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List of Abnormal Hemoglobins Recorded in the World

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Hemoglobinopathy is a congenital abnormality of hemoglobin synthesis, in which the α or the non-α polypeptide chains of abnormal amino acid sequence are produced owing to the mutational change of the structural gene of the hemoglobin polypeptides. Hereditary suppression of the production of the α or the non-α polypeptide chains due to mutation of their operator or regulator gene, namely thalassemia, is also included into the category of hemoglobinopathy, although it is not accompanied by abnormal hemoglobins.

Pauling and his associates are credited for the pioneer work of exploring the vast area of hemoglobinopathy. In 1949[1] they discovered a slow-moving hemoglobin, which was named Hb S later, in the hemolysate of a patient with sickle cell anemia by moving boundary electrophoresis, and established that Hb S which is different from the normal adult hemoglobin in molecular structure was responsible for "sickling" and clinical manifestations of this disease. They coined the word "molecular disease" for sickle cell anemia in order to characterize it properly. Sickle cell anemia was the first instance of hemoglobinopathy. Pauling's discovery gave a great impetus to the survey of hemoglobinopathy in the world, and within a few years a considerable number of electrophoretically abnormal hemoglobins, such as Hbs C, D, E, etc., were reported from various countries.

Schroeder and his associates[2] demonstrated two different sorts of polypeptides, the α and the β chains, in the molecule of hemoglobin. In 1958 Ingram[3] invented an ingenious method called finger-printing for the analysis of polypeptides, which enabled him to reveal the characteristic abnormality in Hb S molecule, i.e. the substitution of valine for the glutamic acid at the sixth residue of the β chain. The abnormal β chain of Hb S, namely the β^S chain, is discriminated from the β^A chain of normal adult hemoglobin (Hb A) only by this amino acid substitution. The remainder of the amino acid sequence is entirely the same between the β^S and the β^A chains. However, the presence of valine in the place of glutamic acid residue (β 6) leads to build an intramolecular ring (Val-His-Leu-Thr-Pro-Val) between the sixth amino acid residues and the N-terminal end of the β^S chain. In deoxygenated state a pair of these rings of a Hb S molecule are fitted to a pair of pockets belonging to the α chains of another Hb S molecule. In this way the connection of deoxygenated Hb S molecule extends endlessly to form a filament. Several (six) of the filaments snuggle together to form a bundle and the

bundles thus produced create crystal-like structure called "tactoid" which is extremely insoluble. The tactoids push and deform the stroma of an erythrocyte from inside to give rise to fish-fin or foliate spicules on the surface. This is the phenomenon of "sickling" which is characteristic of the erythrocytes containing Hb S.[4]

The basic study on the chemistry of hemoglobinopathy was almost completely accomplished in 1965, by which year the amino acid sequences had been established for all of the polypeptide chains composing the molecules of the normal human hemoglobins, namely the α^{A}[5], the β^{A}[5], the γ^{F}[6] and the δ^{A2}[7] chains. The erythrocytes of the normal adults contain three kinds of hemoglobins, (1) Hb A = $\alpha_2^A\beta_2^A$, the major component occupying about 95 per cent, (2) Hb F = $\alpha_2^A\gamma_2^F$, a minor component which is alkali-resistant, comprising about 1 per cent and (3) Hb A_2 = $\alpha_2^A\delta_2^{A2}$, a slow moving hemoglobin forming about 2.5 per cent of the total hemoglobin respectively, in the foetal period Hb F makes the principal component of hemoglobins.

As many as 199 sorts of abnormal hemoglobins have hitherto been recorded in the world. They are listed in Table I. Most of them are not associated with clinical symptoms (symptomless hemoglobinopathies). However, some abnormal hemoglobins, which are represented by Hb S, give rise to diseases showing characteristic clinical manifestations. They are classified into the following major groups: ... (1) Sickle cell hemoglobins, (2) unstable hemoglobins producing congenital Heinz body hemolytic anemia, (3) hemoglobin M's causing congenital cyanosis, (4) hemoglobins with low oxygen affinity, and (5) hemoglobins with high oxygen affinity entailing polycythemia.

