminished for up to 3 years in a number of patients. The SI obtained with EBV did not directly correlate to that of anti-Ig. Some patients responded to anti-Ig, whereas others first responded to EBV.

**Immunoglobulins in vivo.** As shown in Table 1, the median serum IgG level was significantly lower than in controls ($P < .006$) for 1 year following ABMT. The IgM level was lower than normal in the majority of the patients before and during the 6 months following ABMT, whereas IgA serum levels were abnormal for more than 2 years after ABMT. We did not find a statistically significant
correlation between number of B cells and levels of immunoglobulins or between in vitro activation and proliferation and serum IgG, IgA, or IgM levels.

DISCUSSION

In the present report we have examined immunologic reconstitution following high-dose chemoradiotherapy and anti-B-cell MoAb-purged ABMT. By cell-surface phenotypic analysis, the majority of patients had normal percentages of NK cells, monocytes, and CD8+ T cells at 1 month post-ABMT. In contrast, the percentage of CD4+ T cells was reduced for at least 3 years, and the CD4:CD8 ratio reflects this imbalance. B-cell reconstitution was slightly prolonged, with normal percentage of CD20+ B cells evident by 3 months. Although normal absolute numbers of B cells were observed by 3 months, in vitro assessment of B-cell function demonstrated impairment of proliferative responses to either anti-Ig, anti-Ig plus IL-2, or EBV during the first year and with anti-Ig plus BCGF for approximately 2 or more years. Moreover, in vivo B-cell reconstitution demonstrated a more selective defect, with normal levels of IgM returning at 6 months, IgG at 12 months, and IgA after 2 years. These studies suggest that following anti-B-cell MoAb-purged ABMT, there are long-lasting defects in both T- and B-cell reconstitution as measured by phenotypic and functional analysis. Moreover, these defects are similar to those observed following nonpurged autologous and allogeneic BMT, although the interval of immune impairment appears more prolonged.

There are many similarities in the sequence of phenotypic reconstitution observed following anti-B-cell-purged ABMT with published series of syngeneic BMT, nonpurged ABMT, and even allogeneic BMT. In all series, CD8+ T cells return early, and CD4+ cells reconstitute very slowly. Other investigators have similarly observed the reversal of the CD4:CD8 ratio; however, in the majority of studies this reversal persists for only 6 to 12 months. The prolongation to greater than 36 months in our series is striking, and to date we have no explanation for this observation. Preliminary studies from this laboratory have further examined these

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**Table 1. Median Serum Levels for IgG, IgM, and IgA Before and After ABMT**

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>IgG (mg/dl)</th>
<th>IgM (mg/dl)</th>
<th>IgA (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1,300</td>
<td>155</td>
<td>258</td>
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<tr>
<td></td>
<td>(1,175-1,412)</td>
<td>(98-212)</td>
<td>(169-332)</td>
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<tr>
<td>Pre-ABMT</td>
<td>894</td>
<td>58</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>(602-1,125)</td>
<td>(48-169)</td>
<td>(68-281)</td>
</tr>
<tr>
<td>1-3</td>
<td>839*</td>
<td>68*</td>
<td>84*</td>
</tr>
<tr>
<td></td>
<td>(640-1,100)</td>
<td>(40-102)</td>
<td>(50-111)</td>
</tr>
<tr>
<td>4-6</td>
<td>730*</td>
<td>84*</td>
<td>84*</td>
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<td>(613-1,160)</td>
<td>(50-102)</td>
<td>(74-177)</td>
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<tr>
<td>7-12</td>
<td>848*</td>
<td>104</td>
<td>93*</td>
</tr>
<tr>
<td></td>
<td>(761-1,147)</td>
<td>(85-123)</td>
<td>(57-158)</td>
</tr>
<tr>
<td>13-18</td>
<td>725</td>
<td>95</td>
<td>98*</td>
</tr>
<tr>
<td></td>
<td>(669-963)</td>
<td>(57-170)</td>
<td>(55-182)</td>
</tr>
<tr>
<td>19-24</td>
<td>912</td>
<td>118</td>
<td>70*</td>
</tr>
<tr>
<td></td>
<td>(616-1,303)</td>
<td>(77-177)</td>
<td>(51-158)</td>
</tr>
<tr>
<td>25-36</td>
<td>950</td>
<td>104</td>
<td>82</td>
</tr>
<tr>
<td></td>
<td>(595-1,165)</td>
<td>(40-171)</td>
<td>(48-85)</td>
</tr>
<tr>
<td>37</td>
<td>1,195</td>
<td>96</td>
<td>114</td>
</tr>
<tr>
<td></td>
<td>(680-1,481)</td>
<td>(52-199)</td>
<td>(108-226)</td>
</tr>
</tbody>
</table>

