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Center for Disease Control Diagnostic Immunology Proficiency Testing Program Results for 1978

ROGER N. TAYLOR,[1]* KAREN M. FULFORD,[1] VINCENT A. PRZYBYSZEWSKI,[1] AND VICTORIA POPE[2]

Diagnostic Immunology Section, Proficiency Testing Branch,[1] and Venereal Disease Serology Laboratory, Bacterial Immunology Branch,[2] Center for Disease Control, Atlanta, Georgia 30333

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Data from about 1,000 laboratories participating in the Diagnostic Immunology portion of the 1978 Center for Disease Control Proficiency Testing Program provided information dealing with laboratory performance and trends in testing protocols. Ninety specimens were distributed in scheduled quarterly and semiannual shipments, and five additional specimens were provided in a special survey. The specimens offered both qualitative and quantitative challenges for a wide variety of analytes which included syphilis serology, rheumatoid factor, bacterial agglutinins, hepatitis B surface antigen, immunoglobulins and other serum proteins, infectious mononucleosis, rubella, toxoplasma, antinuclear antibodies, and streptococcal exoenzymes. This paper summarizes the results of the 1978 program.

Under the Clinical Laboratories Improvement Act of 1967, the Center for Disease Control (CDC) Proficiency Testing Program was given the responsibility for measuring and improving clinical laboratory performance in the United States. The goal of the program is to improve performance by analyzing results, detecting deficiencies, evaluating methods, and disseminating results and other pertinent information to the participants.

Specimens prepared by the Diagnostic Immunology Section personnel are distributed to all participants, which include licensed laboratories and some nonlicensed (special study and reference) laboratories. A few laboratories located outside the United States also participate. In instructions accompanying the specimens, regular laboratory staff members are asked to test the specimens in a routine manner and to perform all of the tests that they normally perform. Participation in the program is mandatory for laboratories that provide interstate testing services.

In this report, data obtained from the 1978 Diagnostic Immunology Program are summarized. The overall trends and changes that became apparent after the year's accumulation of test data was evaluated are noted.

MATERIALS AND METHODS

Most of the sera or plasmas used for specimen preparations were purchased from commercial suppliers on government contract. Other sources donated pools of human serum of known reactivity in specific tests.

The Diagnostic Immunology Section of the Proficiency Testing Branch or an appropriate CDC specialty laboratory, or both, tested the sera for acceptability for use in the program. All sera were tested for hepatitis B surface antigen (HBsAg) reactivity, and only sera negative for HBsAg by radioimmunoassay were used as specimens other than those to be tested in HBsAg surveys. Specimens obtained as plasma were defibrinated with calcium chloride or thrombin.

Details of specimen preparation and tabulations of results for each survey are included in appropriate summary analyses and critiques (8-14, 16-20). Briefly, specimens were adjusted to the desired reactivity, filtered through sterile membrane filters, and dispensed into suitable vials or tubes. Many of the specimens were lyophilized. The adequacy of samples was confirmed independently by the Diagnostic Immunology Section, by other CDC specialty laboratories, and by reference laboratories. A continuous quality control program insures that all specimens satisfy preestablished criteria for sterility, antibody titer and stability, and between-vial variability.

Each specimen shipment was packaged and mailed in accordance with postal regulations and included appropriate instructions and report forms. Completed reports were to be postmarked within 2 weeks of the initial shipping date. Responses were compiled and graded, and individual performance rankings were reported to participants within 3 to 4 weeks after responses were received. Acceptable responses were determined from reference laboratory results. Overall response data were evaluated and compiled in summary analyses or published as separate reports and were sent to all participants.

RESULTS

Table 1 shows the tests that the participants were requested to perform and the number of

laboratories that participated for each test. The list includes a wide variety of tests commonly performed in diagnostic immunology laboratories. The Diagnostic Immunology Program is divided into three divisions: syphilis serology, HBsAg, and immunology, which includes all the remaining tests. Participants enrolled in immunology received samples for all of the tests in that division but were requested to test and report only those that they routinely perform.

Table 2 shows a comparison of reference and participant laboratory performance. The mean of the geometric standard deviations for each test is presented as a measure of interlaboratory precision. To translate those values into numbers that are more meaningful to the laboratorian, examples of the corresponding two standard deviation ranges for selected titers are given. In every case there was better interlaboratory comparability among the reference laboratories than there was among the other participants. In some cases the differences were slight, but in others they were substantial. Analytes showing the greatest differences in interlaboratory precision were: antistreptolysin O (ASO), heterophile, antinuclear antibody, brucella, tularemia, and rheumatoid factor (RF).

