

Appendix One

Additional historic UK NEQAS data in support of ‘Macroprolactin(s): composition and reactivity in immunoassays and laboratory interpretation of results of an unusual patient serum’

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Macroprolactin positive serum specimens issued previously by UK NEQAS and interpretative exercises undertaken

Macroprolactin positive specimens issued

The UK NEQAS for prolactin provides proficiency testing for laboratories that measure prolactin by immunoassay. Distributions are identified by sequential code number and are issued monthly. The serum specimens generally comprise material that is known not to contain macroprolactin. However, several macroprolactin positive sera have been distributed over the recent years. Typically, sufficient material has been available to permit only limited distribution to a sub-set of participants, as is the case for the index case described in the body of this paper. However, occasionally sufficient material has been available to permit distribution to all participants. The materials distributed are described in Table 1. Recently, recipients have been invited to

interpret their results too. The immunoassay values observed are shown in Figures 1–8.

Gel filtration profiles

The specimens listed in Table 1 were all examined by Sephacryl™ S300 gel filtration, as described in the paper. The gel profiles are shown in Figures 9–16.

Hyperprolactinaemic specimens without hypermacroprolactinaemia

Several interpretative exercises involving specimens exhibiting hyperprolactinaemia without macroprolactinaemia have been conducted. These are listed in Table 2.

Summary of interpretative exercises

Table 3 describes briefly all the interpretative exercises issued through the UK NEQAS for prolactin between 1996 and 2002, and summarizes the outcomes.

Table 1 *Macroprolactin positive specimens issued, 1996–2003*

Dist.	Date	Full or limited	Source	Interpretation included	Figure number	
					Immunoassay	Gel profile
199A	August 1996	L	Single patient	No	1	9
199B	August 1996	L	Single patient	No	2	10
199C	August 1996	L	Single patient	No	3	11
214	November 1997	L	Single patient	No	4	12
226	November 1998	F	Single patient	Yes	5	13
254	March 2001	L	Single patient	Yes	6	14
261	October 2001	F	Pooled serum	Yes	7	15
281	June 2003	L	Single patient	Yes	8	16

F – Distributed to all participants; L – Distributed to a sub-set of participants.

