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Tγ lymphocytosis is clinically non-progressive but immunologically heterogeneous

F. MIEDEMA, F. G. TERPSTRA, J. W. SMIT,* J. P. W. VAN DER VEEN & C. J. M. MELIEF *Central Laboratory of the Netherlands Red Cross Blood Transfusion Service; Laboratory for Experimental and Clinical Immunology of the University of Amsterdam, Amsterdam and *Division of Hematology, Department of Internal Medicine, University Hospital Groningen, The Netherlands*

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SUMMARY

Immunological studies were performed with the expanded Tγ cells of five patients with Tγ lymphocytosis. All patients showed a stable clinical picture with persistent Tγ lymphocytosis and neutropenia, with or without recurrent infections. The expanded Tγ cells in the blood had the $T1^-3^+4^-8^+11^+M1^-$ phenotype, with the exception of one patient whose cells lacked the T8 marker. The expanded Tγ cell population did not proliferate in response to T cell mitogens and did not show immunoregulatory activity on pokeweed mitogen driven immunoglobulin synthesis. In four of the five patients the Tγ cells had killer cell activity against IgG sensitized mouse mastocytoma cells. Taken together, these results and the data from the literature, it is concluded that Tγ lymphocytosis represents a spectrum of T cell expansions clearly distinct from clinically progressive mature T cell neoplasias.

Keywords Tγ lymphocytosis immunological studies

INTRODUCTION

Within the spectrum of chronic T cell lymphocytic leukaemia (T-CLL), Tγ lymphocytosis is now a well recognized T cell disorder (Bom-van Noorloos *et al.*, 1980; Schlimok *et al.*, 1982; Rümke *et al.*, 1982; Itoh *et al.*, 1983; Palutke *et al.*, 1983). Tγ lymphocytosis is characterized by chronic persistent lymphocytosis of T cells with Fc receptors for IgG, Tγ cells. Clinically these patients suffer from neutropenia (Bom-van Noorloos *et al.*, 1980; Hooks *et al.*, 1982; Rümke *et al.*, 1982; Chan *et al.*, 1984) with or without recurrent infections, and/or anaemia (Rümke *et al.*, 1982; Itoh *et al.*, 1983) or no symptoms at all (Schlimok *et al.*, 1982; Rümke *et al.*, 1982; Pandolfi *et al.*, 1982, 1983). In most patients the expanded T cell has an $E^+Fc\gamma^+T3^+4^-8^+11^+M1^-$ phenotype (Melief *et al.*, 1980; Palutke *et al.*, 1983; Rümke *et al.*, 1982; Chan *et al.*, 1984). In some patients the proliferating Tγ cells have a $T1^-3^-4^-8^-11^+M1^+$ phenotype (Rümke *et al.*, 1982), a $T3^+4^-8^-M1^-$ phenotype (Itoh *et al.*, 1983) or a $T3^+4^-8^+M1^+$ phenotype (Schlimok *et al.*, 1982).

In the cases tested, it was found that the Tγ cells lacked the T1 marker (Rümke *et al.*, 1982; Aisenberg *et al.*, 1981; Callard *et al.*, 1981) and that an elevated percentage of the peripheral blood lymphocytes (PBL) expressed the HNK-1 antigen (Pandolfi *et al.*, 1983; Itoh *et al.*, 1983; Palutke *et al.*, 1983).

With respect to the functional properties of the expanded Tγ cells, we have previously described

Correspondence: Dr C. J. M. Melief, c/o Publication Secretariat, Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, PO Box 9406, 1006 AK Amsterdam, The Netherlands.

Tγ-K, Tγ-S and Tγ NK/K lymphocytosis with Tγ cells mediating killer (K) cell activity, suppressor cell activity (S) and both natural killer (NK) cell activity and K cell activity (Melief *et al.*, 1981; Rümke *et al.*, 1982), respectively. In most patients the Tγ cells are Tγ-K cells (reviewed in Melief, 1984 and Rümke *et al.*, 1982), whereas until now in only two patients the expanded T cell population were shown to be of the Tγ-K/NK type (Rümke *et al.*, 1982; Schlimok *et al.*, 1982). In these two patients the Tγ cells showed a hybrid marker phenotype, expressing both lymphocytic and myelomonocytic differentiation antigens. Tγ-S lymphocytosis was reported in a small number of cases (Nagasawa, Abe & Nakagawa, 1981; Thien *et al.*, 1982; Rümke *et al.*, 1982). In two patients the Tγ cells had both suppressor activity and NK cell activity (Itoh *et al.*, 1983; Palutke *et al.*, 1983), a new phenotype of the expanded cells in Tγ lymphocytosis that are designated as Tγ-NK/S cells.

