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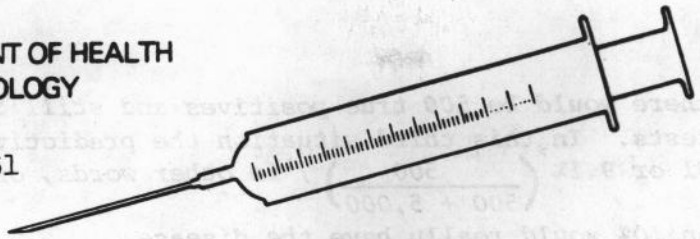

EPIDEMIOLOGY BULLETIN

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PREDICTIVE VALUE OF SYPHILIS SEROLOGIES

As the incidence and prevalence of syphilis declines, a physician is faced with more and more difficulty making the correct diagnosis in the absence of classical symptoms and signs of the disease. Other than the traditional dark field examination of primary and secondary lesions, one has to rely solely on serological tests. Most physicians are familar with the VDRL (Venereal Disease Research Laboratory) and the RPR (Rapid Plasma Reagin) tests. These have been the mainstays in screening and diagnosing syphilis. They are good, sometimes very good, but they are not perfect. No matter how good a test is, there will be some false positives and false negatives for various reasons. With serological tests for syphilis the false positive tests have reached the status of a recognized independent entity, the Biological False Positives (BFP's), which are frequently discussed.

As the proportion of a population with a disease (prevalence) decreases and becomes smaller and smaller, the actual number of cases of that disease in that population also becomes smaller. However, if one relies on a positive laboratory test as the only basis for a correct diagnosis and the laboratory test is being applied to large, unselected segments of the population, then the <u>percentage</u> of false positive tests will remain the same despite the decline in the number of cases of true disease, and the actual number of false positive tests will depend on the sample size of the population being tested. Therefore, even if the percentage of false positives is very small, when a test is applied to a large population, there still may be a considerable number of people with false positive test results. As the actual number of true disease cases decreases, the number of people with false positive test results becomes a larger and larger portion of all those people who have positive results. The ratio of those people with <u>disease</u> who have a positive test result to all people who have a positive test result (true positives/true positives + false positives) is referred to as the predictive value of a positive test result. The sensitivity and specificity of any given test are fixed values; however, the predictive value of a test varies, depending on the disease prevalence in the population being screened.

As a simplistic example, suppose there is a test which results in 0.1% false positives (a specificity of 99.9%), and that it identifies 100% of those individuals with true disease (sensitivity of 100%). If this test were performed on every person in Virginia, one would expect about 5,000 false positive results (5,000,000 x .001). If there were 45,000 people in the state with the true <u>disease</u>, and who thus would all be identified in this survey by positive test results, then there would be 50,000 positive tests of which 45,000 would be true positives and the predictive value of a positive test representing a case of true disease would be .90 or 90% $\left(\frac{45{,}000}{45{,}000 + 5{,}000}\right)$. But now suppose that instead of 45,000 people with true disease there were actually only 5,000 people with the disease in Virginia. Then there would be 5,000 true positives, still 5,000 false positives and the predictive value of the positive test would be only .50 or 50% $\left(\frac{5{,}000}{5{,}000 + 5{,}000}\right)$. If one further supposes that only 500

people have the true disease, there would be 500 true positives and still 5,000 false positives for a total of 5,500 positive tests. In this third situation the predictive value of the positive test would be only .091 or 9.1% $\left(\frac{500}{500 + 5,000}\right)$; in other words, of all those with positive test results, less than 10% would really have the disease.

Considering the examples above, what is the situation with respect to syphilis serologies? As syphilis in the general population has declined over the years, the predictive value of a positive serological test has also declined. In Virginia each year there are about 500-600 cases of primary and secondary syphilis reported. These are a portion of the 1500-1600 cases of all types of syphilis reported in the state each year. Assuming that all cases are reported, this means that only 0.01% of the population of Virginia truly has primary or secondary syphilis each year and only 0.03% has some form of syphilis reported each year. The predictive value of a positive serology, therefore, lies somewhere between 9.1% and 23.1% (and this assumes a test with a sensitivity of 100% and a specificity of 99.9%!). Therefore, when used as a screening test in the unselected general population, a positive serology indicates a true case of syphilis in fewer than 25% of the patients with a positive serological test for syphilis.