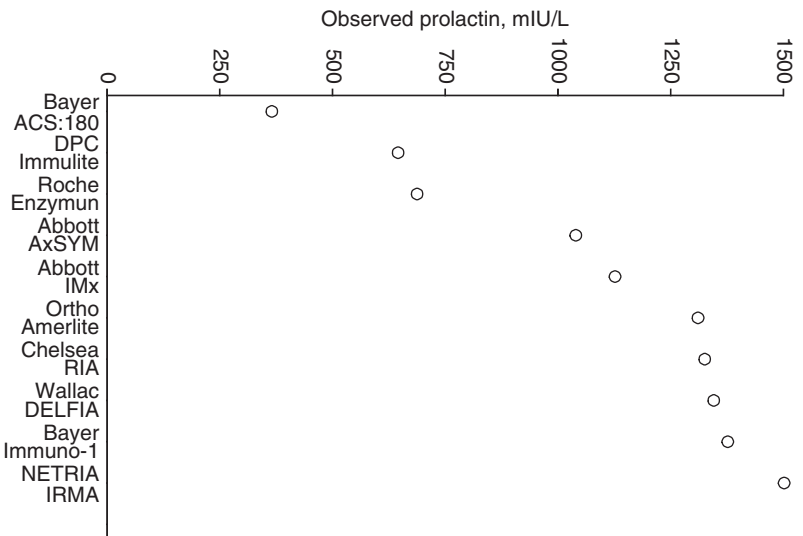


Figure 1 Method mean prolactin, distribution 199A

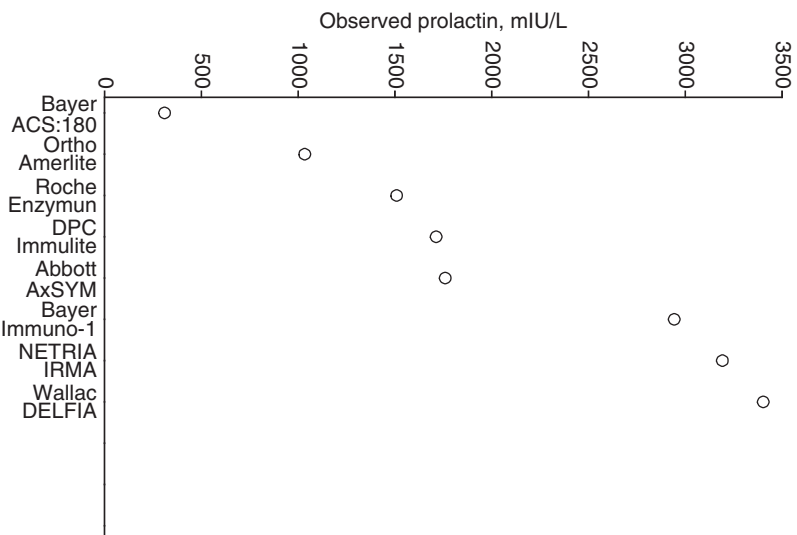


Figure 3 Method mean prolactin, distribution 199C

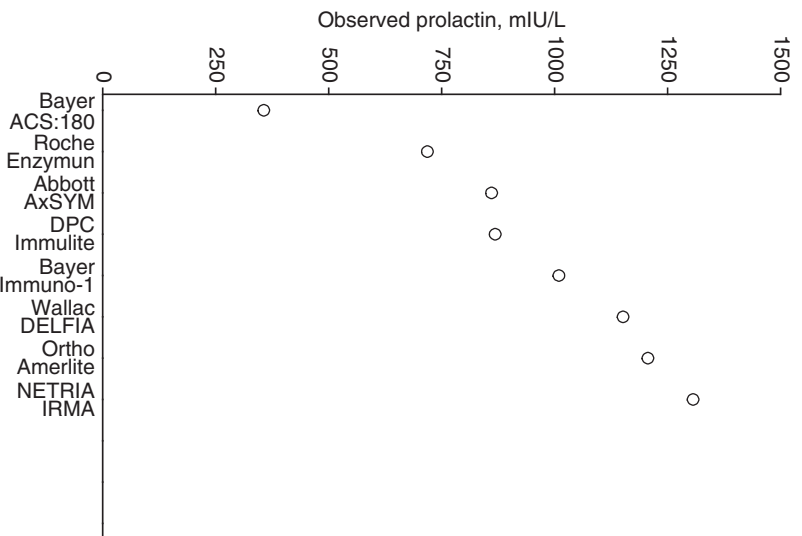


Figure 2 Method mean prolactin, distribution 199B

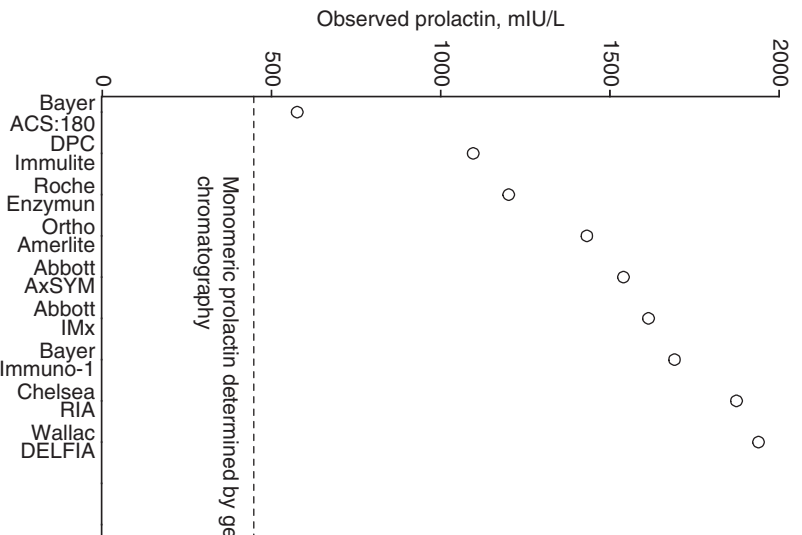


Figure 4 Method mean prolactin, distribution 214

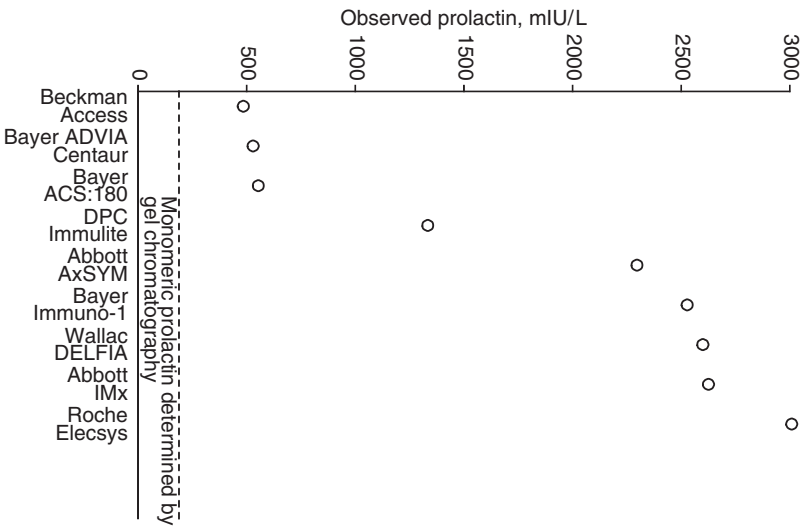


Figure 5 Method mean prolactin, distribution 226

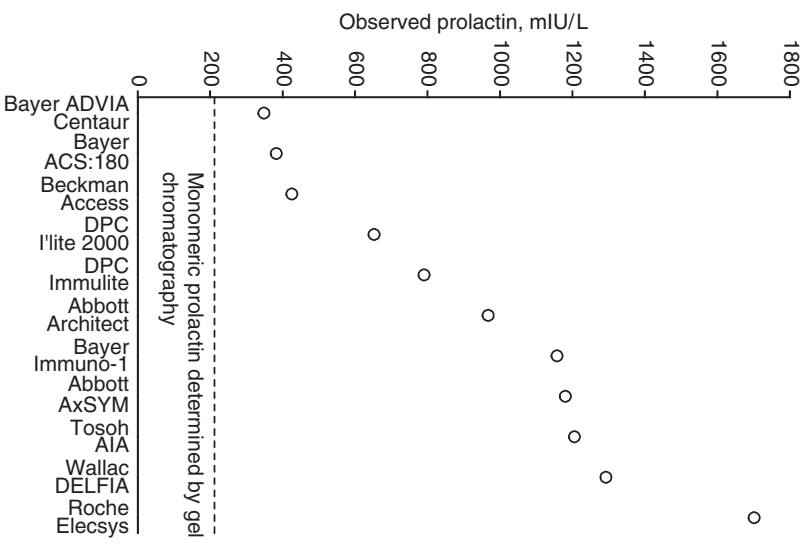


Figure 7 Method mean prolactin, distribution 261