We now report immunological studies with the cells of five Tγ lymphocytosis patients who were not included in previous reports. Studies of surface marker phenotype and of functional properties of the expanded Tγ cells from these patients confirm the heterogeneity of Tγ lymphocytosis as a nosological entity. A clinically benign course was seen in all patients.

In four of the five patients the proliferating cells were of the Tγ-K type whereas in the fifth patient the Tγ cells were non-functional in all *in vitro* tests performed.

PATIENTS

Tables 1 and 2 summarize the clinical and laboratory findings in the five Tγ lymphocytosis patients. In all patients Tγ lymphocytosis existed with moderate to severe granulocytopenia. Leucocytosis was only observed in patient 5. **Patient 1** has lymphocytosis and granulocytopenia that was stable

Table 1. Longitudinal haematological findings in five Tγ lymphocytosis patients

Patient (Age, sex)	Time of sample	Leucocytes ($\times 10^9$/l)	Lymphocytes (%)	Granulocytes (%)	Monocytes (%)
1 Foe (69, M)	12/20/80	8·2	80	12	8
	2/82	14·1	82	12	6
	12/82	13·6	81	12	6
	3/31/83	8·2	85	12	3
2 Ha (69, F)	1/11/83	3·9	84	15	0
	5/02/83	4·6	89	9	2
	10/06/83	6·4	88	12	0
3 Li (72, F)	10/18/82	8·2	91	2	7
	12/27/82	7·1	91	0	9
	1/24/83	7·2	99	1	0
	7/13/83	7·3	94	6	0
	11/10/83	4·7	70	10	20
	6/03/84	5·1	97	3	0
4 Wa (76, M)	7/31/79	3·1	75	21	4
	9/17/79	5·2	95	4	1
	9/22/80	6·0	92	4	4
	10/30/81	7·0	90	4	7
	5/10/82	7·5	79	9	12
	5/02/83	5·9	85	8	7
	10/28/83	7·2	76	8	7
5 Ke (61, M)	12/08/82	13·6	81	12	6
	4/15/83	28·1	86	8	5
	9/14/83	16·1	78	19	3
Normal range		4–11	20–45	45–70	0–8

Table 2. Main clinical findings in five Tγ lymphocytosis patients

Patient	Lymphocyte infiltration BM	Liver	Spleen	LN	Other symptoms during clinical course	Duration of disease (years)
(1) Foe	+	–	–	–	Fatigue	3·5
(2) Ha	+	–	–	–	Leg ulcers, fever	1
(3) Li	+	–	–	–	Multiple infections	2
(4) Wa	–	–	–	–	None	5
(5) Ke	+	+	+	–	Anaemia, chronic aspecific respiratory disease	3

for 3 years. The only symptom was a vague complaint of fatigue. Bone marrow aspirates showed a moderate infiltration with lymphocytes (30%). **Patient 2** presented in August 1982 with an ulcus cruris of the right leg that had started in February 1982, accompanied by fever. The patient was hospitalized from August 1982 until December 1982 and routine hematological laboratory investigations revealed Tγ lymphocytosis and neutropenia. Apart from the open leg wound no other infections were noted. Bone marrow examinations on several occasions showed infiltration with atypical lymphocytes and myelodysplasia. As of this writing her condition had not changed. She still suffers from ulcus cruris of the leg. **Patient 3** was hospitalized for vitrectomy of the left eye from 24 September to 21 October 1982, when she developed fever and complained of a sore throat. Laboratory investigations demonstrated Tγ lymphocytosis and severe neutropenia. The patient suffered from sinusitis maxillaris and candida oesophagitis. A slight erythrodermia was observed. The bone marrow was moderately infiltrated with lymphocytes. In July 1983 a colon carcinoma was diagnosed for which she underwent extensive surgery and was hospitalized from July until October 1983. Until June 1984 her haematological picture has remained essentially unchanged. In **Patient 4** lymphocytosis was first observed in September 1979 when he was an outpatient at the dermatological department because of dermatitis e.c.i. The patient had moderate complaints of an itching skin and was seen as an out-patient since. A persistent Tγ lymphocytosis with neutropenia and without serious disease symptoms was observed until the moment of writing. **Patient 5** was admitted in February 1982 because of anaemia. The patient had a history of tuberculosis and chronic respiratory illness. Examinations showed hepatosplenomegaly, lymphocytosis, neutropenia and a moderate anaemia. The bone marrow was infiltrated with lymphocytes. In December 1982 the patient was hospitalized for 2 weeks because of anaemia, fatigue and weight loss but no further complaints. As of this writing his clinical and haematological condition remain essentially unaltered.