Fewer laboratories had results outside the reference ranges for rubella this year than in 1977. The percentage of participants that used standardized methods and recommended serum treatments for rubella hemagglutination-inhibition (HAI) testing remained approximately the same throughout the year. In each survey, poor performance (results outside of the reference laboratory range) was linked with failure to use recommended procedures for serum treatment (Table 3). In the past, the percentage of results outside the acceptable limits for laboratories using kaolin serum treatment was larger than the percentage for those using the recommended treatments (6, 7, 21, 22). Similar results were evident again in 1978 (Table 3). The geometric means of the kaolin titers were usually at the lower limit of the acceptable range or below it; this demonstrates once again the inadequacy of this treatment.

The geometric means of titers obtained with trypsinized human cells were higher than the means obtained with other cells, regardless of the serum treatment used. Mean titers were about 36% lower when baby chicken cells were used and 39% lower when Abbott "Duracytes" were used (Table 4). The titers of the antigens used in rubella HAI tests have increased over the past 2 years, and the majority of the laboratories are now using antigens with titers of 64 or greater. Some of the problems previously associated with low-titered antigens are not prevalent now.

TABLE 1. *Summary of CDC Diagnostic Immunology Proficiency Testing Program, 1978*

Determination	No. of challenges	No. of surveys per year	Mean no. of labs responding per survey
Rubella antibody	8	4	334
Streptococcal antibodies			
ASO	4	2	338
ADN-B	4	2	40
Multiple-enzyme test	4	2	181
RF	4	2	540
Infectious mononucleosis serology	4	2	493
Antinuclear antibodies	2	1	380
Salmonella agglutinins	2	1	418
Brucella agglutinins	2	1	399
Tularemia agglutinins	2	1	236
Rickettsial antibodies			
Weil-Felix test	2	1	353
CF	2	1	37
Toxoplasma antibodies	2	1	167
Carcinoembryonic antigen	2	1	115
Immunoglobulin quantitation			
IgG	2	1	334
IgA	2	1	334
IgM	2	1	334
Complement			
C3	2	1	269
C4	2	1	197
Alpha-1-antitrypsin	2	1	212
Haptoglobin	2	1	212
Ceruloplasmin	2	1	86
HBsAg	10	2	273
Syphilis serology	40	4	475
Special study surveys			
IgG, IgA, IgM	5	1	115
IgD	5	1	42
IgE	5	1	54
Coccidioides antibody	5	1	75
Histoplasma antibody	5	1	68

Use of a common reference serum for RF has been shown to improve the comparability of RF test results from different laboratories (2, 15, 16). Each shipment that contained samples for RF testing in 1978 included a vial of standardized RF serum. After testing the standard and the unknowns, the participants were asked to convert their titers for the unknowns to international units on the basis of the titers obtained on the standardized sample. Results from different laboratories have continued to be more comparable (less interlaboratory variation) when they are standardized in this manner (Table 5).

Immunoglobulins (immunoglobulin G [IgG], IgA, IgM) were quantitated primarily by radial immunodiffusion. Approximately 78% of the participating laboratories used this technique, but nephelometric and fluorometric methods are increasing in popularity. The geometric means of

TABLE 2. *Comparison of reference and participant laboratory interlaboratory precision*

Analyte	Titer	Reference labs		Participants	
		Mean S_G[a]	$2S_G$ range[b]	Mean S_G	$2S_G$ range
Rubella	20	1.58	8–50	1.88	6–71
Alpha-1-antitrypsin	100	1.10	83–121	1.20	69–144
Haptoglobin	100	1.23	66–151	1.32	57–174
Ceruloplasmin	100	1.49	45–222	1.68	35–282
IgG	1,000	1.16	743–1,346	1.17	730–1,369
IgA	100	1.16	47–134	1.25	64–156
IgM	100	1.22	67–148	1.35	55–182
C3	100	1.05	91–110	1.28	61–164
C4	100	1.17	73–137	1.30	59–169
ASO	60	1.34	33–108	1.88	17–212
ADN-B	60	1.20	42–86	1.40	31–118
Heterophile	60	1.49	27–133	2.31	11–320
Ox cell hemolysin	60	2.11	13–267	2.14	13–274
Antinuclear antibody	20	1.44	10–41	2.70	3–146
Brucella	20	1.41	10–40	2.21	4–98
Tularemia	20	1.52	9–46	2.02	5–82
Weil-Felix (*Proteus* OX19)	20	1.92	5–73	2.26	4–102
Salmonella	20	1.76	6–62	2.16	4–93
RF	20	1.51	9–46	2.58	3–133
Toxoplasma indirect immunofluorescence	20	1.70	7–58	2.94	2–173
Toxoplasma passive hemagglutination	20	2.11	4–89	2.35	3–110