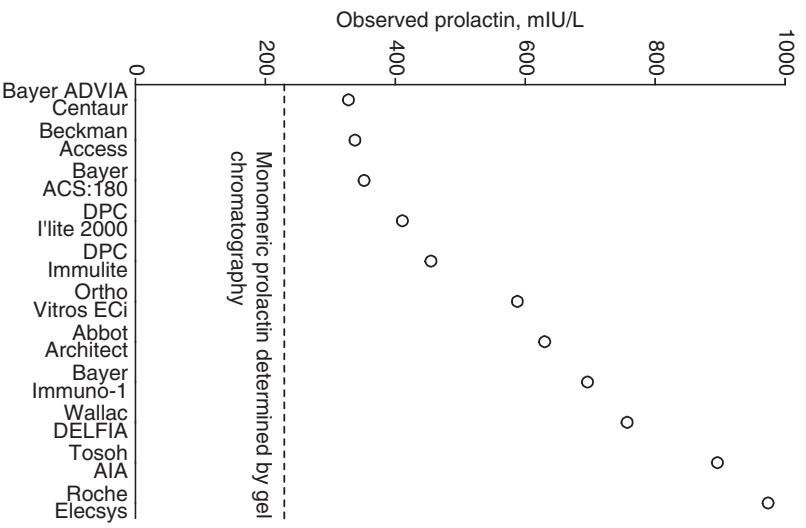


Figure 6 Method mean prolactin, distribution 254

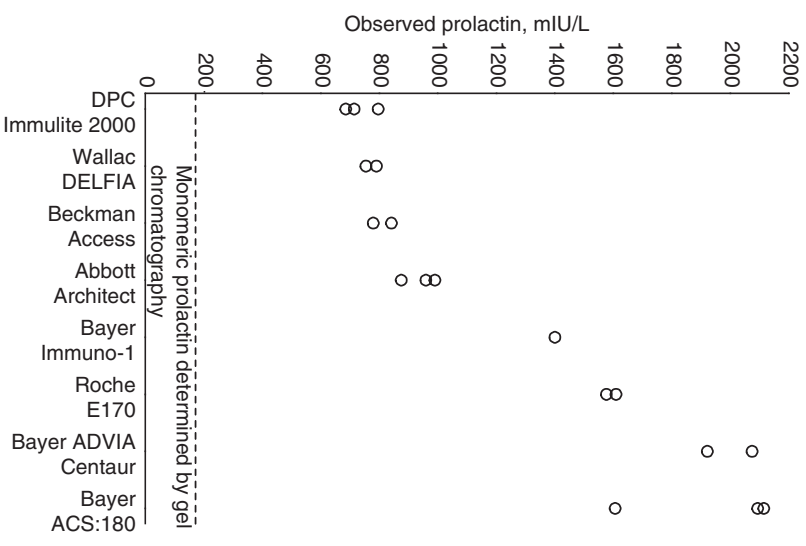


Figure 8 Method mean prolactin, distribution 281

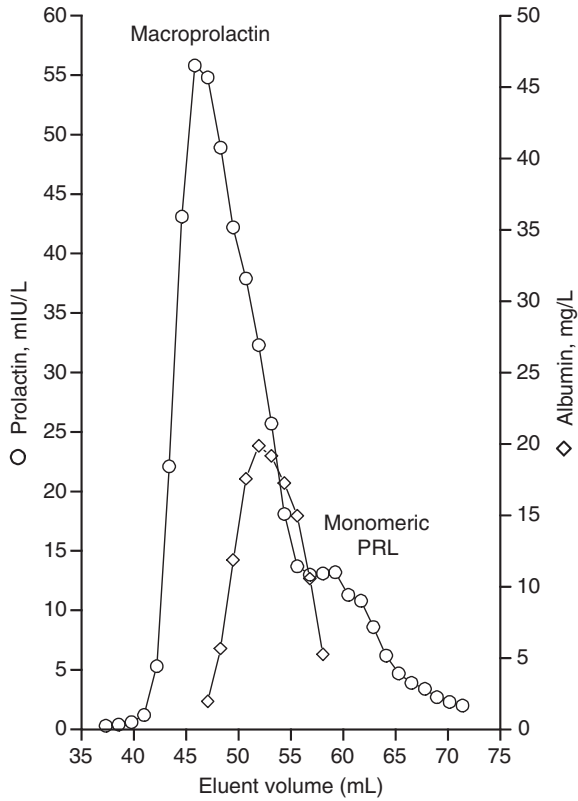


Figure 9 Gel filtration profile, distribution 199A

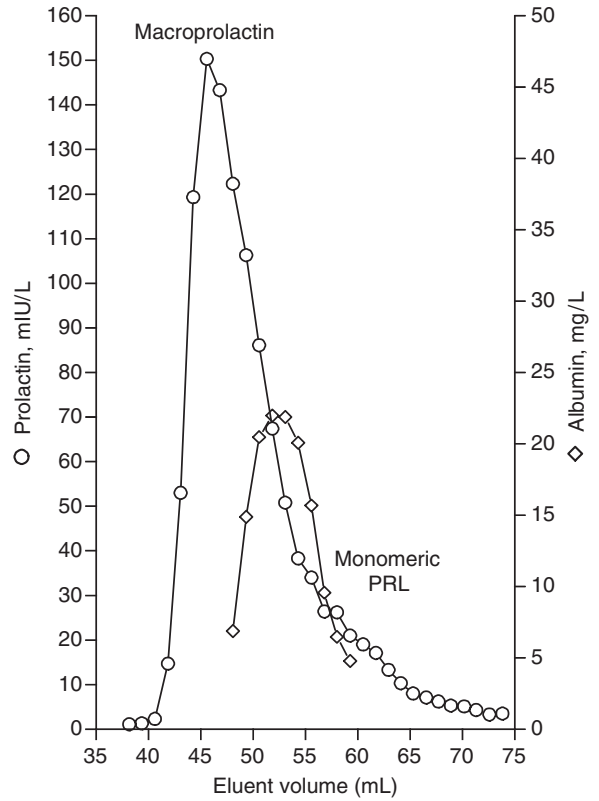


Figure 11 Gel filtration profile, distribution 199C

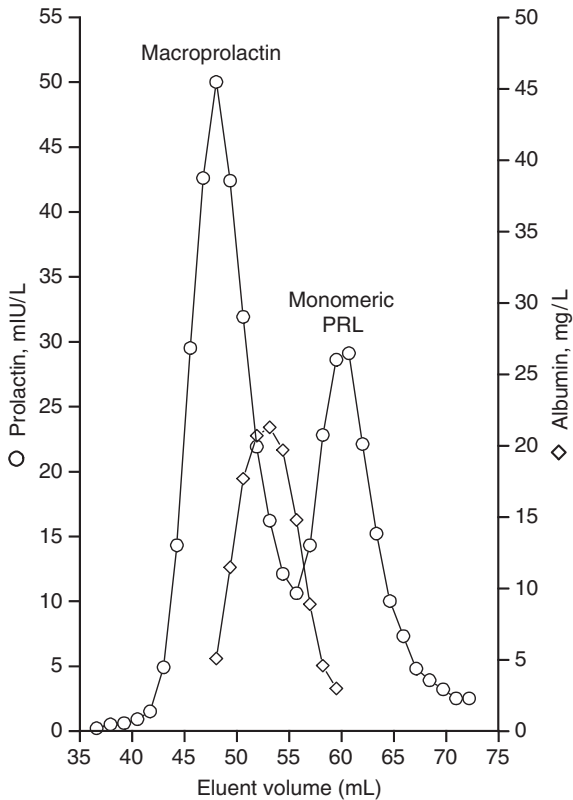


Figure 10 Gel filtration profile, distribution 199B

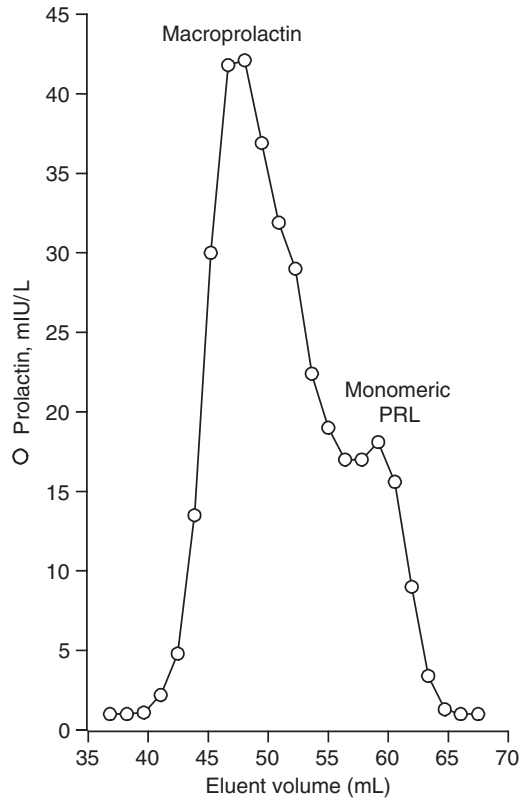


Figure 12 Gel filtration profile, distribution 214