MATERIALS AND METHODS

Isolation of lymphocytes and separation of T cell subsets. Blood of patients and normal donors was either defibrinated or anti-coagulated with heparin. Peripheral blood mononuclear cells (PBL) were isolated by means of Ficoll-Isopaque density gradient centrifugation. T and non-T cells were separated by E rosette sedimentation. T cells of patients and normal donors were separated in to $T4^+$ cells and $T8^+$ cells by means of a panning technique with the OKT4 and OKT8 monoclonal antibodies (MoAb), as described (Rümke) *et al.*, 1982). $T4^+$ cells were always $<3\%$ $T8^+$ and 75–90% $T4^+$ whereas $T8^+$ cells were always $<3\%$ $T4^+$ and over 75% $T8^+$. Tγ cells from normal donors were isolated as described (Rümke *et al.*, 1982).

Surface marker analysis. Receptors for sheep erythrocytes (E) and the Fc receptor for IgG (EA) were evaluated in rosette tests with sheep erythrocytes and human IgG sensitized erythrocytes. Phenotypic analysis of all cell populations with OKT, Leu 7 and 3A1 MoAb was performed by

indirect immunofluorescence with fluorescein conjugated goat anti-mouse IgG on an Ortho FC200 cytofluorograph as described (de Bruin *et al.*, 1981).

Functional studies. Proliferative responses of patient cells to the polyclonal mitogens phytohaemagglutinin (PHA), concanavalin A (Con A) and anti-lymphocyte serum (ALS) were performed as described in detail elsewhere (van Oers, Pinkster, Zeijlemaker, 1979). K cell activity and NK cell activity (antibody-dependent cell-mediated cytotoxicity ADCC) were tested as previously described (Rümke *et al* 1982). Helper and suppressor activity of patient cells and normal T cell subsets on pokeweed mitogen (PWM)-induced polyclonal IgM synthesis by healthy donor non-T cells were measured in a microculture system described before (Rümke *et al.*, 1981, 1982). IgM synthesis was measured in cell culture supernatants with an ELISA technique. In all functional studies cryopreserved patient cells and normal donor T cells were used. Viability of the cell suspensions was always over 90% as tested before use.

RESULTS

Surface marker analysis

The patients' PBL were analysed with MoAb and rosette techniques for surface marker expression. In all patients an expanded Tγ cell population was present that was homogeneous with respect to surface marker phenotype. Longitudinal studies demonstrated a persistent and stable marker expression (Table 3). PBL of all patients showed a markedly decreased percentage of cells reactive with OKT1, compared to normal donors. In all patients, except patient 2, the PBL had the $E^{+}EA^{+}T3^{+}4^{-}8^{+}11^{+}M1^{-}$ phenotype. The Tγ cell population in patient 2 lacked the T8 marker. In some of the patients (2, 3 and 4) the Tγ cells expressed the Leu 7 marker, which was demonstrable only on a subset of the cells of patient 5. In 2 out of 3 patients tested the Tγ cells lacked the 3A1 marker, a marker shown to be absent on T cells in Sézary syndrome and adult T cell leukaemia/lymphoma (ATLL) (Haynes *et al.*, 1981; Miedema *et al.*, 1984a, 1984b).

Table 3. Surface marker analysis

Patient	Time of sample	Cell fraction	% rosette E	% rosette EA	Binding of MoAb T1	T3	T4	T6	T8	T11	M1	I1	Leu 7	3A1
1 Foe	3/31/82	PBL	67	57	4	96	10	2	87	98	3	9	nt	nt
		T	74	87	6	96	7	2	85	98	< 1	< 1	nt	nt
	7/5/83	PBL	50	39	15	66	9	nt	78	69	15	10	38	nt
2 Ha	11/25/82	PBL	nt	50	27	76	12	nt	12	68	4	6	nt	nt
		T	nt	65	21	70	9	nt	8	64	5	5	nt	nt
	5/2/83	PBL	75	60	15	91	12	1	8	83	7	9	52	13
3 Li	11/25/82	PBL	nt	48	51	75	11	nt	71	63	5	9	nt	nt
		T	nt	71	34	70	15	nt	75	60	12	13	nt	nt
	5/2/83	PBL	72	75	6	70	13	1	70	77	4	15	47	67
4 Wa	5/2/83	PBL	79	65	8	67	11	2	66	76	10	10	47	28
	11/10/83	PBL	88	57	16	61	12	nt	50	64	12	15	29	nt
5 Ke	12/6/82	PBL	42	86	47	66	11	1	63	65	9	6	17	37
	9/29/83	PBL	68	39	8	85	5	nt	93	83	7	8	22	nt
Healthy donor mean ($n = 3$–6)		PBL	70	20	83	80	66	< 10	21	91	23	15	15	70
		T	90	11	90	85	58	< 10	33	94	11	15	15	81
		Tγ	83	60	75	30	17	nt	16	83	70	nt	21	64