[a] Mean of geometric standard deviation (S_G) for each test.
[b] Two standard deviation range: titer × S_G^2 to titer/S_G^2.

TABLE 3. *Rubella proficiency testing performance, 1978*

Sample no.	Acceptable range	Heparin-$MnCl_2$ or dextran sulfate		Kaolin	
		No. of participants	Results outside acceptable range (%)	No. of participants	Results outside acceptable range (%)
BI8-A01	8–16	162	24.7	87	35.6
BI8-A02	16–32	163	29.5	102	40.2
BI8-B01	16–64	183	16.9	82	37.8
BI8-B02	16–64	183	17.5	82	39.0
BI8-C01	≤16	152	8.6	88	4.6
BI8-C02	16–64	158	23.4	88	52.3
BI8-D01	32–128	155	18.6	87	19.5
BI8-D02	32–128	155	16.7	89	23.0
Average			19.5		31.5

the immunoglobulin results for different manufacturers indicate that additional improvement could be made in the standardization of these reagents. Reagents for other serum proteins, however, are in greater need of standardization. Complement C3 results vary with the antibody source mainly because some will detect only the βIA component but others will detect both the βIA and βIC components. Alpha-1-antitrypsin, haptoglobin, and ceruloplasmin results were also dependent on the source of the antibody used. The geometric mean values for a single sample varied with the manufacturer and ranged from 188 to 385 mg/dl for alpha-1-antitrypsin, from 103 to 158 mg/dl for haptoglobin, and from 26 to 81 mg/dl for ceruloplasmin. There are no readily available standards for these tests (Table 6).

There was variation in the geometric means of ASO titers obtained with streptolysin reagents from different manufacturers. Although the differences were not consistent in both surveys, some reagents do appear to give higher titers than others (20). Rabbit erythrocytes gave lower titers than sheep erythrocytes, which gave lower titers than human erythrocytes.

The number of laboratories performing the antideoxyribonuclease-B (ADN-B) test has re-

TABLE 4. *Comparison of rubella HAI results by serum treatment and cell type*[a]

Serum treatment and cell type	BI8-A01			BI8-A02			BI8-B01 and BI8-B02			BI8-C01			BI8-C02			BI8-D01 and BI8-D02		
	N	$\bar{x}_G$	S_G	*N*	$\bar{x}_G$	S_G	*N*	$\bar{x}_G$	S_G	*N*	$\bar{x}_G$	S_G	*N*	$\bar{x}_G$	S_G	*N*	$\bar{x}_G$	S_G
Heparin-$MnCl_2$																		
Chick	36	10	1.72	37	28	2.05	65	20	1.74	28	8	2.15	33	18	1.98	30	54	1.74
Duracytes	52	13	1.71	53	28	1.68	98	18	1.73	64	7	1.66	66	19	1.60	136	52	1.94
Human, trypsinized	54	16	1.68	57	37	1.49	154	32	1.72	42	9	2.11	41	28	2.13	84	98	1.76
Other	5	12	2.20	5	57	1.36	8	27	1.37	2	16	—	2	32	—	4	90	1.49
Total	147	13	1.76	152	31	1.71	330	25	1.88	136	8	1.92	142	21	1.98	254	65	1.97
Dextran sulfate																		
Chick	7	10	1.40	8	21	1.43	16	39	2.50	8	7	1.78	8	29	1.78	12	81	1.40
Human	6	13	1.43	6	32	1.55	16	45	1.85	6	8	2.13	6	40	1.43	10	147	1.55
Goose	2	8	—	2	23	2.00	4	32	2.22	2	6	—	2	16	—	2	640	—
Total	15	11	1.42	16	25	1.53	36	41	2.16	16	7	1.85	16	31	1.71	64	123	1.98
Kaolin																		
Chick	23	9	1.46	24	21	1.83	43	15	1.38	23	6	1.45	24	15	1.90	50	44	1.48
Duracytes	58	10	1.56	72	22	1.70	113	16	1.55	56	6	1.50	61	14	1.60	118	39	1.81
Other	4	13	2.16	5	28	1.36	2	20	—	3	10	2.88	3	20	2.88	8	62	1.21
Total	85	10	1.56	101	22	1.71	164	16	1.51	82	6	1.54	88	14	1.72	176	41	1.71
Acceptable range	8–16			16–32			16–64			16			16–64			32–128		