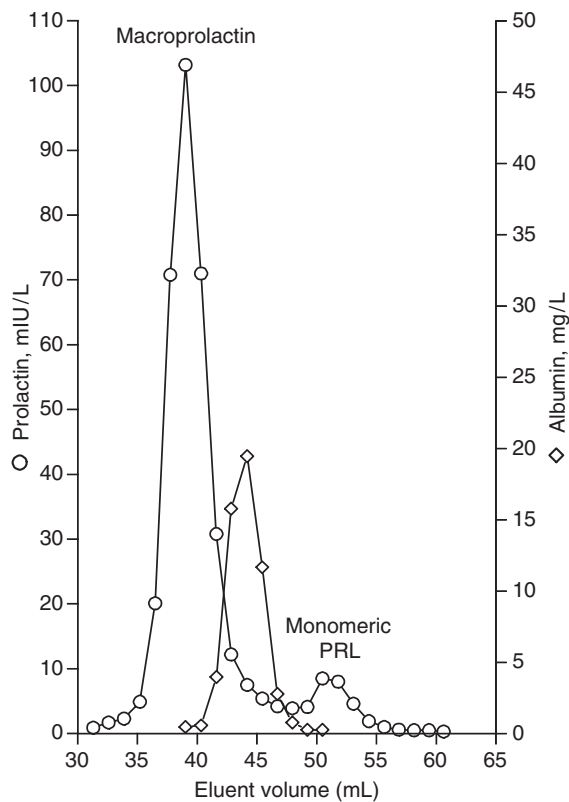


Figure 13 Gel filtration profile, distribution 226

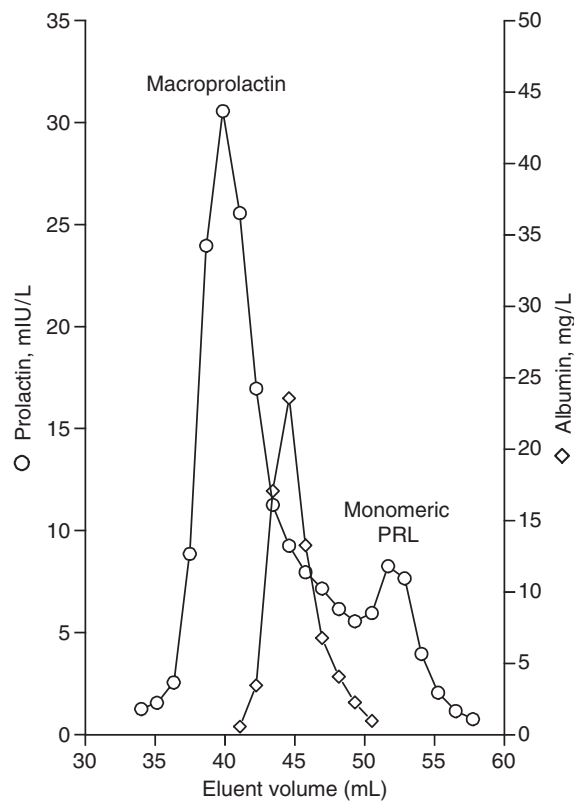


Figure 15 Gel filtration profile, distribution 261

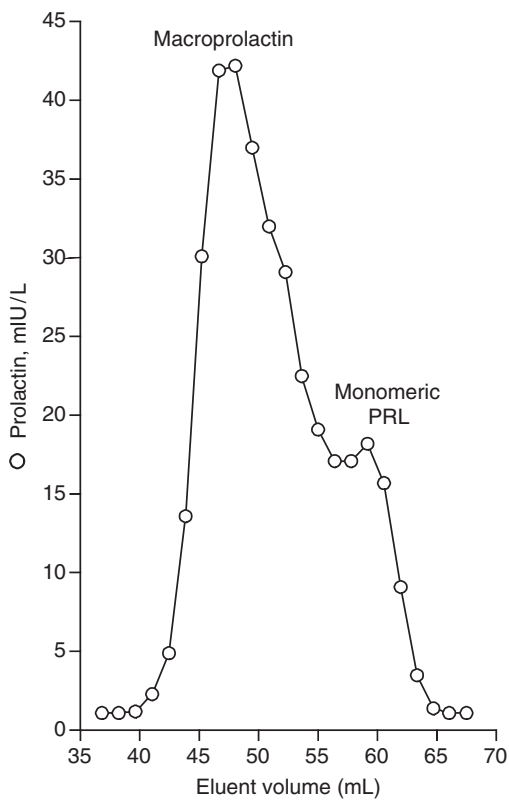


Figure 14 Gel filtration profile, distribution 254

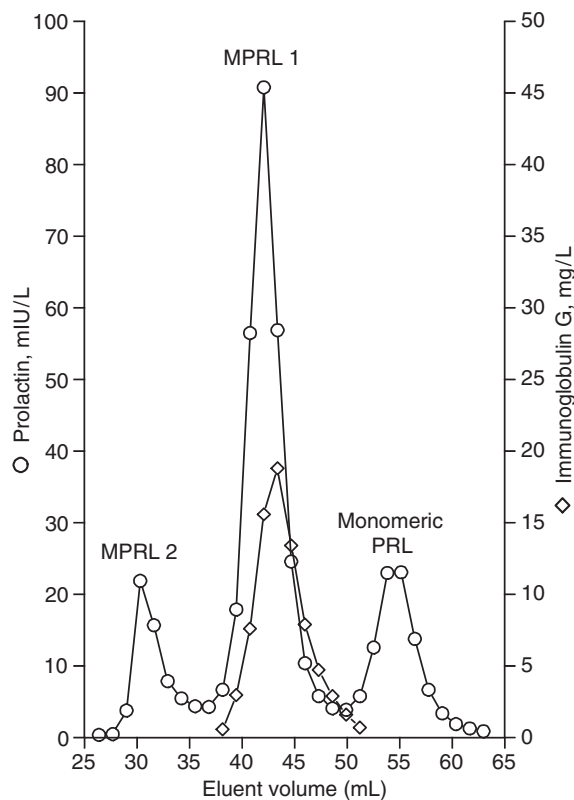


Figure 16 Gel filtration profile, distribution 281

Table 2 *Interpretative exercises involving specimens exhibiting hyperprolactinaemia without macroprolactinaemia, 1996–2003*

Distribution	Date	Source
197	June 1996	Routine pools