1. Sickle cell hemoglobins. This is represented by Hb S (β 6 Glu→Val). Sickle cell hemoglobins are listed in Table II. They give positive result to sickling test of blood drop with reducing agent (2 per cent sodium metabisulfite solution). Hb I was once said to cause sickling, but recent study revealed it to be an artifact[8].

2. Unstable hemoglobins. These hemoglobins are so unstable that they undergo irreversible oxidation and denaturation spontaneously even while they are contained in living erythrocytes, yielding intraerythrocytic inclusion bodies (Heinz bodies). Occasionally denaturation becomes manifest only when drugs (sulfonamide) which enhance the oxidation process in the erythrocytes are given to the carrier. Hb Zürich (β 63 His→Arg) is such an example. The hemoglobins are precipitated when they are warmed at 50–60°C. Accordingly, heat denaturation test of the hemolysate containing these abnormal hemoglobins are used for their detection. A few hemoglobins belonging to this group such as Hb Hammersmith, Hb Torino, Hb Mie, Hb Kanazawa and Hb Chiba are not demonstrable by electrophoresis. Table III presents the list of unstable hemoglobins. It is worth while to mention that almost all the unstable hemoglobins have β chain anomaly.

3. Hb M's. Hb M is the oldest example of abnormal hemoglobins that have

ever been detected from the Caucasians and the Asian races. They were for the first time reported from Germany by Hörlein and Weber in 1948[9], a year before the discovery of Hb S by Pauling[1] and his associates. Hb M's are characterized by their chocolate brown color reminiscent of methemoglobin. So, they are demonstrable by the spectroscopic examination of the hemolysates (of O_2 Hb and metHb types). Irreversible oxidation of heme iron as a result of the amino acid substitution in the α or β chains at a residue which is in intimate relation to heme is responsible for the causation of this peculiar color. It is thought that half a moiety of the molecule of this hemoglobin relevant to the abnormal polypeptide chains (the α or the β) is methemoglobinized. Substitution of tyrosine for the proximal (α 87, β 92) or the distal (α 58, β 63) histidine is commonly found in Hb M's. Agar gel or starch block electrophoresis (pH 7.0) of the methemoglobin type hemolysate is convenient for the demonstration of the Hb M's. Hb M's are listed in Table IV.

4. Hemoglobins with low O_2 affinity. Hb Kansas is the representative of this group (Table V). Like Hb M's it causes cyanosis. However, another hemoglo bin belonging to this group, i.e. Hb E is not related to cyanosis.

5. Hemoglobins with high O_2 affinity. The molecules of these hemoglobins are difficult in releasing O_2 when they are exposed to lowered oxygen tension. Presumably the amino acid substitution in the abnormal chains seen in these hemoglobins result in altered conformation of the α or β subunit pair which hampers their interrelated to-and-fro shift inherent in oxygenation and deoxygenation of hemoglobin molecule. Chronic oxygen deficit in the tissues will stimulate production of erythropoietin, thus causing polycythemia. Hemoglobins with high O_2 affinity are seen in Table VI.

Theoretically 2151 sorts of abnormal hemoglobins are expected from the consideration of possible amino acid substitution on the α or the β chains.[15] Only 687 kinds of these are demonstrable by electrophoresis which is, at present, the most useful measure for their detection. The remaining variants are thought to be buried until new procedures except electrophoresis which enable us to disclose electrically inert abnormality of hemoglobins, because the amino acid substitutions in their abnormal polypeptide chains are of the one which does not entail the positive or negative change in electrical charge. Perhaps, heat denaturation test of the hemolysate may be mentioned as one of such procedures, although it has only a limited usefulness. Further efforts should be made along this line to promote the study of abnormal hemoglobins.