(*) = interquartile range.

*Difference versus control significant (P < .006).*

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Fig 6. The proliferation of enriched B cells to EBV. The SI is represented for each patient, and the median is depicted for each time interval. The dotted line represents one third of the median value obtained in controls. SI below the dotted line is considered abnormal. Differences between controls and patients is statistically significant before and up to 6 months post-ABMT at a level of $P < .006$.
T-cell subsets.\textsuperscript{49} The majority of CD4\textsuperscript{+} cells are CD29\textsuperscript{+}, which defines the helper-inducer population with a relative decrease in the inducers of suppression (CD4\textsuperscript{+}CD45R\textsuperscript{+}). The majority of CD8\textsuperscript{+} cells were cytotoxic (S6F1\textsuperscript{+}), with a relative decrease in the proportion of CD8 suppressor cells. Whereas NK cells return rapidly postautologous and allogeneic BMT, the percentage of NK cells in our series is significantly less than that observed following anti-T-cell MoAb-purged allogeneic BMT.\textsuperscript{50} From 3 to 24 months following ABMT, the majority of patients reconstituted normal absolute numbers of CD20\textsuperscript{+} cells. At least one time during the first 2 years after ABMT, approximately 20% of patients had increased absolute numbers of B cells (>400/\mu L), and approximately 15% had persistently diminished numbers (<60/\mu L). Our results in best approximation are not substantially different from those previously published,\textsuperscript{51-54} suggesting that in vitro purging may not alter quantitative reconstitution. The expression of the CD21 Ag lagged 1 month behind that of the CD20 Ag. This is reminiscent of normal B-cell ontogeny where the acquisition of CD21 follows the expression of CD20.\textsuperscript{55} The delay in CD21\textsuperscript{+} cells may also be due to early reconstitution with a CD21 negative subset of B cells. For example, CD5\textsuperscript{+} B cells are reported to appear early in reconstitution following ABMT, and these cells may lack or weakly express CD21.\textsuperscript{56}

B cells before and within the first 6 months following ABMT did not proliferate in response to anti-Ig or EBV. The observation that proliferation of enriched B cells after EBV stimulation had a similar temporal pattern of recovery to that of PBMC activated with anti-Ig supports the hypothesis of a primary B-cell defect. Although it cannot be formally excluded, it is less likely that T-cell or monocyte "suppression" might contribute to these results. One explanation for this defect might be insufficient or aberrant expression of one or more cell-surface molecules, including CD19, CD20, and CD22, which have been shown to be involved in signal transmission and in the regulation of B-cell activation.\textsuperscript{57} An alternative explanation might be that a particular B-cell subset may predominate during early reconstitution, and that population may have different responsiveness to B-cell stimuli. The delay in attaining normal responses to added growth factors may similarly be due to either the lack of growth factor receptors (IL-2 or BCGF) or the hyporesponsiveness of a particular B-cell subset. Again, the heterogeneous responses seen to anti-Ig and EBV stimulation might be due to recovery of different B-cell subsets or heterogeneous-expression cell-surface receptors.