[a] N, Number of samples; $\bar{x}_G$, geometric mean; S_G, geometric standard deviation. —, Not calculated.

TABLE 5. *RF proficiency testing performance, 1978*

Test	Sample no.	Acceptable range (IU/ml)	No. of participants	Results outside acceptable range (%)
Slide	BI8-B03[a]	200–400	130	28.5
	BI8-B04[a]	200–400	128	31.2
	BI8-D03	100–400	158	27.8
	BI8-D04	Neg	158	10.8
	Average			24.6
Tube	BI8-B03[a]	200–400	208	26.4
	BI8-B04[a]	200–400	208	27.4
	BI8-D03	100–400	205	17.1
	BI8-D04	Neg	205	13.6
	Average			21.1

[a] Samples BI8-B03 and BI8-B04 are duplicates.

TABLE 6. *Serum-specific protein proficiency testing performance, 1978*

Analyte	Sample no.	Acceptable range	No. of participants	Results outside acceptable range (%)
Alpha-1-Antitrypsin	BI8-A09	206–280	213	26.7
	BI8-A10	206–280	211	29.1
Haptoglobin	BI8-A09	96–187	212	28.8
	BI8-A10	96–187	209	27.6
Ceruloplasmin	BI8-A09	10–29	86	47.3
	BI8-A10	10–29	85	53.3
IgG	BI8-B09	875–1,424	315	9.8
	BI8-B10	445–768	312	13.1
IgA	BI8-B09	150–237	330	16.9
	BI8-B10	74–124	329	24.3
IgM	BI8-B09	180–300	329	24.3
	BI8-B10	41–78	327	21.4
C3 (βIA)	BI8-D07	43–58	112	62.5
	BI8-D08	24–36	112	87.5
C3 (βIA/βIC)	BI8-D07	74–83	157	60.5
	BI8-D08	61–70	157	65.6
C4	BI8-D07	13–20	197	26.5
	BI8-D08	12–21	197	28.9

mained about the same as last year. This test is a good supplement to the ASO test for detecting streptococcal infections, particularly of the skin. Multiple-enzyme tests continue to be popular, and qualitative results agreed well with the ASO and ADN-B test results for the samples submitted this year.

Most laboratories in the Diagnostic Immunology program used slide tests to screen sera for infectious mononucleosis antibodies. Quantitative results for the slide infectious mononucleosis tests cannot be compared between laboratories because the results are given either as the reciprocal of the dilution of serum giving a positive result or as a titer equivalent to a heterophile titer (the actual titer multiplied by some factor). When qualitative results for each kit were compared with the reference laboratories' results, agreement was from 95 to 98% (20).

Variation in the method of reporting results was also seen for the ox cell hemolysin test. Some participants reported titers based on the serum dilution before addition of other reagents, but others based their titers on the final dilution, which is threefold higher than the serum dilution.

Quantitative results of indirect immunofluorescence tests for antinuclear antibodies varied according to the substrate species and tissue (17, 20). Use of mouse kidney or rat liver cells gave the highest geometric mean titers. Latex agglutination tests were positive about half of the time for the sample that was positive by indirect immunofluorescence, but the percentage of positive results varied with the reagent.

Most laboratories used similar procedures for all the bacterial agglutination tests. Slide test results (geometric means) were 17 to 38% lower than tube test results for brucella and 40% lower for salmonella agglutination. Differences in the antigens produced by commercial manufacturers remained a major reason for much of the variability in test results (20, 21). Titers of 80 to 160 were considered significant by over 90% of the reporting laboratories, and between 77 and 83% of the laboratories considered a change in titer between acute- and convalescent-phase sera to be more definitive. These data are similar to results in previous years. Over half of the laboratories using slide tests for detecting salmonella agglutinins reported two samples as negative (Table 7), although the reference laboratories reported titers of 40 to 160 (geometric mean = 101). About 20% of the participants that used the tube test also reported negative results for these samples. A similar situation was noted in 1977 (22).