211	August 1997	Routine pools
275	December 2002	Pooled pregnancy sera
287	November 2003	Routine pools

Routine pools were prepared by adding serum from hyperprolactinaemic individuals to base pools with normal prolactin. The pregnancy sera came from the second trimester.

Table 3 *Distributions including an interpretative element, 1996–2002*

Distribution	Date	Specimens issued (mean observed prolactin, mIU/L IS 84/500)	Centres (%) mentioning possible presence of macroprolactin	Notes
197	June 1996	Routine pools (178, 591, 1073 & 3481 mIU/L)	0	
211	August 1997	Routine pools (180, 1689, 4453 & 6434 mIU/L)	0	
226	November 1998	Single patient, macroprolactin positive (476–3212 mIU/L, depending on method)	22%	Amongst participants regarding the observed prolactin concentration as raised, 30% considered the presence of macroprolactin.
254	March 2001	Single patient, macroprolactin positive (320–980 mIU/L, depending on method)	65%	Centres had prior knowledge that the prolactin as determined by Bayer Immuno-1 on a previous specimen was 1352 mIU/L.
261	October 2001	Pooled pregnancy serum (989 mIU/L); macroprolactin positive pools (1230 & 887 mIU/L); macroprolactin negative donation (2590 mIU/L)	33%	
275	December 2002	Pooled pregnancy serum (774 mIU/L)	14%	Many centres thought that pregnancy should be excluded before considering macroprolactin.
281	June 2003	Single patient, macroprolactin positive (680–2110 mIU/L, depending on method)	78%	
287	December 2003	Routine pools (1415 & 579 mIU/L)	77%	Of the 28% centres that thought the prolactin concentration was raised, 68% mentioned macroprolactin.

Analysis of centres mentioning macroprolactin as a possible cause of hyperprolactinaemia.