This primary B-cell defect has been previously observed following ABMT and allogeneic BMT.\textsuperscript{33,34,58} These studies have examined only small numbers of patients, and very few patients who had been followed for greater than 1 year. Kiesel et al\textsuperscript{28} examined functional B-cell reconstitution following ABMT using patients who had received either bone marrow or peripheral-blood stem-cell grafts. Using enriched B-cell populations stimulated with staphylococcal Cowan Strain I (SAC), BCGF, and anti-Ig plus BCGF in 11 ABMT patients and 10 controls, there was a significant reduction of H-TdR incorporation for all stimuli in the majority of patients during the first 12 months post-ABMT. Matsue et al\textsuperscript{81} observed severely impaired proliferation to SAC within the first 90 days postallogeneic BMT, which normalized at 1 year. Addition of T-cell supernatants as a source of B-cell growth factor did not lead to enhanced proliferation at 90 days, which also normalized at 1 year. Both of these functional studies employing enriched B-cell populations triggered with B-cell–restricted mitogens concluded that a primary defect in B-cell triggering was observed early following ABMT and allogeneic BMT.

B-cell reconstitution in vivo was evaluated by examining serum immunoglobulin levels. Our observations are not different from that previously reported for patients following allogeneic transplantation\textsuperscript{42-45} and purged ABMT.\textsuperscript{29} In two studies Ig isotypes were studied, and these investigators observed that IgM and total IgG returned early. However, the normal level of total IgG was a result of increased secretion of IgG1 and IgG3 and very low levels of IgG2 and IgG4.\textsuperscript{59} The levels of IgG2 and IgG4 were very low, and reconstitution was prolonged. Aucourtier et al\textsuperscript{21} observed that in addition to the late return of IgG2 and IgG4, there is a very prolonged defect in IgA. Both studies suggested that the high rates of late infections following allogeneic BMT might be due to these selected immunodeficiencies. Although we have demonstrated low IgA, we have not thus far examined IgG isotype deficiency in our B-cell–purged ABMT patients. However, we should note that unlike allogeneic BMT patients with GVHD, we have not observed late bacterial infections.

It is not clear whether anti–B-cell MoAb purging contributes to B-cell deficiency observed in vitro and in vivo.\textsuperscript{56,59} Very little data have been published for the immunologic reconstitution following ABMT using unpurged marrow. From the study of Kiesel et al\textsuperscript{28} it appears that purging does not prolong the length of immunosuppression following ABMT. A very preliminary study comparing patients in the first 6 months following anti–B-cell–purged ABMT with patients with solid tumors undergoing unpurged ABMT suggests that there is no difference in phenotypic reconstitution and in vitro proliferative response to anti-Ig, anti-Ig plus IL-2, or anti-Ig plus BCGF. These preliminary studies must be expanded, confirmed, and formally compared in NHL patients whose bone marrows, either purged or unpurged, are treated with the same ablative regimen.

REFERENCES

5. Schroff RW, Gale RP, Fahey JL: Regulation of T cell subpopulations after bone marrow transplantation: Cytomegalovirus


41. Armitage RJ, Goldstone AH, Richards JDM, Cawley JC:
Lymphocyte function after autologous bone marrow transplantation (BMT): A comparison with patients treated with allogeneic BMT and with chemotherapy only. Br J Haematol 63:637, 1986


48. Verdonck LF, de Gast GC: Is cytomegalovirus infection a major cause of T cell alterations after (autologous) bone marrow transplantation? Lancet 1:932, 1984


52. Toetterman TH, Bengtsson M, Gordon J, Smedmyr B, Oeberg G, Simonsson B: B cell regeneration in marrow and blood after purged ABMT: Kinetics of serum B cell growth factor and B cell markers. Bone Marrow Transplant 3:130, 1988 (suppl 1, abstr)


Anti-B-cell monoclonal antibody-purged autologous bone marrow transplantation for B-cell non-Hodgkin's lymphoma: phenotypic reconstitution and B-cell function

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