Considerable variation was seen in the results of tests for toxoplasma antibodies. IIF test results ranged from 270 to 1,625 by antigen source, and almost 30% of the results were outside the acceptable range (512–2,048). Titers were somewhat lower with the indirect hemagglutination test, and fewer labs were outside the acceptable range (20).

Nearly all laboratories in the program used at least one third-generation test for HBsAg, which resulted in correct results for 95 to 99% of the reports. Second-generation tests were positive with samples of low reactivity only 60% of the time. The more sensitive latex tests gave results comparable to other third-generation tests. Participants were asked to test the HBsAg samples for anti-HBs in 1978. There was 75 to 93% agreement as to the presence or absence of antibody in the samples submitted (Table 8).

In 1978 the percentage of participants using the Rapid Plasma Reagin (RPR) card test remained fairly constant throughout the year (at

TABLE 7. *Bacterial agglutinins proficiency testing performance, 1978*

Analyte	Test	Sample no.	Acceptable range	No. of participants	Results outside acceptable range (%)
Brucella	Slide	BI8-A07	48–80	201	47.8
		BI8-A08	320–640	272	25.7
		Average			36.8
	Tube	BI8-A07	40–80	146	36.3
		BI8-A08	320–640	182	33.0
		Average			34.6
Proteus OX19 (Weil-Felix)	Slide and tube	BI8-B07	Neg–40	275	13.8
		BI8-B08	Neg–40	235	15.7
		Average			14.8
Tularemia	Slide	BI8-C07[a]	40–160	167	9.6
		BI8-C08[a]	40–160	164	11.6
		Average			10.6
	Tube	BI8-C07[a]	40–160	115	12.2
		BI8-C08[a]	40–160	113	13.3
		Average			12.8
Salmonella—group D	Slide	BI8-D09[a]	40–160	351	53.3
		BI8-D10[a]	40–160	351	51.6
		Average			52.4
	Tube	BI8-D09[a]	40–160	146	29.4
		BI8-D10[a]	40–160	146	34.9
		Average			32.2

[a] Samples BI8-C07 and BI8-C08, and BI8-D09 and BI8-D10 are duplicates.

about 56%), but the percentage of laboratories using the Venereal Disease Research Laboratory (VDRL) test and fluorescent treponeal antibody absorption test dropped significantly, from 52 and 43% to 39 and 29%, respectively. This was probably due primarily to the large number of Medicare laboratories added. Many of these are small private laboratories using only the qualitative RPR card test. The actual number of laboratories using the VDRL and the fluorescent treponemal antibody absorption tests remained about the same.

Tables 9 and 10 show that the overall qualitative performance was better in the RPR, with the correct answer given 96.3% of the time as opposed to 92.2% of the time for the VDRL. Both are above the acceptable level of 90%. In the fluorescent treponemal antibody absorption test the correct answer was given 92.7% of the time (Table 11).

Several laboratories which had been using more than one nontreponemal test for syphilis are now using only one. Many of the laboratories were performing both the VDRL and RPR but are now doing only the RPR. The reasons for choice of the RPR are probably twofold: ease in performing and reading the test, and stability of the antigen, which makes it less costly.

A special survey for immunoglobulins and fungal serology was provided to selected laboratories. Forty-nine laboratories reported IgE results on the five samples. Most participants used radioimmunoassay for quantitation of IgE, and they were evenly split between those using Sephadex as the solid phase and those using paper disks. The results for those using Sephadex were an average of 35% higher than for those using paper disks.

Of the 71 laboratories that reported results for coccidioides antibodies, 42 performed immunodiffusion, 45 did complement fixation (CF) tests, and 4 performed latex tests. Sample BI8-SO1 contained a higher level of antibody to coccidioides than did BI8-SO2. CF appeared to be the most sensitive test, because 95% reported positive results for BI8-SO1 and 46% reported positive for BI8-SO2. Only 50 and 27% of the laboratories using immunodiffusion found the same samples to be positive. There were some differences in sensitivity of immunodiffusion with reagents from different manufacturers. The positive results ranged from 36 to 80% for BI8-SO1 and from 11 to 71% for BI8-SO2.