Response of patient lymphocytes to T cell mitogens
Proliferative responses of the patients' PBL after 3 days of culture in the presence of PHA, Con A or ALS were compared with the responses of normal donor PBL and T cell subpopulations. An impaired response to all mitogens was found (Table 4). The proliferative response of patient PBL was not increased by adding normal irradiated non-T cells as an accessory cell source (not shown). The residual proliferative response observed with the patients' PBL was due to admixed normal $T4^+$ cells.

K and NK cell activity
In all patients, except patient 5, the $T\gamma$ cells showed increased K cell activity on IgG sensitized mouse mastocytoma cells (Table 5). With the PBL of patients 2 and 3 a low cytolytic activity in the NK cell assay was observed compared to the NK activity of normal donors. The cells of patient 5 never mediated either K or NK cell activity.

Helper and suppressor activity
The capacity of the patients' PBL to act as helper cells in PWM driven immunoglobulin synthesis was evaluated in a microculture system. In this system Ig production is strictly helper T cell-dependent. Helper activity of the patients' PBL was compared with the help provided by normal $T4^+$ T cells (Table 6). The patients' PBL showed only marginal or suboptimal helper activity compared to the helper activity delivered by normal $T4^+$ cells. The helper activity provided by the patients' PBL was mediated by the residual normal $T4^+$ cells in the PBL population, because patient PBL depleted for $T4^+$ cells by a panning technique were devoid of significant helper activity, as demonstrated with the cells of patient 1 (Table 6). These findings confirm the results obtained with PBL from other $T\gamma$ lymphocytosis patients (Rümke *et al.*, 1982).

We therefore conclude that the expanded $T\gamma$ cell populations did not mediate helper activity. It

Table 4. Proliferative responses of patient cells to polyclonal mitogens

Patient	Time of sample	Cell fraction	Expt no.	% response of normal donor PBL*		
				PHA	Con A	ALS
1 Foe	31/3/82	PBL	1	5	11	15
		T		26	19	32
		T	2	4	3	11
		T-4		2	3	4
2 Ha	25/11/82	PBL	1	3	5	4
	2/5/83	PBL	1	46	nt	36
3 Li	25/11/82	PBL	1	11	10	4
	2/5/83	PBL	1	45	nt	
			2	44	nt	23
4 Wa	2/5/83	PBL	1	15	nt	15
			2	62	nt	58
5 Ke	6/12/83	PBL	1	14	nt	7
			2	11	nt	9
Normal donor		T		160	272	108
		T-4		123	162	108
		T-8		134	156	129
Normal donor		PBL		6,649	2,695	7,419
ct/mean (n=9–12) and s.d.				(3,455)	(147)	(3,502)

* Measured at day 4 of culture after 24 h ^{3}H-thymidine incorporation.

Table 5. K and NK cell activity of patient cells

Patient	Time of sample	Cell fraction	Expt No.	K cell activity 2·5*	K cell activity 1·25	NK cell activity 10*	NK cell activity 2·5
1 Foe	3/31/82	PBL	1	57	47	3	1
		T	1	51	34	1	0
	7/5/83	PBL	1	14	14	1	1
2 Ha	5/2/83	PBL	1	62	60	32	10
			2	45	20	10	2
			3	35	25	35	15
3 Li	5/2/83	PBL	1	45	33	12	6
			2	32	25	15	2
			3	35	20	15	10
	11/10/83	PBL	1	60	45	24	27
4 Wa	5/2/83	PBL	1	55	40	10	3
			2	24	17	2	0
			3	22	17	12	5
	11/10/83	PBL	1	15	12	6	3
5 Ke	12/6/82	PBL	1	0	0	0	0
			2	0	0	0	0
	9/29/83	PBL	1	10	3	1	1
Healthy donor mean ($n=20$)		PBL		29 (±3)	20 (±2)	50 (±3)	21 (±3)

* Effector to target cell ratio.

was next tested whether the patients' cells were able to suppress immunoglobulin production by a mixture of normal T4⁺ cells and normal B cells. Although a strong suppression was observed with normal T8⁺ cells, suppression could not be demonstrated with the PBL of the patients in this series (data not shown).