Furthermore, if one assumes more realistic values for sensitivity and specificity (for example 86% and 97% respectively[1]) the predictive value of a positive test is then <u>less than 1.0%!</u> Even if one wishes to assume that 10 times as many people actually have syphilis than are reported, the predictive value of a positive test utilizing a realistic sensitivity and specificity would be about 8%. These problems must be kept in mind in evaluating patients and interpreting the meaning of a positive syphilis serology in anyone on whom the test was performed strictly as a screening test.

Of course, if one does not use syphilis serology testing on an <u>unselected</u> population, but uses it for those in whom there are signs, symptoms or history compatible with syphilis, the predictive value increases greatly, e.g., if 5% of the tested group has syphilis, then the predictive value of a positive test is 98% (when one assumes 100% sensitivity and 99.9% specificity) and only falls to 60% when one assumes 86% sensitivity and 97% specificity.

Some physicians will attempt to resolve this problem by ordering a treponemal test such as the FTA-ABS because it has a higher sensitivity and specificity, probably 98-99% for both. However, when using this test and by-passing the non-treponemal tests (VDRL, RPR), one still is faced with the same problems of false negatives and false positives described above. When used on an unselected general population, the predictive value of a positive FTA-ABS test will be less than 3% (assuming sensitivity and specificity of 99%). However if one first clinically selects the patients on whom to perform an initial non-treponemal syphilis serology test and <u>then</u> obtains an FTA-ABS only on those who are RPR or VDRL positive, the predictive value is greatly improved . To use the previous example, assume a clinically selected group in which at least 5% have syphilis. Then the predictive value of a positive non-treponemal serologic test (e.g., RPR or VDRL) is 60%, assuming realistic sensitivity and specificity of 86% and 97% respectively. If the FTA-ABS is subsequently performed on that selected group with positive serologies, of whom 60% actually have syphilis, the predictive value of a positive FTA-ABS (again assuming a sensitivity of 99% and a specificity of 99%[1]) rises to 99.3%.

Therefore, from these calculations it is obvious that doing syphilis serology testing on unselected populations results in exceedingly poor predictive values of positive tests. The serological tests should be done in sequence, with the more sensitive and more specific FTA-ABS being done only on those sera which have been shown to be positive by non-treponemal tests. In this way one can achieve high predictive values for positive test results and help avoid the all-to-frequent dilemma of being forced to treat positive laboratory tests and perhaps stigmatize patients who do not have the disease. Recent discussions of this problem in interpreting positive test results appear in Griner, P. F. <u>et alia</u>, Selection and Interpretation of Diagnostic Tests and Procedures.[1]

Reference: 1. <u>Annals of Internal Medicine</u> 94:553-600 (April 1981, Part 2)

FOOD HANDLERS AND HEPATITIS B

What infection control strategy should be practiced when a food handler is shown to be positive for hepatitis B surface antigen?

There is no evidence that HBsAg-positive food handlers pose a health risk to the general public; hepatitis B infection has never been documented as being foodborne. The principal sources of infectious virions are blood, plasma, and bodily secretions or excretions which, under normal conditions or traumatic injury, could contain blood or serum. Disease transmission would be possible only if food were grossly contaminated with large quantities of these fluids, and this would be a remote possibility. Although HBsAg has been identified in many body fluids in addition to blood and blood derivatives, and although saliva and semen have been shown in experimental animals to be potentially infective, as yet there is no conclusive proof that exposure to such fluids results in a significant number of clinical cases of hepatitis B.

It is prudent, of course, to restrict any food handler from working while ill with "acute" hepatitis B. However, food handlers with persistent HBsAg, like all other antigen-positive persons, should be educated about HBV transmission, the need for good personal hygiene, and the avoidance of hand injuries. Their personal procedures and practices should always reflect an awareness of their potential for transmitting the disease, and must include rigorous efforts to reduce any chance that transmission might occur.