Sixty-five laboratories performed tests for histoplasma antibodies; 38 used immunodiffusion,

TABLE 8. *Anti-HBs test results*

Sample no.	No. of labs	Correct responses	
		No.	Percent
BH8-A01	60	14	77
BH8-A02	58	45	78
BH8-A03	58	45	78
BH8-A04	58	45	78
BH8-A05	60	14	77
BH8-B01	74	58	78
BH8-B02	74	59	80
BH8-B03	72	67	93
BH8-B04	71	18	75
BH8-B05	71	66	93

TABLE 9. *RPR card test: syphilis serology test performance*

Sample no.	Acceptable result[a]	Qualitative		Quantitative	
		No. of participants	% Incorrect	No. of participants	% Incorrect
BV8-A01	N	212	1	92	1
BV8-A02	R4	212	1	92	39
BV8-A03	N	212	3	92	3
BV8-A04	R2	212	1	92	28
BV8-A05	R2	212	1	92	27
BV8-A06	N	212	1	92	0
BV8-A07	R1-R2	212	2	92	2
BV8-A08	N	212	7	92	9
BV8-A09	R1-R2	212	1	92	2
BV8-A10	R2	212	1	92	20
BV8-B01	R1-R2	219	2	101	3
BV8-B02	N	219	2	101	3
BV8-B03	R1	219	5	101	31
BV8-B04	N	219	4	101	3
BV8-B05	R2	219	0	101	25
BV8-B06	R1	219	5	101	27
BV8-B07	N	219	3	101	4
BV8-B08	R2	219	1	101	28
BV8-B09	R1-R2	219	2	101	5
BV8-B10	N	219	2	101	2
BV8-C01	R2-R4	250	<1	113	5
BV8-C02	R1-R2	250	8	113	20
BV8-C03	N	250	1	113	1
BV8-C04	R2-R4	250	<1	113	7
BV8-C05	N	250	3	113	1
BV8-C06	R1-R2	250	8	113	12
BV8-C07	N	250	2	113	2
BV8-C08	N	250	1	113	1
BV8-C09	R1-R2	250	9	113	11
BV8-C10	R1-R2	250	11	113	14
BV8-D01	R2-R4	304	1	124	6
BV8-D02	N	304	13	124	10
BV8-D03	R1	304	26	124	36
BV8-D04	N	304	1	124	0
BV8-D05	N	304	2	124	1
BV8-D06	R2-R4	304	1	124	10
BV8-D07	R1-R2	304	7	124	5
BV8-D08	R2-R4	304	3	124	32
BV8-D09	N	304	4	124	2
BV8-D10	N	304	2	124	0
Average for 1978			3.7		11.0

[a] N, nonreactive; R, reactive.

TABLE 10. *VDRL test: syphilis serology test performance*

Sample no.	Acceptable result[a]	Qualitative		Quantitative	
		No. of participants	% Incorrect	No. of participants	% Incorrect[b]
BV8-A01	N	195	3	164	0
BV8-A02	R2	195	1	164	26
BV8-A03	N	195	1	164	0
BV8-A04	R1-R2	195	1	164	2
BV8-A05	R1-R2	195	2	164	3
BV8-A06	N	195	2	164	0
BV8-A07	W_0-R1	195	2	164	2
BV8-A08	N	195	7	164	0
BV8-A09	W_0-R1	195	2	164	4
BV8-A10	R1	195	16	164	22
BV8-B01	W_0	187	29	154	39
BV8-B02	N	187	2	154	0
BV8-B03	W_0	187	31	154	25
BV8-B04	N	187	3	154	1
BV8-B05	R1	187	4	154	25
BV8-B06	W_0	187	22	154	19
BV8-B07	N	187	4	154	0
BV8-B08	R1	187	18	154	23
BV8-B09	W_0	187	26	154	23
BV8-B10	N	187	1	154	0
BV8-C01	R1	195	2	155	24
BV8-C02	W_0	195	21	155	6
BV8-C03	N	195	3	155	1
BV8-C04	R1	195	2	155	39
BV8-C05	N	195	3	155	0
BV8-C06	W_0-R1	195	2	155	1
BV8-C07	N	195	1	155	0
BV8-C08	N	195	3	155	1
BV8-C09	W_0	195	20	155	6
BV8-C10	W_0-R1	195	4	155	1
BV8-D01	R1-R2	208	<1	157	5
BV8-D02	N	208	20	157	0
BV8-D03	W_0	208	22	157	5
BV8-D04	N	208	1	157	0
BV8-D05	N	208	1	157	0
BV8-D06	R2	208	0	157	23
BV8-D07	W_0-R1	208	<1	157	4
BV8-D08	R1	208	27	157	30
BV8-D09	N	208	4	157	0
BV8-D10	N	208	0	157	0
Average for 1978			7.8		9.0

[a] N, Nonreactive; W_0, weakly reactive; R, reactive.