Table I. List of known hemoglobin substitutions and deletions

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
A'_2 (B_2)[10]	delta	16	A 13	Gly⟶Ala
A_2 Babinga[11]	delta	136	H 14	Gly⟶Asp
A_2 Flatbush[12]	delta	22	B 4	Ala⟶Glu
A_2 N.Y.U.[13]	delta	12	A 9	Asn⟶Lys
A_2 Sphakia[14]	delta	2	NA 2	His⟶Arg
Abiko[15]	beta			
Aegina[16]	gamma ?			
Agenogi =Izumo[17]	beta	90	F 6	Glu⟶Lys
Alexandra[18]	gamma ?			
Ann Arbor[19]	alpha	80	F 1	Leu⟶Arg
Atago[199]	alpha	85	F 6	Asp⟶Tyr
Augusta I[20]	beta			β_4^S (tetramer)
Augusta II[20]	beta			β_4^C (tetramer)
Bart's[21]				γ_4 (tetramer)
Bibba[22]	alpha	136	H 19	Leu⟶Pro
Boras[23]	beta	88	F 4	Leu⟶Arg
Broussais[24]	alpha	90	FG 2	Lys⟶Asn
C[25]	beta	6	A 3	Glu⟶Lys
C Georgetown[26]	beta	6 core	A 3 —	Glu⟶Val —
C Harlem[27]	beta	6 73	A 3 E 17	Glu⟶Val Asp⟶Asn
Cardeza[28]	alpha			
Caserto[29]	beta			
Chad[30]	alpha	23	B 4	Glu⟶Lys
Chesapeake[31]	alpha	92	FG 4	Arg⟶Leu
Chiapas[32]	alpha	114	GH 2	Pro⟶Arg
Chiba[33]				
Chicago I[34]				
Cyprus I[35]	gamma			
D Bushman[36]	beta	16	A 13	Gly⟶Arg
D Frankfurt[37]	beta			
D Hollywood[38]	beta			
D Ibadan[39]	beta	87	F 3	Thr⟶Lys
D Punjab[40] =D Caucasian =D Chicago =D Cyprus =D Los Angeles =D North Carolina =D Portugal	beta	121	GH 4	Glu⟶Gln

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
Dakar[41]	alpha	112	G 19	His⟶Gln
Dhofar[42]	beta	58	E 2	Pro⟶Arg
Douglas et al[43]	beta			
E[44]	beta	26	B 8	Glu⟶Lys
E Saskatoon[45]	beta	22	B 4	Glu⟶Lys
Etobicoke[46]	alpha	84	F 5	Ser⟶Arg
F Akashi[15]	gamma			
F Alexandra[19]	gamma	12	A 9	Thr⟶Lys
F Houston[47]	gamma			
F Hull[48]	gamma	121	GH 4	Glu⟶Lys
F Jamaica[200]	gamma gamma	61 136	E 5 H 14	Lys⟶Glu Ala
F Roma[49]	gamma			
F Texas I[50] =F Galveston	gamma	5	A 2	Glu⟶Lys
F Texas II[51]	gamma	6	A 3	Glu⟶Lys
Fessas-Papaspyrou[52] =Bart's				γ_4 (tetramer)
Freiburg[53]	beta	23	B 5	Val deleted
Fukuoka[54]				
G Accra[55]	beta	79	EF 3	Asp⟶Asn
G Audhali[56]	alpha	23	B 4	Glu⟶Val
G Baltimore[57]	alpha	Tp-9		Asp⟶His
G Chinese[58] =G Hong Kong =G Honolulu =G Shingapore	alpha	30	B 11	Glu⟶Gln
G Copenhagen[59]	beta	47	CD 6	Asp⟶Asn
G Coushatta[60] =G Saskatoon =G Hsin-Chu	beta	22	B 4	Glu⟶Ala
G Galveston[61] =G Port Arther =G Texas	beta	43	CD 2	Glu⟶Ala
G Georgia[201]	alpha	95	G 2	Pro⟶Leu
G Ibadan[62]	alpha			
G Makassar[202]	beta	6	A 3	Glu⟶Ala
G Norfolk[63]	alpha	85	F 6	Asp⟶Asn
G Paris[64]	alpha	Tp-7		
G Philadelphia[65] =D Azuokoli =D Baltimore =D St. Lous =D Washington =G Bristol =Stanleyville I	alpha	68	E 17	Asn⟶Lys