DISCUSSION

The immunological studies performed with the PBL of the five Tγ lymphocytosis patients in this series emphasize the usefulness of identifying Tγ lymphocytosis as a distinct clinical entity of a relatively benign nature. On the other hand, Tγ lymphocytosis constitutes a spectrum of T cell expansions with heterogeneous marker expression and functional properties as summarized in Table 7.

Whereas in the present series all patients showed similar clinical features, e.g. expanded Tγ cell populations with moderate bone marrow infiltrations and moderate to severe neutropenia, a heterogeneity was found in the immunological studies. In four out of five patients the Tγ cells had a $T1^-3^+4^-8^+11^+M1^-$ phenotype like the first two Tγ lymphocytosis patients described (Melief *et al.*, 1980; Rümke *et al.*, 1982). The expanded Tγ cell population in patient 2 lacked the T8 marker of this phenotype. So far in all Tγ lymphocytosis patients studied in our laboratory (Rümke *et al.*, 1982) and in the patients reported by Aisenberg *et al.* (1981) and Callard *et al.* (1981), the Tγ cells lacked the T1 marker or only a small proportion of the cells expressed T1, whereas this marker was found to be expressed on a large series of mature T-cell neoplasias (Miedema *et al.*, 1984a, 1984b

Table 6. Helper activity of patient cells

Patient	Time of sample	Cell fraction	Expt No.	Control†	Helper activity*: Patient cells	Normal T4+	Normal T8+
1 (Foe)	31/3/82	T	1	<20‡	600‡	1,250‡	100‡
		T-4§		<20	40	1,250	100
		T	2	<20	200	1,300	80
		T-4§		<80	80	1,300	80
2 (Ha)	25/11/82	PBL	1	<20	450	3,850	600
	2/5/83	PBL	1	<20	300	3,350	100
			2	<20	1,500	2,900	50
			3	<20	<20	1,355	<20
3 (Li)	25/11/82	PBL	1	<20	750	3,850	600
	2/5/83	PBL	1	<20	340	3,350	100
			2	<20	1,800	2,900	50
			3	<20	<20	1,355	<20
4 (Wa)	2/5/83	PBL	1	<20	50	3,350	100
			2	<20	1,800	2,900	50
			3	<20	<20	1,355	<20
5 (Ke)	6/12/82	PBL	1	<20	150	2,900	50
			2	<20	<20	1,355	<20

* Expressed as the IgM production induced by 20×10^3 patient cells or healthy donor T4+ or T8+ cells.
† Healthy donor non-T cells and 1:200 PWM alone.
‡ Nanogram IgM per culture well.
§ T-4 = <3% T4+, 80–92% T8+.

and unpublished observations). In normal donors Tγ cells have been shown to consist of two major populations: (1) $T3^+4^+8^-11^+M1^+$ and $T3^+4^-8^+11^+M1^+$ and (2) $T3^-4^-8^-11^+M1^+$ (van de Griend *et al.*, 1982). Whether the $T1^-3^+4^-8^+11^+M1^-$ and the $T3^+4^-8^-11^+M1^-$ cells represent the expansions of minor subsets hardly detectable in normal blood is unclear. It could well be that the Tγ cells lost the T1 marker or the T8 marker (patient 2) during the clonal expansion. Normal Tγ cells contain a large percentage (>80%) of cells bearing T1 (Table 3). The phenotypic heterogeneity on the other hand could be a reflection of different maturation stages correlated with phenotypic changes (Horwitz & Bakke, 1984). Upon maturation Tγ cells lose T cell markers, the OKM1 antigen (C3bi receptor) is expressed on immature and mature cells. It is postulated that T3 (T1) and T8 are lost early, whereas T11 is lost late in Tγ cell maturation. Immature cells predominantly are $T3^+8^+M1^+$, mature Tγ cells are $T3^-8^-11^+M1^+$ and precursor Tγ cells are $T3^+8^+M1^-$ (Horwitz & Bakke 1984). It is important to notice that a Tγ lymphocytosis patient with a Tγ cell population expressing the same markers as found in patient 2 has been described before (Itoh *et al.*, 1983).