[b] In determining percent incorrect for quantitative results, "W_0" responses are considered as "N" responses.

and 46 used CF. Both yeast and mycelial antigens were used in CF tests by most participants. The CF test was again more sensitive than immunodiffusion: 96% of the CF results were positive for samples BI8-SO1, BI8-SO2, and BI8-SO5, whereas 3 to 40% of the immunodiffusion results were positive. The three samples contained different levels of histoplasma antibodies.

DISCUSSION

The Diagnostic Immunology portion of the CDC Proficiency Testing Program includes a wide variety of immunological tests. Several factors are considered when selecting tests for the program: (i) the number of laboratories that provide the test, (ii) the number of times the test is performed per year, (iii) the importance of the test in diagnosis or treatment of disease, (iv) the degree of difficulty in obtaining useful results from the test, and (v) the availability of resources.

TABLE 11. *Fluorescent treponemal antibody absorption test: syphilis serology test performance*

Sample no.	Acceptable result[a]	No. of participants	% Incorrect
BV8-A01	N	163	5
BV8-A02	R(3-4+)	163	4
BV8-A03	B-R(1-2+)	163	14
BV8-A04	R(3-4+)	163	2
BV8-A05	R(3-4+)	163	1
BV8-A06	N	163	2
BV8-A07	R(3-4+)	163	2
BV8-A08	B-R(1+)	163	25
BV8-A09	R(3+)	163	1
BV8-A10	R(3-4+)	163	1
BV8-B01	R(1-3+)	163	13
BV8-B02	N	163	11
BV8-B03	R(3-4+)	163	2
BV8-B04	B-R(1-2+)	163	21
BV8-B05	R(2-4+)	163	3
BV8-B06	R(2-3+)	163	1
BV8-B07	B-R(1-2+)	163	21
BV8-B08	R(2-4+)	163	1
BV8-B09	R(1-3+)	163	4
BV8-B10	N	163	12
BV8-C01	R(3-4+)	169	1
BV8-C02	R(2-3+)	169	4
BV8-C03	N	169	6
BV8-C04	R(3-4+)	169	1
BV8-C05	B-R(1-2+)	169	18
BV8-C06	R(2-4+)	169	1
BV8-C07	B-R(1-2+)	169	18
BV8-C08	N	169	4
BV8-C09	R(2-3+)	169	5
BV8-C10	R(2-4+)	169	2
BV8-D01	R(3-4+)	156	1
BV8-D02	R(1-3+)	156	19
BV8-D03	R(2-4+)	156	5
BV8-D04	N	156	4
BV8-D05	N	156	12
BV8-D06	R(3-4+)	156	0
BV8-D07	R(2-4+)	156	2
BV8-D08	R(4+)	156	0
BV8-D09	R(1-3+)	156	37
BV8-D10	N	156	5
Average for 1978			7.3

[a] N, Nonreactive; B, borderline; R, reactive.

Standardization in serological tests is encouraged by the Proficiency Testing Program. Reference laboratories are selected from laboratories which use standard methods when they are available, and all participants are urged to consider adopting standard methods for use in their laboratories. Use of standards or reference materials is also recommended when they are available. The results from laboratories which use standard methods or reference materials are generally more comparable than the results from other laboratories.

Several manufacturers voluntarily submit samples of their products to CDC for premarket evaluation to be sure that their reagents meet CDC specifications. The CDC Diagnostic Products Evaluation Branch publishes a monthly report listing control/lot number of those reagents that have met the specifications; the report is available upon request. Laboratorians ordering from these manufacturers should request that they supply reagents from lots that meet these specifications. Some of the reagents evaluated in this program are rubella HAI reagents, bacterial antigens and control sera, viral antigens and antisera, and syphilis serology reagents.