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
G San Jose[66]	beta	7	A 4	Glu⟶Gly
G Taegu[67]				
G Taichung[203] =Mahidol	alpha	74	EF 3	Asp⟶His
G Taipei[68]	beta	22	B 4	Glu⟶Gly
G Taiwan Ami[69]	beta	25	B 7	Gly⟶Arg
Genova[70]	beta	28	B 10	Leu⟶Pro
Gifu[71] =G Szuhu[72] =Ichnomiya	beta	80	EF 4	Asn⟶Lys
Gower I[73]	epsilon			ε_4 (tetramer)
Gower II[74]				$\alpha_2\ \varepsilon_2$
Gun Hill[75]	btea	91-95 or 92-96 or 93-97	F7-FG2 or F8-FG3 or F9-FG4	(Leu, His, Cys, Asp, Lys) deletion
H[76]				β_4 (tetramer)
Hammersmith[77]	beta	42	CD 1	Phe⟶Ser
Hasharon[78]	alpha	47	CD 6	Asp⟶His
Hikairi[79]	beta	61	E 5	Lys⟶Asn
Hirose[80]	beta	37	C 3	Try⟶Ser
Hiroshima[81]	beta	146	H 21	His⟶Asp
Hijiyama[82]	beta	120	GH 3	Lys⟶Gln
Hofu[83]	beta	126	H 4	Val⟶Glu
Honolulu[84]				
Hope[85]	beta	136	H 14	Gly⟶Asp
Hopkins I[86]	beta			
Hopkins II[87]	alpha			
I[88]	alpha	16	A 14	Lys⟶Glu
I Burlington[89]	alpha			
I Toulouse[90]	beta	66	E 10	Lys⟶Glu
Ichinomiya[91] =Gifu	beta	80	EF 4	Asn⟶Lys
J[92] =Mexico	alpha	54	E 3	Gln⟶Glu
J Baltimore[93] =New Heaven No. 2 =J Trinidad =J Ireland	beta	16	A 13	Gly⟶Asp
J Bangkok[94] =J Korat =J Meining	beta	56	D 7	Gly⟶Asp
J Cambridge[59]	beta	69	E 13	Gly⟶Asp
J Cape Town[95]	alpha	92	FG 4	Arg⟶Gln

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
J Georgia[96]	beta			
J India[97]	alpha			
J Iran[98]	beta	77	EF 1	His⟶Asp
J Jamaica[38]	beta			
J Kaohsiung[204]	beta	59	E 3	Lys⟶Thr
J Korat[99]	beta	56	D 7	Gly⟶Asp
J Malaya[97]	alpha			
J Medellin[100]	alpha	22	B 3	Gly⟶Asp
J Meining[99]	beta	56	D 7	Gly⟶Asp
J Oxford[101] =I Interlaken	alpha	15	A 13	Gly⟶Asp
J Paris[102]	alpha	12	A 10	Ala⟶Asp
J Sardegna[103]	alpha	50	CD 8	His⟶Asp
J Taichung[198]	beta	129	H 7	Ala⟶Asp
J Tongariki[104]	alpha	115	GH 3	Ala⟶Asp
J Toronto[105]	alpha	5	A 3	Ala⟶Asp
K Calcutta[97]	alpha			
K Cameroon[106]	beta	Tp-8		Ala⟶Glu or Asp
K Ibadan[106]	beta	46	CD 5	Gly⟶Glu
K Liberia[38]	beta			
K Madras[38]	alpha			
K Woolwich[106]	beta	132	H 10	Lys⟶Gln
Kanazawa[107]				
Kansas[108]	beta	102	G 4	Asn⟶Thr
Kempsey[109]	beta	99	FG 6	Asp⟶Asn
Khartoum[110]	beta	124	H 2	Pro⟶Arg
Koelliker[111]	alpha	141	HC 3	Arg deleted
Köln[112]	beta	98	FG 5	Val⟶Met
Kokura[113] =L Ferrara =Beilinson =Umi =Tagawa II =Yukuhashi II =L Gaslini	alpha	47	CD 6	Asp⟶Gly
Korle Bu[114]	beta	73	E 17	Asp⟶Asn
Kumamoto[115]	alpha			
L[116]	beta			
L Bombay[117]	alpha	Tp-8,9		
L Ferrara[118] =Kokura	alpha	47	CD 6	Asp⟶Gly
L Persian Gulf[205]	alpha	57	E 6	Gly⟶Arg