In summary, it is important to distinguish between infection--which is what is indicated by an HBsAg-positive test, and communicability--which is evidenced by transmission of the disease to others. There is no documented evidence that food handlers have transmitted HBV infection in an occupational setting.

REFERENCES

1. Center for Disease Control. Hepatitis surveillance Report no. 45. Atlanta, Center for Disease Control, 1980 May.

2. Center for Disease Control. Viral hepatitis type B, tuberculosis, and dental care of Indochinese refugees. Morbidity Mortality Weekly Rep 1980; 29: 1-3.

3. Bradley, DW, Fields HA, McCaustland KA, et al. Serodiagnosis of viral hepatitis A by a modified competitive binding radioimmunoassay for immunoglobulin M anti-hepatitis A virus. J Clin Microbiol 1979;9: 120-7.

4. Center for Disease Control. Pseudo outbreak of hepatitis A--Louisiana. Morbidity Mortality Weekly Rep 1979;28: 473-4.

SOURCE

1. Centers for Disease Control Hepatitis Surveillance Report no. 46. Atlanta, Center for Disease Control, 1981 March.

ERRATA:

In the April 1981 Epidemiology Bulletin the article "Rabies in Cats: A New Problem" said that . . . "Tennessee and North Carolina now require rabies immunization for cats . . ." Tennessee has had a law requiring rabies immunization for cats since 1972. However, in North Carolina only Wake County, Forsythe County, Alamance County and Charlotte City currently have laws requiring rabies immunization for cats (about one-fifth of the human population of North Carolina lives in these localities). A state-wide law requiring rabies immunization for cats has been introduced into the North Carolina legislature but was referred back to committee during the last legislative session.

MONTH: JUNE

DISEASE	STATE					REGIONS				
	THIS MONTH	LAST MONTH	TOTAL TO DATE 1981	TOTAL TO DATE 1980	MEAN 5 YEAR TO DATE	THIS MONTH N.W.	N.	S.W.	C.	E.
CHICKENPOX	191	151	1483	314	703.2	10	17	10	22	132
MEASLES	3	--	6	294	1,190.6		3			
MUMPS	18	6	83	47	97.4				2	16
PERTUSSIS	--	--	2	2	6.2					
RUBELLA	1	1	5	39	246.2					1
MENINGITIS – ASEPTIC	4	5	39	34	34.6		2		1	1
BACTERIAL	10	16	116	98	75.0	1	3	1	1	4
ENCEPHALITIS – INFECTIOUS	2	2	17	3	8.2	2				
POST-INFECTIOUS	--	--	2	2	5.2					
HEPATITIS A (INFECTIOUS)	18	7	95	157	142.2		7	2	2	7
B (SERUM)	51	49	245	268	177.6	6	13	1	11	20
SALMONELLOSIS	140	171	642	471	340.8	14	30	19	49	28
SHIGELLOSIS	167	304	917	53	63.2	10	6	2	148	2
TUBERCULOSIS – PULMONARY	38	25	273	261	--					
EXTRA-PULMONARY	5	5	53	59	--					
SYPHILIS (PRIMARY & SECONDARY)	56	56	397	282	280.8	2	10	7	10	27
GONORRHEA	1882	1786	12,032	10,245	11,186.2					
ROCKY MOUNTAIN SPOTTED FEVER	20	12	32	22	41.6	4	8	3	5	
RABIES IN ANIMALS	8	9	34	6	9.4	3		5		
MENINGOCOCCAL INFECTIONS	6	8	60	32	35.6	1	3			2
INFLUENZA	16	47	4844	756	4,478.8		1	15		
MALARIA	1	1	11	33	13.6		1			
OTHER: Hepatitis, Unspecified	13	10	89	83	84.4	2	5	2	1	3

COUNTIES REPORTING ANIMAL RABIES: Fauquier-1 cat, 1 skunk; Scott-5 skunks; Rockingham-1 gray fox

OCCUPATIONAL ILLNESSES: Occupational pneumoconioses 23; Occupational dermatoses 4; Occupational hearing loss 8; Asbestosis 1; Byssinosis 1; Chlorine gas inhalation 1

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