The number of laboratories using the standardized HAI test for rubella antibodies (heparin-manganous chloride or dextran sulfate serum treatments) increased slightly for the second survey, but declined for the third and fourth. The number using the kaolin serum treatment remained the same during the year. There was a shift from the HAI test to passive hemagglutination and fluorometric assay. These tests have not been thoroughly compared with the HAI test, but the passive hemagglutination test seems to result in higher titers than the HAI. Results for the fluorometric test appear to be similar to HAI results. Since neither the passive hemagglutination nor the fluorometric rubella test is recommended by the manufacturers as a diagnostic test for recent rubella infections, their use should be restricted to immunity screening.

Standardization of reagents has helped to make immunoglobulin results more comparable than they were a few years ago. The absence of standards for other serum proteins, such as alpha-1-antitrypsin, haptoglobin, ceruloplasmin, and complement components, is reflected by considerable variation in the geometric means of results obtained with reagents from various sources. Complement C3 results should be recognized as being determinations of different components depending on the specificity of the antiserum used, i.e., either βIA or βIA/βIC.

The ASO and ADN-B are currently the most suitable serological tests for detecting infection by group A beta-hemolytic streptococci (3, 4). Both have good reproducibility, reagents are commercially available, and the antigens are produced by most strains of group A streptococci. Multiple-enzyme tests can be useful as screening tests when used as adjuncts to the ASO test. These tests are rapid and can be used to check sera with low ASO or ADN-B titers for elevated levels of antibodies to other streptococcal exoenzymes (5). For the present, the best approach to serological detection of group A streptococcal infection is to use the ASO test and another test, such as the ADN-B test, multiple-enzyme test, or a test for another streptococcal enzyme.

Several inquiries have been made about the use of plasma in preparation of syphilis serology proficiency testing samples and in routine testing. Plasma is not recommended because it tends to give rough negatives in the nontreponemal tests (especially in the RPR), which in turn makes them difficult to distinguish from weakly reactive or minimally reactive sera.

Samples containing low-reactivity levels of HBsAg may or may not be detected by second-generation tests. These kinds of samples are deliberately included in CDC hepatitis surveys to emphasize the importance of using third-generation tests by demonstrating their superior sensitivity over second-generation tests.

The value of standardization is well illustrated in the RF test. Even though laboratories used substantially the same methods to test for RF, results were considerably more comparable when they were converted to and reported in international units. Comparison of results reported in international units per milliliter with those reported as raw titers showed that the use of a serum reference preparation could eliminate most of the interlaboratory variation in results (15). A national standard RF preparation containing 1,000 IU/ml is now available from CDC to be used in preparing secondary reference preparations. Requests for the standard should be addressed to:

Center for Disease Control
Attention: Bureau of Laboratories
Biological Products Division
Building 6, Room 185
Atlanta, GA 30333

The largest source of variation in the bacterial agglutination tests was the antigen, a repeat of the pattern observed in 1976 and 1977. The need to develop and use standard antigens for bacterial agglutination tests persists. The insensitivity

of the slide test for salmonella agglutinins continues to be a problem.

The variation in substrate sensitivity for antinuclear antibody detection is also a continuing problem in comparing results with this test. CDC has listed certain tests that could improve, through standardization, the reliability of results for laboratories that want to improve their performance (1).

One of the reasons for poor performance that has been reported previously and still persists is the lack of a good quality control program. Frequently, deviations from the recommended procedures are noted on returned report forms which indicate that test results are reported in spite of the fact that the test is "out of control." CDC has recently published a quality control monograph for immunological tests. Its purpose is to help stimulate quality control consciousness among immunologists and to provide guidelines for upgrading quality control procedures (23).

The ultimate purpose of proficiency testing is to improve the quality of clinical laboratory results and in turn improve the quality of health care. To achieve these goals the CDC Proficiency Testing Program has used and will continue to use a number of approaches. These activities can benefit the participants by: (i) providing them with stable reference test samples; (ii) providing an external component to supplement their internal quality control program; (iii) providing feedback concerning their performance; (iv) providing interlaboratory comparison data; (v) providing evaluations of methods, reagents, kits, and procedural variables and the relative importance of each; (vi) providing information on what tests are currently being used; (vii) encouraging standardization of units and reporting methods; (viii) providing estimates of the level of performance being achieved; (ix) determining the need for standard and reference materials and methods; and (x) distributing educational materials. The success of these endeavors depends on both the Proficiency Testing Program sponsor and the participants. If improvements in the quality of clinical laboratory results are to be achieved, it will require cooperation among all those involved.

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