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
Leiden[119]	beta	6 or 7	A3 or A4	Glu deleted
Lepore Boston[120]				$\alpha_2(\delta\text{-}\beta)_2$
Lepore Hollandia[121]				$\alpha_2(\delta\text{-}\beta)_2$
M Boston[122] (Osaka[123]) =M Gothenberg =M Kiskunhalas[124] =M Leipzig II =M Norin =M Osaka	alpha	58	E 7	His⟶Tyr
M Hyde Park[125] (Akita[126]) =M Akita	beta	92	F 8	His⟶Tyr
M Iwate[127] (Kankakee[128]) =M Kankakee =M Oldenburg	alpha	87	F 8	His⟶Tyr
M Leipzig I[129]				
M Leipzig II[130]				
M Milwaukee I[122] =M Mineapolis	beta	67	E 11	Val⟶Glu
M Milwaukee II[122]	beta			
M Reserve[131]	alpha			
M Saskatoon[122] (Kurume[132]) =M Chicago =M Emory =M Elberfeld =M Hamburg =M Kurume =M Radom =M Arhus =M Yonago	beta	63	E 7	His⟶Tyr
Malmö[210]	bata	97	FG 4	His⟶Gln
Manitoba[133]	alpha	102	G 9	Ser⟶Arg
Matsue[134]	alpha	Tp-9		
Memphis[135]	alpha	23	B 4	Glu⟶Gln
Mexico[32] =J	alpha	54	E 3	Gln⟶Glu
Mie[136]				
Miyada[115]				$\alpha_2(\beta\text{-}\delta)_2$
N Baltimore[137] =N Memphis =N New Haven =Jenkins =Kenwood	beta	95	FG 2	Lys⟶Glu
N New Haven[138]	bata	95	FG 2	Lys⟶Glu
N Seattle[139]	beta	61	E 5	Lys⟶Glu
Nagasaki[15]	beta	17	A 14	Lys⟶Glu
New York[140]	beta	113	G 15	Val⟶Glu
Nishiki IV[141] =Waziro ?	beta	Tp-3		