The functional properties of the Tγ cells of patients 1–4 were quite similar to those of three Tγ-K cell patients described by us before (Rümke *et al.*, 1982). They were active as effector cells in the K cell assay but not in the NK cell assay, but lack immunoregulatory activity in *in vitro* immunoglobulin synthesis and also fail to respond to T cell mitogens.

Although phenotypically the expanded Tγ cell population in patient 5 could not be distinguished from the Tγ cells in patients 1–4, the cells of this patient were functionally different. This is the first Tγ lymphocytosis patient with a non-functional Tγ cell population in all tests

Table 7. Phenotype and functional properties of Tγ cells in Tγ lymphocytosis. Survey of the literature

Number of patients	Phenotype of expanded Tγ cells								Functional properties				Reference
	T1	T3	T4	T6	T8	T11	OKM1	OKI1	K	NK	Helper	Suppressor	
3	−	+	−	−	+	+	−	−	+	−	−	−	Bom *et al.*, 1980; Rümke *et al.*, 1982
1	−	−	−	−	−	+	+	+	+	+	−	−	Rümke *et al.*, 1982
1	−	+	−	−	+	+	−	−	−	−	−	+	Rümke *et al.*, 1982; Thien *et al.*, 1982
1		+	−	−	+		−	+	+	−	−	−	Pandolfi *et al.*, 1980; Strong *et al.*, 1981
1									+		−	+	Nagasawa *et al.*, 1981
1	−	+	−	−	+	+	−	−	+	−			Aisenberg *et al.*, 1981
2	+*	+	−	−	+	+		+	+		−	−	Callard *et al.*, 1981; Linch *et al.*, 1981
2		+	−	−	+	+		+/−			−	−	Linch *et al.*, 1981
1		+	−	−	+			−	+	−	−	−	Hooks *et al.*, 1981
1		+	−		+	+	+	−	+	+	−	−	Schlimok *et al.*, 1982
3		+	−	−	+	+	−	−	+		−	+	Pandolfi *et al.*, 1982, 1983
1		+	−		−		−		−	+			Itoh *et al.*, 1983
1		+	−	−	+	+	−	−	+	±	−	+	Palutke *et al.*, 1983
4		+	−		+	+	−	−	+	−	−	−	Chan *et al.*, 1984
2	−	+	−	−	+	+	−	−	+	−	−	−	This study
1	−	+	−	−	−	+	−	−	+	−	−	−	This study
1	−	+	−	−	+	+	−	−	−	−	−	−	This study

* Very weak expression.

performed, but with a similar clinical syndrome as in the Tγ-K syndrome, i.e. anaemia and granulocytopenia. This patient illustrates that ADCC as a cause of the cytopenias is unlikely. Moreover, anti-granulocyte antibodies were detectable only in a minority of patients with Tγ-K cell expansions and granulocytopenia.

Detailed immunological studies with the expanded T cells in various lymphoproliferative conditions have resulted in the recognition of Tγ lymphocytosis as a distinct entity within the spectrum of the mature T cell disorders (Aisenberg *et al.*, 1981; Rümke *et al.*, 1982; Melief, 1984). This distinction is of clinical relevance and has implications for treatment and therapy of the disease (Rümke *et al.*, 1982). It has furthermore been shown that Tγ lymphocytosis is heterogeneous with respect to the functional properties and the phenotype of the expanded Tγ cells (Table 7). Here we demonstrated that indeed this heterogeneity could be found in a series of five Tγ lymphocytosis patients without major clinical differences. With respect to a possible causal relation between the Tγ cell proliferation and infiltration of the bone marrow and the neutropenia, a direct regulatory activity of the Tγ cells on the CFU GM colony growth has not been demonstrated thus far (Linch *et al.*, 1981).

Recently, two patients with chronic persistent $T8^+$ cell lymphocytosis with neutropenia were reported. The expanded $T8^+$ cells in these patients lacked the Fc γ receptor (Starkebaum *et al.*, 1983; Brisbane *et al.*, 1983). Neither K nor NK cell activity was reported in these two patients. In one of them there were anti-neutrophil antibodies with evidence for shortened intravascular survival (Starkebaum *et al.*, 1983). An unexpected finding in both patients was a very good helper activity on PWM-induced immunoglobulin synthesis mediated by the expanded $T8^+$ cell population. Hence, the patients described in those studies are clearly different from the Tγ lymphocytosis patients with respect to the properties of the expanded T cells, although a striking similarity does exist in the clinical pictures of the patients.

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