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
Norfolk[142] =Kagoshima =Nishiki I, II, III	alpha	57	E 6	Gly⟶Asp
O Arab[143] =O Bulgaria =O New York	beta	121	GH 4	Glu⟶Lys
O Indonesia[143]	alpha	116	GH 4	Glu⟶Lys
Oak Ridge[144]	beta	94	FG 1	Asp⟶Asn
Okayama[15]	alpha			
Oki[15]	alpha			
Olmsted[145, 210]	beta	141	H 19	Leu⟶Arg
Omori[15]	beta	6 or 7	A3 or A4	Glu⟶Gly
Otsu[146] =E	beta	26	B 8	Glu⟶Lys
P[147]	beta	117	G 19	His⟶Arg
Philly[148]	beta	35	C 1	Tyr⟶Phe
Picardy[149]				
Port Alegre[150]	beta	9	A 6	Ser⟶Cys
Portland 1[151]				$\gamma_2\ \chi_2$
Pylos[152]				$\alpha_2(\delta\text{-}\beta)_2$
Q Chinese[153]	alpha			
Q Iran[211]	alpha	75	EF 4	Asp⟶His
Q Thailand[212]	alpha	74	EF 3	Asp⟶His
R[154] =Durham No. 1	beta	Tp-1		
Rainier[155]	beta	145	HC 2	Tyr⟶Cys
Rambam[156]	beta	69 or 74	E13 or E18	Gly⟶Asp
Riverdale-Bronx[157]	beta	24	B 6	Gly⟶Arg
Russ[158]	alpha	51	CD 9	Gly⟶Arg
S[159]	beta	6	A 3	Glu⟶Val
Santa Ana[160]	beta	88	F 4	Leu⟶Pro
Sabine[161]	beta	91	F 7	Leu⟶Pro
Salt Lake City[162]				
Sawara[206]	alpha	6	A 4	Asp⟶Ala
Sealy[163] =Sinai =Hasharon	alpha	47	CD 6	Asp⟶His
Seattle[164]	beta	76	E 20	Ala⟶Glu
Shepherds Bush[207]	beta	74	E 18	Gly⟶Asp
Shimonoseki[165,166] =Hikoshima =Mobara	alpha	54	E 3	Gln⟶Arg

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
Singapore [110]	alpha	141	HC 3	Arg⟶Pro
Singapore-Bristol [167]	gamma			
Siriraj [168]	beta	7	A 4	Glu⟶Lys
Sogn [169]	beta	14	A 11	Leu⟶Arg
Stanleyville II [170]	alpha	78	EF 7	Asn⟶Lys
St. Mary [171]	beta	core ?		
Sud-Vietnam [172]				
Sydney [173]	beta	67	E 11	Val⟶Ala
Tacoma [133]	beta	30	B 12	Arg⟶Ser
Tagawa I [115]	alpha	Tp-10		
Ta-Li [208]	beta	83	EF 7	Gly⟶Cys
Tochigi [174]	beta	56-59	D7-E3	deleted
Tokuchi [115]	beta			
Tokyo [115]	beta			
Torino [175]	alpha	43	CD 1	Phe⟶Val
Tsukiji [176]	beta			
Ube I [177]	beta	93	F 9	Cys SH blocked
Ube II [178]	alpha	68	E 17	Asn⟶Asp
Warren [179]	gamma			
Wajiro [180]	alpha			
Wien [133]	beta	130	H 8	Tyr⟶Asp
Yakima [181]	beta	99	FG 6	Asp⟶His
Yatsushiro [15]	beta			
Yoshizuka [15]	beta	108	G 10	Asn⟶Asp
Ypsilanti [182]				
Yukuhashi [15]	beta	58	E 2	Pro⟶Arg
Zambia [209]	alpha	60	E 9	Lys⟶Asn
Zurich [183]	beta	63	E 7	His⟶Arg

Table II. List of sickling hemoglobins

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
S [159]	beta	6	A 3	Glu⟶Val
C Georgetown [26]	beta	6 core	A 3	Glu⟶Val
C Harlem [27]	beta	6	A 3	Glu⟶Val
		73	E 17	Asp⟶Asn
G Philadelphia/S [184]	alpha	68	E 17	Asn⟶Lys
	beta	6	A 3	Glu⟶Val

Memphis/S [185]	alpha	23	B 4	Glu⟶Gln
	beta	6	A 3	Glu⟶Val
Stanleyville II/S [186]	alpha	78	EF 7	Asn⟶Lys
	beta	6	A 3	Glu⟶Val

Table III. List of unstable hemoglobins

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
Bibba [22]	alpha	136	H 19	Leu⟶Pro
Chiba [33]				
Genova [70]	beta	28	B 10	Leu⟶Pro
Gun Hill [75]	beta	91-95 or 92-96 or 93-97	F7-FG2 or F8-FG3 or F9-FG4	(Leu, His, Cys, Asp, Lys) deleted
Hammersmith [77]	beta	42	CD 1	Phe⟶Ser
Kansas [108]	beta	102	G 4	Asn⟶Thr
Köln [112]	beta	98	FG 5	Val⟶Met
L Ferrara [118]	alpha	47	CD 6	Asp⟶Gly
Mie [136]				
Olmsted [145]				
Philly [148]	beta	35	C 1	Tyr⟶Phe
Sabine [161]	beta	91	F 7	Leu⟶Pro
Salt Lake City [162]				
Santa Ana [160]	beta	88	F 4	Leu⟶Pro
Seattle [164]	beta	76	E 20	Ala⟶Glu
Sealy [163]	alpha	47	CD 6	Asp⟶His
Shepherds Bush [207]	beta	74	E 18	Gly⟶Asp
Sogn [169]	beta	14	A 11	Leu⟶Arg
St. Mary's [171]	beta	core ?		
Sydney [173]	beta	67	E 11	Val⟶Ala
Tacoma [133]	beta	30	B 12	Arg⟶Ser
Tochigi [174]	beta	56-59	D7-E3	deleted
Torino [175]	alpha	43	CD 1	Phe⟶Val
Ube 1 [177]	beta	93	F 9	Cys SH blocked
Wien [133]	beta	130	H 8	Tyr⟶Asp
Zurich [183]	beta	63	E 7	His⟶Arg

Table IV. List of hemoglobin M diseases

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
M Boston[122]	alpha	58	E 7	His⟶Tyr
M Hyde Park[125]	beta	92	F 8	His⟶Tyr
M Iwate[127]	alpha	87	F 8	His⟶Tyr
M Milwaukee 1[122]	beta	67	E 11	Val⟶Glu
M Saskatoon[122]	beta	63	E 7	His⟶Tyr

Table V. List of hemoglobins with low oxygen affinity

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
E[44, 187]	beta	26	B 8	Glu⟶Lys
Kansas[108]	beta	102	G 4	Asn⟶Thr

(Hb M's of α chain anomaly will also be classified into this group.)[203]

Table VI. List of hemoglobins with high oxygen affinity

Name	Chain anomaly	Residue no.	Helical no.	Amino acid substitution
A_2[7, 188]				
$A'_2(B_2)$[10, 188]	delta	16	A 13	Gly⟶Ala
Bart's[21, 189]				γ_4 (tetramer)
C Harlem[27]	beta	6 73	A 3 E 17	Glu⟶Val Asp⟶Asn
Chesapeake[31, 190]	alpha	92	FG 4	Arg⟶Leu
D Punjab[40, 191]	beta	121	GH 4	Glu⟶Gln
Freiburg[53]	beta	23	B 5	Val deleted
Gun Hill[75]	beta	91-95 or 92-96 or 93-97	F7-FG2 or F8-FG3 or F9-FG4	(Leu, His, Cys, Asp, Lys) deleted
H[76, 192]				β_4 (tetramer)
Hiroshima[81]	beta	143	H 21	His⟶Asp
J Cape Town[95, 193]	alpha	92	FG 4	Arg⟶Gln
Kempsey[109]	beta	99	FG 6	Asp⟶Asn
Köln[112, 194]	beta	98	FG 5	Val⟶Met
Lepore[120, 121, 195]				$\alpha_2(\delta\text{-}\beta)_2$
*M Hyde Park[125, 126, 196]	beta	92	F 8	His⟶Tyr
Rainier[155]	beta	145	HC 2	Tyr⟶His
Tacoma[133]	beta	30	B 12	Arg⟶Ser
Yakima[181, 197]	beta	99	FG 6	Asp⟶His
Zurich[183]	beta	63	E 7	His⟶Arg

*Hb M's of β chain anomaly are inferior to normal adult hemoglobin in the capacity of transporting oxygen in spite of slightly increased oxygen affinity of their normal α chain, because their abnormal β chains can not carry oxygen.

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